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## Genetic Quirks May Increase Your Needs for Vitamins and Other Micronutrients

Forty years ago, Roger Williams, PhD, proposed his theory of biochemical individuality. In essence, he contended that people required the same nutrients, but in dramatically different amounts.

Williams, who discovered the B-vitamin pantothenic acid, drew on a wealth of anatomical, physiological, and genetic data. Just as people look different on the outside, Williams wrote, they are different on the inside as well. Internal organs vary greatly in size, shape, and location, reflecting their genetic and anatomical individuality. That uniqueness is the basis of people's biochemical and nutritional individuality.

As obvious as the link between our genetic heritage and our nutritional individuality might seem, it wasn't until recently that scientists carefully linked subtle genetic defects—quirks, if you wish—with the inability to properly use specific nutrients. Nutritional supplements, however, can often overcome these inherited or congenital genetic weaknesses.

The confirmation that genetics influences our nutritional requirements came out of research on folic acid and birth defects, a subject studied extensively over the past 25 years. Deficiencies of folic acid, a B vitamin, in pregnant women dramatically increased their risk of delivering infants with neural tube birth defects, such as spina bifida. Folic acid supplements reduced the risk, and most scientists and physicians assumed that the supplements corrected a nutritional deficiency among women.

However, a few researchers wondered whether part of a woman's

risk of delivering infants with neural tube defects might have a genetic basis. A number of factors pointed in that direction. For example, women in Finland and Ireland eat about the same amount of folic acid, but the incidence of spina bifida ranges five to ten times higher in Ireland. And many women delivering infants with spina bifida had normal levels of the vitamin.

Recently, independent teams of Irish and Dutch researchers identified the nature of that genetic defect: the gene that programs production of the enzyme 5,10 methylenetetrahydrofolate reductase. In women with the defective gene, the enzyme behaves sluggishly and does not efficiently convert dietary folic acid to 5-methyltetrahydrofolate, the form of the nutrient found in the blood.

But extra amounts of folic acid—as in supplements—prime the enzyme and raise blood levels of the vitamin, according to the researchers' reports in *QJ Medicine* (Whitehead AS, et al., Oct 1995;88:763-6) and *Lancet*

(van der Put NMJ, Oct. 21, 1995;346:1070-1).

At this point, a clear link between a specific genetic defect and higher requirement for a micronutrient has been confirmed for only folic acid. But the implications are far broader than a birth defect affecting several thousand infants annually in the United States.

The researchers believe the same defective gene probably predisposes large numbers of women and men to heart disease and stroke. Large quantities of homocysteine, a compound that initiates and promotes cardiovascular disease, are produced when the body either doesn't obtain enough folic acid or can't properly use it. Researchers have estimated that 10 to 40 percent of cardiovascular disease might be related to inadequate intake of folic acid.

The same principal of defective genes and sluggish enzymes likely affects everyone to one extent or another—and may increase dietary

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## Fish Oils Prevent Arrhythmias

Increased consumption of the omega-3 fatty acids could dramatically reduce the incidence of arrhythmias, ventricular fibrillations, and "sudden death," according to Alexander Leaf, MD, of Massachusetts General Hospital and the Harvard Medical School.

In a short, focused review article, Leaf related the anti-arrhythmic benefits of omega-3 fatty acids, or fish oils. In one experiment, he and his colleagues showed that a glycoside, ouabain, could induce arrhythmias in laboratory animals. Small quantities of eicosapentaenoic

acid (EPA) and docosahexaenoic acid (DHA), however, completely prevented the heart spasms.

Leaf's primary interest was in determining whether omega-3 fatty acids could prevent deadly ventricular fibrillation after heart attacks. This type of arrhythmia accounts for about half of the 600,000 heart attack deaths annually in the United States.

In one experiment, Leaf used fish oils to prevent arrhythmias after artificially inducing heart attacks in dogs.

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# High-Potency Multivitamins Improve Mood, Reaction Times After One Year of Supplementation

In studies of college age men and women, a team of European researchers has found that a daily high-potency vitamin supplement significantly improves both mood and cognitive function. The effect was more pronounced in women than in men, and the benefits took a year before they became statistically significant.

