

The Nutrition Reporter™

© Jack Challem January 2004 Vol 15 No 1

The independent newsletter that reports vitamin, mineral, and food therapies

B Vitamin Supplements Modify Gene Behavior, Apparently for the Better

Years ago, we were taught that our genetic traits, everything from hair color to risk of disease, were fixed. But as researchers explore the relationship between genes and nutrition—nutrigenomics—it is becoming increasingly clear that the foods we eat affect the activity of our genes and very likely those of our children.

Some of the relationships between nutrition and genes are already well understood. For example, a common genetic variation that reduces the metabolism of folic acid, a B vitamin, can increase the risk of birth defects, heart disease, cancer, and depression. Similarly, another genetic variation lowers vitamin D activity, increasing the risk of osteoporosis and cancer. In both instances, greater intake of the affected nutrient offsets the genetic weakness.

Recently, two teams of researchers took research in this field a step further. They investigated how giving extra amounts of several B vitamins to pregnant mice dramatically altered the activity of a key gene in their offspring, with profound consequences.

Folic acid, vitamin B12, and choline feed into methylation, one of the body's most basic molecule-building processes. Methylation generates large numbers of molecules known as methyl groups, which contain three hydrogen atoms and one carbon atom. These methyl groups help construct new molecules, including the antioxidant glutathione and the neurotransmitter taurine.

But, according to the researchers, vitamin-derived methyl groups also regulate the activity of some genes. Most of the time, methyl groups suppress unneeded gene activity, such as that of cancer-causing oncogenes.

In the most recent experiment, Robert A. Waterland, PhD, and Randy L. Jirtle, PhD, of the Duke University Medical Center, Durham, N.C., fed a group of pregnant "agouti" mice extra amounts of folic acid, vitamin B12, and choline to increase their reservoir of methyl groups. These mice carry the agouti gene, which typically programs for yellow fur

and obesity, and the obesity increases the animals' risk of developing diabetes and cancer.

Although the pregnant mice were not apparently affected by the vitamins, their offspring were. A large percentage of them were born thin and had brown fur.

Waterland and Jirtle noted that the DNA sequence in the agouti gene was not changed by the vitamins. Rather, the vitamins merely suppressed the activity of the agouti gene in most of the offspring, so they did not develop yellow fur or obesity.

According to Craig A. Cooney, PhD, of the University of Arkansas for Medical Sciences, Little Rock, and lead author of an earlier article on agouti mice, vitamin-dependent methyl groups are essential for maintaining normal DNA activity and preventing cancer in rodents and humans.

References: Waterland RA, Jirtle RL. Transposable elements: targets for early nutritional effects on epigenetic gene regulation. *Molecular and Cellular Biology*, 2003;23:5293-5300. Cooney CA, Dave AA, Wolff GL. Maternal methyl supplements in mice affect epigenetic variation and DNA methylation of offspring. *Journal of Nutrition*, 2002;132:2392S-2400S. □

Calcium and Vitamin D Work Together to Lower Risk of Large-Bowel Cancer

Calcium and vitamin D work hand-in-hand to increase and maintain normal bone density. Now, research shows that these two nutrients also work in tandem to lower the risk of colorectal cancer.

Previous studies have associated high intake of calcium and vitamin D, separately, with a reduced long-term risk of colorectal cancer. In the latest study, Maria V. Grau, MD, of Dartmouth Medical School, Lebanon, New Hampshire, and her colleagues investigated how the two nutrients interacted in lowering cancer risk.

Grau and her colleagues studied 803 men and

Continues on next page

women who had a precancerous large-bowel adenoma removed within three months of joining in the study. Subjects were given either a placebo or supplements containing 3 grams of calcium carbonate, yielding 1,200 mg of pure calcium. In addition, the subjects' blood levels of vitamin D were measured twice during the study.

It turned out that neither nutrient by itself reduced the risk of colorectal cancer.

Calcium supplements reduced the risk of new adenomas by an average of 29 percent, but only when subjects' vitamin D levels ranged from normal to high. People who took calcium supplements, but had low vitamin D levels, gained no benefits.

Conversely, subjects with high vitamin D levels were protected only when they also took calcium supplements.

"Calcium supplementation and vitamin D status appear to act largely together, not separately, to reduce the risk of colorectal adenoma recurrence," wrote Grau and her colleagues.

