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Gamma-Linolenic Acid: The Overlooked, Yet Potent Anti-Inflammatory Dietary Fat

Of all the dietary fats we consume or supplement with, gamma-linolenic acid (GLA) may be the most misunderstood.

GLA is a member of the omega-6 family of polyunsaturated fats. Some of the omega-6 fats, such as linoleic acid and arachidonic acid, abound in modern diets rich in corn, cottonseed, and sunflower, as well as in processed and fast foods. But not GLA.

Many byproducts of the omega-6s can be powerful promoters of inflammation, involved in arthritis, cancer, diabetes, and heart disease. Often, people try to counter the effects of excess dietary omega-6s by taking omega-3 supplements or eating coldwater fish, which are rich in omega-3s.

But given the chance, GLA has potent anti-inflammatory properties of its own. It serves somewhat like an internal control within the omega-6 family that, under ideal circumstances, prevents other family members from becoming too inflammatory.

According to a recent article by Rakesh Kapoor, PhD, of Bioriginal Food & Science Corporation, Saskatoon, Canada, the activity of GLA depends on a single enzyme, delta-6-desaturase (D6D). Without D6D, the body cannot convert linoleic acid to GLA.

Yet even in the best of circumstances, the conversion of linoleic acid to GLA is very slow, according to Kapoor. The conversion is further reduced by deficiencies of vitamin B12, zinc, and other nutrients, as well as in inflammatory diseases such as arthritis and psoriasis.

"Hypertension, diabetes, and several other diseases also impair the activity of this enzyme, leading to insufficient production of GLA in the body," wrote Kapoor and his colleague, Yung-Sheng-Huang, PhD, in *Current Pharmaceutical Biotechnology*.

Still other factors interfere with the D6D enzyme, including trans fats, smoking, alcohol, and stress. In fact, researchers have known since 1982 that trans fats disable D6D and related enzymes, in the process disrupting the anti-inflammatory activities of both omega-6 and omega-3 fats.

Once formed in the body, or taken as supplements, GLA is rapidly converted to dihomogamma-linolenic acid (DGLA), the "activated" form of GLA. In turn, DGLA provides the chemical foundation of cyclooxygenases (COX) and lipoxygenases (LOX), enzymes that can either promote or dampen inflammation. However, trans fats also inhibit the conversion of GLA to DGLA.

In addition to its anti-inflammatory benefits, particularly in rheumatoid arthritis, GLA may reduce the risk of cancer, as well as be an adjunct to other cancer therapies, according to Kapoor. It also appears to play a role in regulating insulin activity and therefore may be helpful in preventing diabetes.

The richest natural sources of GLA are the seed oils from borage, black currant, and evening primrose. Clinical trials have used between 500 mg and 2.8 grams of GLA daily.

References: Kapoor R, Huang YS. Gamma linolenic acid: an anti-inflammatory omega-6 fatty acid. *Current Pharmaceutical Biotechnology*, 2006;7:531-534. Costa AG, Bressan J, Sabarense CM. Trans fatty acids: foods and effects on health. *Archivos Latinoamericanos de Nutricion*, 2006;56:12-21. Hill EG, Johnson SB, Lawson LD, et al. Perturbation of the metabolism of essential fatty acids by dietary partially hydrogenated vegetable oil. *Proceedings of the National Academy of Sciences*, 1982;79:953-957. □

Perspectives...

Epigenetics: The New Face of Genetics

Sometimes revolutions in science come all too quietly. For more than 50 years, we've been taught that the genetic code—the biological blueprint of life—would be the key unlocking the secrets of health, disease, and longevity.

Given the complexity of human biology, scientists were dismayed several years ago when they discovered that humans had only about 20,000 genes, about the same number of genes found in the lowly

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roundworm. Obviously, there's more at play than the simple number of genes we have.

Each of us inherits our own unique variation of the genetic code. We can't change the hardwiring of our genetic code, but epigenetic factors can radically change what our genes do.

If our genetic code is a little like biological hardware, epigenetics is like software that can be modified on the fly. Like the genetic code, epigenetic changes can be passed onto subsequent generations. Unlike the genetic code, they can also be reversed.