In the mood study, David Benton, MD, of the department of psychology, University College Swansea (Wales), asked 129 healthy students, ages 17-27, to take either a dummy pill or a daily multivitamin containing 10 times the Recommended Dietary Allowance (RDA) for vitamins B1, B2, B3, B6, B12, C, E, and biotin. The supplement contained approximately RDA levels of vitamin A.

In a previous paper, Benton contended that psychological symptoms are usually the first sign of a vitamin deficiency. The reason, he explained, is that many of the B vitamins and vitamin C are involved in the production of neurotransmitters.

The students' moods were assessed with two tests, the Profile of Mood States questionnaire, which measured "feelings" during the previous week, and the General Health Questionnaire, which screened for psychiatric disorders.

The study was double blind, meaning that neither the subjects nor the providers of the supplements knew which were the vitamins or the placebos. When queried at the end of the study, students had no idea whether they had been taking vitamins or placebos.

When Benton analyzed the results of the year-long study, he found that men taking vitamins described themselves as feeling more "agreeable" during the previous 12 months. The women who took vitamins said their moods had improved significantly and they had much more restful sleep. They

also described themselves as more agreeable, more composed, and in better mental health, according to Benton's article in *Biological Psychology/Pharmacopsychology* (1995;32:98-105).

Notably, these improvements in mood peaked after 12 months, even though blood levels of the vitamin reached a plateau at three months. Benton determined that the improvement in mood was most closely associated with higher blood levels of vitamins B2 and B6.

In a separate paper, Benton

reported that taking the same high-potency vitamin supplement improved cognitive function—again, more impressively in women than in men. Writing in *Psychopharmacology* (Aug 1995;117:298-305), he reported that women who took vitamins had faster reaction and decision times than did women taking placebos.

Although other studies cited by Benton described the role of vitamins B1, B2, B6, and B12 in cognition, his study found B1 to be the most important nutrient. □

## Vitamin B12 Problems in Strict Vegans

Vegans—people who eat no animal products whatsoever—run a serious risk of developing vitamin B12 deficiency, according to a recent study conducted by Finnish researchers.

Anna-Liisa Rauma, PhD, and her colleagues at the University of Kuopio, Finland, analyzed B12 levels in two ways: first by comparing the vitamin's levels in vegans and meat eaters and, second, by tracking levels in nine vegans over two years.

The vegans selected for the study were strict "living food eaters" in that they consumed all food uncooked, with many of the foods either fermented or spouted. The rationale is that such an approach provides more B12 than an ordinary vegan diet. Overall, the subjects had been eating a vegan diet for an average of five years, and none took B12 supplements.

Compared with meat eaters, all of the vegans had significantly lower levels of B12, according to Rauma's article in the *Journal of Nutrition* (Oct 1995,125:2511-15). However, the vegans eating Nori and Chlorella seaweeds had blood levels of B12 about twice as high as the vegans not eating seaweed.

Two of the vegans were eating large amounts of Nori and Chlorella—above recommended amounts—

which could lead to excessive iodine intake.

In the other part of the study, Rauma found that B12 levels in six of the nine vegans consistently deteriorated over a two-year period.

"On the basis of these results we conclude that some seaweeds consumed in large amounts can supply adequate amounts of bioavailable vitamin B12," Rauma wrote. "However, the average use of seaweeds and fermented foods by 'living food eaters' will not supply enough vitamin B12 to maintain the body vitamin B12 status." □

## Antioxidant Survey

More than half of Americans—57 percent—have heard about antioxidant vitamins, but 82 percent could not name a single one, according to a survey of more than 2,000 people.

Furthermore, almost half—47 percent—were confused by all the vitamin information they read, and 59 percent didn't know the difference between antioxidant vitamins and other vitamins.

Almost half the people surveyed agreed that antioxidant vitamins help prevent cancer and heart disease. But 39 percent believed that antioxidants

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# Vitamin B6 Lowers Death Risk from Heart Attack

Vitamin B6 and folic acid are well established for their roles in reducing blood levels of homocysteine and preventing coronary heart disease. (See THE NUTRITION REPORTER, Nov 1995.) But does taking vitamins for some other condition also reduce the likelihood of dying from heart disease?