Reference: Grau MV, Baron JA, Sandler RS, et al. Vitamin D, calcium supplementation, and colorectal adenomas: results of a randomized trial. *Journal of the National Cancer Institute*, 2003;95:1765-1771. □

Whole Tomato, Not Just Lycopene, May Reduce Risk of Prostate Cancer

Lycopene, an antioxidant carotenoid found in tomatoes, has long been associated with a lower risk of prostate cancer in men. But a new study suggests that the combination of nutrients in tomato may be more protective than lycopene alone.

Steven K. Clinton, MD, of Ohio State University, Columbus, and his colleagues exposed laboratory rats to a chemical combination known to promote the growth of prostate cancers. The rats were also fed one of three diets: a conventional diet, a diet with supplemental synthetic lycopene (containing 161 mg per kg of food), or a diet with supplemental whole tomato powder (containing 15 mg lycopene per kg of food). In addition, some of the rats in each group were placed on a 20 percent calorie-restricted diet.

Rats eating the diet supplemented with whole tomato powder fared the best. They had a 26 percent lower risk of death from prostate cancer, compared with those fed a conventional diet. Rats given lycopene had a slightly reduced risk of death from prostate cancer, but not as much as those eating whole tomato powder.

Whole tomato is rich in several carotenoids besides lycopene, including phytoene, gamma-carotene, neurosporiene, phytofluene, beta-carotene, and zeta-carotene.

In addition, calorie restriction reduced the

proportion of rats that developed prostate cancer. Sixty-five percent of the rats eating a calorie-restricted diet developed prostate cancer, compared with 79 percent of those allowed to eat as much as they wanted.

Reference: Boileau TWM, Liao Z, Kim S, et al. Prostate carcinogenesis in N-methyl-N-nitrosourea (NMU)—testosterone-treated rats fed tomato powder, lycopene, or energy-restricted diets. *Journal of the National Cancer Institute*, 2003;95:1578-1586. □

Trans Fats Increase Numbers of Small and Dangerous LDL Particles

Trans fats, found in partially hydrogenated vegetable oils, are known to increase the risk of heart disease—even more than saturated fats do.

A new study indicates that trans fats might damage blood vessels by increasing the numbers of small, dense particles of low-density lipoprotein (LDL) particles.

LDL is widely considered the "bad" form of cholesterol. But small, dense LDL particles are more likely to be involved in heart disease, compared with larger, less dense particles.

Benoît Lamarche, PhD, of Laval University, Québec, Canada and colleagues, asked 18 men and 18 women to eat five experimental diets, each for 35 days. All of the diets contained 30 percent fat, but the percentage of trans fats varied between the diets.

One of the diets used butter, high in saturated fat, while the others used semiliquid margarine, soft margarine, shortening, and stick margarine, each with increasing percentages of trans fats.

Lamarche found that as trans fat consumption increased so did the percentage of small, dense LDL particles. The greatest number of small, dense LDL particles appeared when subjects consumed the greatest amount of trans fats in stick margarine.

Paradoxically, butter consumption led to the highest blood levels of LDL cholesterol, but larger, less dense LDL particles predominated.

Reference: Mauger JF, Lichtenstein AH, Ausman LM, et al. Effect of different forms of dietary hydrogenated fats on LDL particle size. *American Journal of Clinical Nutrition*, 2003;78:370-375. □

Some Foods, Fats Increase or Decrease the Risk of Macular Degeneration

The type and quantity of dietary fat you eat may increase your risk of age-related macular degeneration (AMD), according to a study by researchers at the Harvard Medical School.

Johanna M. Seddon, MD, and her colleagues tracked the health of 261 men and women over the age of 60 who had early signs of AMD in at least one

eye. AMD, a progressive eye disease, is the leading cause of blindness among seniors in the United States and other developed countries.

The subjects completed extensive dietary questionnaires after being diagnosed with early signs of AMD and being enrolled in the study, and they were followed for an average of almost five years.

People who regularly consumed fish, rich in omega-3 fats had a 66 percent lower risk of developing advanced AMD—but only if their overall diet was also low in omega-6 fats (found in many cooking oils and processed foods). In addition, people who ate one or more servings of nuts each week were 40 percent less likely to develop AMD.