You're probably wondering what any of this has to do with nutrition. Much of what happens in epigenetics originates with chemical compounds known as methyl groups and acetyl groups. Methyl groups attach to genes and suppress gene activity, whereas acetyl groups activate genes. Both methyl and acetyl groups depend on B vitamins, and folic acid appears to be the most important of them.

Animal experiments have revealed the power of epigenetics. Researchers know that "agouti" mice, which have a gene that makes them fat, gives them yellow fur, and increases the risk of diabetes and heart disease. In the experiments, the researchers fed extra B vitamins to pregnant agouti mice. The extra vitamins suppressed the agouti gene, and the litters were born thin and with brown fur.

The science is still young, but I suspect the real future of genetics lies in epigenetics. Once again, the path to health is strongly influenced by nutrition. – JC

Magnesium Supplements Reduce Asthma Symptoms, Medication Needs

Low levels of magnesium have long been associated with wheezing and hyperreactivity of the bronchi. Now a study of children and teenagers has found that magnesium supplements can significantly improve asthma symptoms.

Clesio Gontijo-Amaral, MD, of the State University of Campinas Medical School, Brazil, and his colleagues treated 37 patients with either magnesium supplements or placebos for two months. The patients consisted of boys and girls from seven to 19 years of age.

The magnesium supplements consisted of 300 mg magnesium-glycine, sometimes referred to as a magnesium amino acid chelate. The placebo contained only glycine. Patients were allowed to take asthma medications as needed.

The magnesium supplements significantly reduced bronchial reactivity – by almost 30 percent – and also greatly reduced skin reactions to different allergens. In addition, patients taking magnesium were able to decrease their use of salbutamol, a medication, by almost 40 percent.

Finally, a chemical challenge to the patients found that they were far more resistant to having asthmatic reactions and impaired breathing.

In a separate study, Canadian researchers noted that 13 controlled studies have found that intravenous magnesium sulfate helpful in treating severe asthmatic reactions. They reported that the majority of emergency room physicians knew about the efficacy of magnesium sulfate in treating acute asthma. However, magnesium was used to treat only 2.5 percent of such cases in emergency rooms.

References: Gontijo-Amaral C, Ribeiro MA, Gontijo LS, et al. Oral magnesium supplementation in asthmatic children: a double-blind randomized placebo-controlled trial. *European Journal of Clinical Nutrition*, 2007;61:54-60. Rowe BH, Camargo CA. *Journal of Allergy and Clinical Immunology*, 2006; 117:53-58. □

Folic Acid Supplements Can Slow Age-Related Hearing Loss

Hearing loss affects more than 28 million Americans and half of all seniors. But taking folic acid supplements can slow age-related hearing loss, according to a study by European researchers.

Jane Durga, PhD, of the Nestle Research Center, Switzerland, and her colleagues studied 728 men and women who were 50 to 70 years old. All had moderately elevated blood levels of homocysteine (13 µmol/L or greater), but no serious ear disorders. High homocysteine levels usually indicate inadequate intake of folic acid, a B vitamin.

After measuring the hearing acuity of the subjects, Durga and her colleagues asked them to take either 800 mcg of folic acid or placebos daily. After three years of taking the supplements or placebos, the subjects' hearing was retested.

Durga found that age-related hearing loss continued in both groups, but that it had declined substantially less among people taking folic acid supplements. The subjects taking folic acid had only a 1 dB loss of hearing in the low-frequency range, compared with 1.7 dB loss among those taking placebos. In addition, folic acid supplements resulted in a very slight, though not significant, slowing in the loss of high-frequency hearing.

The researchers also stratified the subjects according to whether they had a normal MTHFR 677 gene or two common variations, which reduce folic acid activity. People with the genetic variations benefited from folic acid supplements much more, compared with people with the normal gene.

In an editorial, Robert A. Dobie, MD, of the University of California, Davis, observed that long-term supplementation with folic acid might be able to

reduce hearing loss by 5 dB over 20 years. But he cautioned that much more research was needed.