That was the thought that guided John M. Ellis, MD, and Kilmer S. McCully, MD in analyzing the deaths of people taking B6 and those who did not take the vitamin.

Before retiring, Ellis practiced medicine in Titus county, Texas, for more than 30 years. He was a pioneer in using the vitamin to treat carpal tunnel syndrome, arthritis, and diabetic symptoms. As a consequence, he attracted a lot of media attention, and many people in Titus county responded by taking B6 supplements.

Several years ago, independent pharmacists in the area reported selling 59,200 tablets containing 50-100 mg of B6 in one (presumably typical) month. Averaged among all 24,000 of the county's residents, this amounted to 4-8 mg of B6 daily, or 2-4 times higher than the Recommended Dietary Allowance (RDA). Of course, some people consumed considerably more than the average, and some consumed much less.

Ellis and McCully suspected that B6 supplements given to treat carpal tunnel syndrome and other conditions would also reduce the risk of death from coronary heart disease. Vitamin B6 helps the body break down homocysteine, a protein byproduct involved in heart disease.

In analyzing hospital patient data in Titus county, Ellis's patients had only one-fourth the risk of being admitted for a heart attack compared with patients of other doctors who were less inclined to recommend B6.

In analyzing 12 of his patients who died from heart attacks, Ellis noted that long-term users of vitamin B6 died at an average age of 84, whereas those

who did not take the vitamin (or took it for less than a year) died at an average age of 76. Patients of other doctors died from heart attacks at an average age of 74 or, if admitted to an emergency room, at the age of 67, according to Ellis and McCully's report in *Research*

*Communications in Molecular Pathology and Pharmacology*, Aug 1995;89:208-20.

In other words, people who took vitamin B6 supplements lived anywhere from eight to 17 years longer than those who did not take the vitamin. □

## Genetic Quirks and Nutritional Needs...

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requirements for any number of other micronutrients. Conversely, some people with very efficient enzymes may actually require fewer micronutrients. This is essentially what Williams proposed back in the 1950s.

Recent studies have shown that genetic defects influencing the body's production of glutathione, an amino acid, increase the risk of prostate cancer (Nelson W, *Proceedings of the National Academy of Sciences of the USA*, Nov. 22, 1994;91: 11733-7). It's conceivable that weak glutathione enzyme systems might prevent the detoxification of carcinogens and increase the risk of disease. The same scenario may be true in breast cancer as well.

Still other research has identified defects in the metabolism of vitamin-like coenzyme Q10 in hereditary disorders related to exercise intolerance (Barak Y, et al., *Israel Journal of Medical Science*, April 1995;31:224-9). As in the case of folic acid, nutritional supplements may stimulate these weak enzyme systems, pushing them into action.

What then of the Recommended

Dietary Allowances (RDAs)?

The RDAs are based on the presumption that people don't require large amounts of vitamins, but the scientific evidence points to a strong association between vitamins and health. Researchers from the late Linus Pauling, PhD, to Paul Lachance, PhD, have pointed out that the RDAs are *not* targets for optimal nutritional intake or for the prevention of heart disease or cancer.

Consider that the latest edition of *Recommended Dietary Allowances* describes the RDAs as appropriate for "practically all healthy persons." But, as Dr. Lachance observed in *Nutrition Reviews* (Aug 1994;52:266-70), "A large proportion of the general population cannot truly be described as 'healthy.' About 30 percent of Americans smoke, and many drink to excess. Others have diabetes, elevated cholesterol levels, or high blood pressure. After age 45, most people are not 'healthy' in the strict sense of the word and relatively few qualify as having no chronic or acute problem." □

## Antioxidant Survey...

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help digestion, which they do not.

The findings of the unpublished study were released in October. It was conducted for BASF, a major supplier of vitamin raw materials used in supplements.

Antioxidants refer to a particular group of vitamins that neutralize dangerous free radicals. Beta-carotene and vitamins C and E are the better

## Omega-3 Fatty Acids...

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Leaf noted in *Prostaglandins Leukotrienes and Essential Fatty Acids* (Feb / March 1995;52:197-8) that increasing omega-3 fatty acids and reducing saturated fats would have a major public health benefit. □

known antioxidants. Vitamin D is not an antioxidant, and vitamin A is a very weak one. □

# Quick Reviews of Recent Research

We're catching up on recent research of interest...