In general, however, the more fat people consumed, the more likely that early signs of AMD would progress to a more serious form of the disease.

People whose diets included a lot of saturated, monounsaturated, polyunsaturated, and trans fats were about twice as likely to develop AMD, compared with those who ate few of these fats.

Those who had a high intake of vegetable fats (mostly omega-6 fats) were almost four times more likely to experience a progression to AMD, compared with those whom consume few vegetable fats.

In addition, people eating processed baked goods, which are typically rich in omega-6 and trans fats, were about two and one-half times more likely to develop AMD.

Seddon and her colleagues wrote that “it is plausible that dietary fat, which is associated with atherosclerosis, could affect ocular blood vessels or could be involved in oxidative processes that contribute to the development of the advanced stage of AMD.”

Reference: Seddon JM, Cote J, Rosner B. Progression of Age-Related Macular Degeneration. Association with dietary fat, transunsaturated fat, nuts, and fish intake. *Archives of Ophthalmology*, 2003;121:1728-1737. □

Women Who Eat Sugar, High-Glycemic Foods Boost Risk of Infant Birth Defects

Researchers and physicians have known for decades that low intake of the B-vitamin folic acid during the first few weeks of pregnancy increases the risk of delivering a child with neural-tube birth defects, such as spina bifida.

But new research shows that women who consume large amounts of either sucrose (table sugar) or high-glycemic foods around the time they become pregnant also have a high risk of delivering a child with birth defects.

High-glycemic foods include potatoes and refined foods, such as sugars, candies, doughnuts,

cookies, cakes, and soft drinks. These foods are rapidly digested, resulting in sharp increases in blood sugar and insulin.

Gary M. Shaw, DrPH, of the California Birth Defects Monitoring Program, Berkeley, and his colleagues interviewed the mothers of 454 infants with neural-tube defects (NTDs) and the mothers of 462 infants born without NTDs. The interviews, including a dietary questionnaire, were conducted within five months of the delivery date.

Shaw found that women who consumed the greatest amount of sucrose or high-glycemic foods around the time of conception were more than twice as likely to deliver infants with NTDs, compared with those who consumed little of these foods.

He noted that high blood sugar levels can lead to free radical damage and a reduction of inositol, a B-vitamin involved in embryonic development.

Shaw also cited earlier research showing that high blood sugar levels increase the risk of preterm delivery, pregnancy complications, and low birth-weight infants.

Reference: Shaw GM, Quach T, Nelson V, et al. Neural tube defects associated with maternal periconceptional dietary intake of simple sugars and glycemic index. *American Journal of Clinical Nutrition*, 2003;78:972-978. □

Researchers Link Higher Vitamin C Levels to Lower Mortality in Seniors

Elderly men and women in Great Britain have a reduced risk of death if they have higher rather than lower blood levels of vitamin C.

Astrid Fletcher, PhD, of the London School of Hygiene and Tropical Medicine, and her colleagues studied 1,214 subjects ranging in age from 75 to 84 years at the start of the study. Blood samples were obtained to measure their levels of vitamin C, vitamin E, vitamin A, and beta-carotene.

After an average of almost four and one-half years of follow up, Fletcher found that people with the lowest levels of vitamin C has experienced the greatest number of deaths during the study. Those with the highest levels of vitamin C had nearly half the risk of death during this time.

While the findings do not clearly show a cause and effect, they are consistent with other studies showing an association between higher vitamin C levels and lower mortality. It is possible that the higher vitamin C levels reflected greater intake of fruit and vegetables, which are rich in many different nutrients.

“Antioxidants act in synergy, and many antioxidants (of which vitamin C is one of the most

Continues on next page

Quick Reviews of Recent Research

• Vitamin E and exercise boost health in seniors

Both exercise and vitamin E supplements are known to provide diverse health benefits. Researchers asked 59 elderly men and women to follow one of four programs: (1) moderate exercise with 800 IU of vitamin E daily, (2) moderate exercise with placebo, (3) sedentary lifestyle with 800 IU of vitamin E daily, and (4) sedentary lifestyle with placebo. By the end of the 16-week study, moderate exercise and vitamin E (independently of each other) led to weight loss of about 2 pounds, lower blood pressure, and less free radical activity. The combination of exercise and vitamin E led to greater blood pressure reductions.