Reference: Durga J, Verhoef P, Anteunis LJC, et al. Effects of folic acid supplementation on hearing in older adults. *Annals of Internal Medicine*, 2007;146:1-9 and 63-64. □

Low Vitamin D Levels Linked to Higher Risk of Multiple Sclerosis

Low levels of vitamin D have long been suspected as a contributing cause of multiple sclerosis (MS), a disease characterized by the breakdown of the protective myelin sheath around nerves. More than 350,000 Americans and more than 2 million people worldwide have MS.

“A striking feature of the global distribution of MS is a multifold increase in incidence with increasing latitude, both north and south of the equator,” wrote Alberto Ascherio, MD, DrPH, of the Harvard School of Public Health.

That pattern of MS incidence points to low vitamin D levels as a potential cause. People make vitamin D when exposed to sunlight, but the ability to produce vitamin D declines with less sun exposure farther from the equator and during winter months.

Ascherio and his colleagues investigated the relationship between vitamin D levels and MS risk by searching through a large medical database from the U.S. military services. Out of seven million entries in the database, they identified 257 cases of MS, then matched each case by sex, age, and other features to two people not diagnosed with MS.

People with the highest vitamin D levels – more than 99.1 nmol/L of blood – were 62 percent less likely to have MS, compared with people who had the lowest levels of the vitamin. Furthermore, the risk of MS decreased by 41 percent with each 50 nmol/L increase in vitamin D blood levels.

Ascherio cited research indicating that almost half of white and two-thirds of African-American adults in the United States have marginal vitamin D levels.

Reference: Munger KL, Levin LI, Hollis BW, et al. Serum 12-hydroxyvitamin D levels and risk of multiple sclerosis. *JAMA*, 296:2832-2838. □

Big Surprise – Good Nutrition Gives People an Edge as They Get Older

By 2030, all of the baby boomers – people born between 1946 and 1964 – will be over 65 years of age. Because aging increases the risk of disability, baby boomers will have a growing – and unprecedented – impact on health care costs.

But adequate nutrition could prevent or delay the onset of disability, according to a study by re-

searchers at Cornell University, Ithaca, New York, and at other institutions.

Benedetta Bartali, RD, and her colleagues tracked the nutritional status and health of 734 women age 65 and older over three years. They paid particular attention to the prevalence of disabilities that affect daily activities, including difficulties in physically getting around, impaired use of arms and hands, and reduced mental functioning related to self-care and managing a household.

Three nutrients had the most significance: vitamins B6 and B12 and selenium. Women with the lowest blood levels of these nutrients were the most likely to have some sort of physical or cognitive disability. Those with the highest levels of these nutrients were, on average, 64 percent less likely to suffer disabilities.

Carotenoids, vitamin A, vitamin D, folic acid, and zinc were also associated with lower rates of disability, but not significantly.

Both vitamins B6 and B12 play key roles in reducing homocysteine levels, thereby protecting against cardiovascular diseases and mental decline. Selenium is needed for normal immune function and breaking down toxins.

Reference: Bartali B, Semba RD, Frongillo EA, et al. Low micronutrient levels as a predictor of incident disability in older women. *Archives of Internal Medicine*, 2006;166:2335-2340. □

Antioxidant-Rich Eating Habits May Preserve Brain Function in the Elderly

Two compelling studies add to the evidence that eating nutrient-rich foods can help maintain normal brain performance as people get older.

Martha Clare Morris, ScD, of the Rush Institute for Healthy Aging, Chicago, and her colleagues analyzed the eating habits and cognitive function of 1,946 people who were 65 years of age or older. Over six years, the subjects underwent two or three tests to track their mental performance.

People who consumed the most servings of vegetables each day had approximately a 38 to 40 percent slowing in age-related mental decline. The greatest benefits were seen in people who consumed about three or more servings of vegetables daily.

Fruit intake did not seem to protect against mental decline.

The slower mental decline was “equivalent to about five years of younger age,” according to Morris. Leafy green vegetables, which are rich in antioxidants and folic acid, were the most protective.