## • CoQ10 and B3 in Parkinson's

MPTP is a chemical that produces the neurological symptoms of Parkinson's disease in animals and people. It depletes adenosine triphosphate (ATP), which generates energy. In a series of experiments, researchers use MPTP to decrease dopamine and energy production. A combination of coenzyme Q10 and vitamin B3, both involved in energy production, protected against MPTP.

Schulz JB, et al., *Experimental Neurology*, April 1995;132:279-83.

## • Vitamin B12 and HIV infections

Low levels of vitamin B12 are often found in patients infected with HIV. In this study, doctors at Montreal General Hospital assessed B12 levels in 200 patients with HIV infections. Abnormally low levels of the vitamin were found in 61 (30.5 percent) of the subjects. B12 deficiencies were more likely in people treated with the drug zidovudine and among those with more advanced disease and gastrointestinal problems.

Paltiel O, et al., *American Journal of Hematology*, 1995;49:318-22.

## • Vitamin B3 and HIV

A number of micronutrients have been shown to inhibit replication of HIV, which causes AIDS. In a recent cell-culture experiment, researchers explored the effect of niacinamide, a form of vitamin B3. They noted that HIV-infected patients have many pellagra-like symptoms, including dermatitis, dementia, and diarrhea. Their experiments showed that niacinamide inhibited HIV replication.

Murray MF, et al., *Biochemical & Biophysical Research Communications*, May 25, 1995; 210:954-9.

## • Flaxseed oil and lupus

Flaxseed is a rich source of alpha-linolenic acid, a precursor of the anti-inflammatory component of fish

oils. In a study of nine patients with lupus erythematosus, physicians found that adding flaxseed to the diet improved kidney function and reduced blood levels of cholesterol.

Clark WF, *Kidney International*, 1995;48:475-80.

## • Vitamin E protects against radiation

Radiation therapy for cancer is meant to destroy tumors but not healthy tissues. In a study using laboratory rats, University of Minnesota researchers compared the effects of radiation exposure on the stomachs of rats given vitamin E and those that were not. They found that dietary vitamin E protected against some of the consequences of radiation damage, including precancerous cell changes.

Felemovicius I, et al., *Annals of Surgery*, Oct 1995;222:504-10.

## • Vitamin B2 and reperfusion

After open-heart surgery, large numbers of free radicals are generated when blood flow to the heart and lungs is resumed. Vitamin E and coenzyme Q10 have been shown to reduce the numbers of free radicals. In this study, researchers found that vitamin B2 is also protective. The vitamin enhances production of flavin reductase, an enzyme that prevents free radical damage.

Mack CP, et al., *Biochemical & Biophysical Research Communications*, July 6, 1995;212:35-40.

## • Diesel exhaust and DNA damage

Researchers found that particles in the exhaust of burned diesel fuel resulted in free radical damage to DNA and tumor formation. Tumor formation was increased in mice fed high-fat diets. Beta-carotene was somewhat protective against the damage.

Nagashima M, et al., *Carcinogenesis*, June 1995;16:1441-5.

## • Ginkgo as a free radical scavenger

Teas and supplements made from the leaves of *Ginkgo biloba* are well-known cerebrovascular dila-

tors. In analyzing a specific extract of Ginkgo, researchers found that it was an efficient scavenger of peroxy free radicals, which attack fats.

Maitra I, et al., *Biochemical Pharmacology*, May 26, 1995;49:1649-55.

## • Dietary fat and eye disease

Recent studies have demonstrated a link between low levels of two antioxidant carotenoids, lutein and zeaxanthin, and macular degeneration. In this study, researchers at the University of Wisconsin analyzed dietary fat intake and the risk of macular degeneration. People with high intakes of saturated fat and cholesterol were more likely to develop macular degeneration at an earlier age, compared with people eating lower fat diets.

Mares-Perlman JA, et al., *Archives of Ophthalmology*, June 1995;113:743-8.

## • Vitamin C and Cancer Prevention

In a 25-year study of diet and cancer in seven countries, researchers found that high vitamin C consumption was strongly associated with protection from cancer.

Ocke MC, et al., *International Journal of Cancer*, May 16, 1995;61:480-4. □

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