Jessup JV, et al. *Biological Research for Nursing*, 2003;5:47-55.

• Vitamin B3 deficiency impair DNA repair

Several B-complex vitamins are necessary for repairing damage to DNA, which contains a cell's genetic code. In particular, vitamin B3 is required for the synthesis of poly(ADP-ribose), a key DNA repair enzyme. In an experiment with laboratory rats, researchers found that a deficiency of vitamin B3 reduced DNA repair processes and increase cell sensitivity to chemical injury.

Spronck JC, et al. *Nutrition and Cancer*, 2003;45:124-131.

• C-reactive protein may increase blood pressure

Coronary heart disease is now regarded as an inflammatory disease of the blood vessels, and elevated blood levels of high-sensitivity C-reactive protein (CRP) are increasingly used as a marker of

Vitamin C and Mortality...

Continues from previous page

powerful) appear to be involved in a cascade of radical quenching reactions. Thus, the best recommendation for older persons, as for middle-aged and younger persons, is to maintain a diet rich in a variety of antioxidant micronutrients," wrote Fletcher. "At older ages, however, several factors, such as reduced appetite and taste, poor dentition, physical and economic barriers to food sources, and lack of motivation, present formidable challenges to this strategy."

Reference: Fletcher A, Breeze E, Shetty PS. Antioxidant vitamins and mortality in older persons: findings from the nutrition add-on study to the medical research council trial of assessment and management of older people in the community. *American Journal of Clinical Nutrition*, 2003;78:999-1010. □

inflammation. In a study of 20,525 women participating in the Women's Health Study, researchers found that elevated CRP levels predicted the subsequent development of hypertension. Women with the highest CRP levels were two and one-half times more likely to be diagnosed with hypertension after an average of eight years follow up. Other research has shown that intake of refined and high-glycemic carbohydrates increases CRP levels.

Sesso HD, et al. *JAMA*, 2003;290:2945-2951.

• Multiple antioxidants reduce free-radical oxidation

Researchers conducted two experiments. In one, they used copper to oxidize human low-density lipoprotein (LDL) cholesterol, mimicking an early step in the development of heart disease. They found that various combinations of vitamin E, vitamin C, and beta-carotene were more effective than individual nutrients in preventing LDL oxidation. In the other experiment, they fed these antioxidants, plus selenium, to laboratory rats for 30 days. These animals experienced lower rates of oxidation in heart and liver cells, compared with animals not fed extra antioxidants.

Konovalova GG, et al. *Bulletin of Experimental Biology and Medicine*, 2003;135:143-146.

• Periodontal disease linked to low antioxidants

In a study of 129 middle-age and elderly men and women in England, researchers found that patients with the most severe periodontal disease has the lowest levels of antioxidants and the greatest amount of oxidized proteins in saliva. The researchers noted that the bacteria involved in periodontal disease stimulate an immune response, resulting in the release of free radicals by white blood cells. They added that free radicals are not likely to cause periodontal disease, but that they probably contribute to its progression.

Sculley DV, et al. *Clinical Science*, 2003;105:167-172.

The Nutrition Reporter™ (ISSN 1079-8609) is published monthly except for August and December and is distributed only by prepaid subscription. This issue, Vol 15 No 1, © January 2004 by Jack Challem. All rights reserved. Reproduction without written permission is prohibited. Phone: (520) 529-6801. Fax: (520) 529-6840. Email addresses: jchallem@aol.com or jack@thenutritionreporter.com. The Nutrition Reporter™ is strictly educational and not intended as medical advice. For diagnosis and treatment, consult your physician. Subscriptions are \$26 per year in the U.S.; either \$33 U.S. or \$48 CAD for Canada; and \$40 for other countries, payable in U.S. funds through a U.S. bank. The Nutrition Reporter is a trademark(TM) of Jack Challem.

THE NUTRITION REPORTER™

Post Office Box 30246 • Tucson AZ 85715-0246 USA

Editor and Publisher: **Jack Challem**

Copy Editor: **Mary E. Larsen**

Medical and Scientific Advisors:

Richard P. Huemer, MD Lancaster, California

Ralph K. Campbell, MD Polson, Montana • **Peter Langsjoen, MD** Tyler, Texas

Marcus Laux, ND San Francisco, California • **James A. Duke, PhD** Fulton, Maryland