In a separate study, Tze-Pin Ng, MD, of the National University of Singapore, investigated the

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Quick Reviews of Recent Research

• Acid-reducing drugs increase risk of hip fracture

In a study of almost 149,000 people from the United Kingdom, researchers reported that the use of proton pump inhibitor drugs, such as Prilosec and Nexium, significantly increased the risk of hip fracture. Taking the drugs for one year raised the risk of fracture by 44 percent, while long-term use increased the risk by 2.6 times. Other acid-reducing drugs also raised the risk of fracture, but not to the

Eating Habits and Brain Function...

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relationship between curry consumption and mental function. Curry uses the spice turmeric, which is rich in the antioxidant curcumin. Increasing research has suggested that curcumin may reduce the risk of heart disease and Alzheimer's disease.

Ng and colleagues studied 1,010 elderly residents of Singapore. The subjects ranged from 60 to 93 years of age and had not been diagnosed with Alzheimer's or any other form of dementia.

In a questionnaire, Ng asked how often the subjects consumed curry. Their cognitive function was assessed with the Mini-Mental State Examination, a standardized test.

People who "occasionally" consumed curry had a 38 percent lower risk of cognitive impairment, compared with those who never or rarely ate curry. People who "often" ate curry had a 49 percent lower risk of cognitive problems.

"Turmeric, the dried rhizome powder from which curcumin is extracted, is the principal ingredient of curry that is consumed by millions of people," wrote Ng and colleagues. "Turmeric is most widely consumed by people in the Indian subcontinent and the Indo-China archipelago. Interestingly, it has also been purported that the prevalence of Alzheimer's disease in India among elderly between 70 and 79 years of age is fourfold less than that of the United States."

Still, Ng cautioned that while the findings suggested a "biologically plausible therapeutic effect," they did not demonstrate a clear cause-and-effect relationship between curry consumption and better mental performance.

References: Morris MC, Evans DA, Tangney CC, et al. Associations of vegetable and fruit consumption with age-related cognitive change. *Neurology*, 2006;67:1370-1376. Ng TP, Chiam PC, Lee T, et al. Curry consumption and cognitive function in the elderly. *American Journal of Epidemiology*, 2006;164: 898-906. □

same extent. The drugs may reduce absorption of calcium, and they may also block the normal breakdown and replacement of older bone.

Yang YX, et al. *JAMA*, 2006;296:2947-2953.

• Fish oils may be better than defibrillators

In an analysis, researchers compared the benefits of supplementing with omega-3 fish oils, distributing emergency defibrillators, or surgically implanting defibrillators to prevent sudden cardiac death. They calculated that fish oils would lower death by 6.4 percent. In contrast, emergency defibrillators would reduce deaths by only 0.8 percent, and implanted defibrillators would lower deaths by 3.3 percent. In addition, omega-3 fish oils would reduce the risk of death among people who did not medically qualify for implanted defibrillators.

Kottke TE, et al. *American Journal of Preventive Medicine*, 2006;31:316-323.

• Sugary foods boost risk of pancreatic cancer

Researchers tracked the health of almost 78,000 middle-age and elderly men and women for an average of seven years. Those with the highest consumption of sugary foods also had the largest incidence of pancreatic cancer. High sugar consumption was associated with a 69 percent greater risk. Soft drink consumption specifically was related to almost twice the risk, and sweetened fruit soups or stewed fruit was related to a 51 percent higher risk of prostate cancer.

Larsson SC, et al. *American Journal of Clinical Nutrition*, 2006;84:1171-1176.

• Magnesium helpful in type 2 diabetes

Researchers analyzed nine studies in which 370 patients with diabetes were given oral daily supplements of magnesium. The average dose was 260 mg daily. Magnesium reduced fasting blood sugar and raised levels of the "good" high-density lipoprotein cholesterol over periods of four to 16 weeks.

Song Y, et al. *Diabetic Medicine*, 2006;23:1050-1056.

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Post Office Box 30246 • Tucson AZ 85715-0246 USA

Editor and Publisher: **Jack Challe**

Copy Editor: **Mary E. Larsen**

Medical and Scientific Advisors:

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