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A Good Reason to Eat Fish and Veggies: Resolvin E1, a Powerful Anti-Inflammatory

Coldwater fish, such as salmon and mackerel, are rich sources of omega-3 fats – which have long been recognized for their anti-inflammatory properties. But recently, researchers at the Harvard Medical School identified a byproduct of the omega-3s with especially powerful anti-inflammatory properties.

The tiny molecule, known as resolvin E1, is made in the body from dietary eicosapentaenoic (EPA), one of the principal omega-3 fats found in fish. Don't bother looking for it on supplement shelves – you won't find it, though there are easy ways to boost your body's production of resolvin E1.

Researchers led by Charles N. Serhan, PhD, had previously identified resolvin E1 in the blood of mice. In his latest study, published in the *Journal of Experimental Medicine*, Serhan found resolvin E1 in the blood of healthy people and then synthesized the molecule in the laboratory. That enabled him to conduct even more detailed analysis of resolvin E1.

Serhan determined that extremely small amounts of resolvin E1 inhibited the activation and movement of human immune cells, changes that would reduce inflammation. It also reduced skin inflammation in rabbits and, in unpublished data, reversed periodontal disease in laboratory mice.

Resolvin E1 appeared to work in part by turning off "nuclear factor kappa beta," which is known to activate pro-inflammatory genes and chemicals known as cytokines.

Serhan also found that aspirin increased the body's production of resolvin E1, which may partly explain the drug's well-known anti-inflammatory benefits.

But while many people take a daily baby aspirin to ward off heart disease, there may be a more natural alternative. Culinary herbs, fruits, and vegetables are rich sources of salicylic acid, the core molecule of aspirin. Previous research has found that people who eat a lot of vegetables have higher blood levels of salicylic acid, compared with those who don't eat as many vegetables.

Serhan reported one other intriguing finding: the often-maligned Cox-2 enzyme is responsible for converting EPA to resolvin E1. When people take Cox-2 inhibitor drugs, such as Vioxx and Celebrex, they reduce resolvin E1 production – which may be one of the reasons why these drugs increase the risk of heart attacks and stroke.

A diet rich in coldwater fish (or one with supplemental omega-3 fish oil supplements) and high-fiber nonstarchy vegetables would provide all the building blocks for making resolvin E1.

References: Arita M, Bianchini F, Aliberti J, et al. Stereochemical assignment, anti-inflammatory properties, and receptor for the omega-3 lipid mediator resolvin E1. *Journal of Experimental Medicine*, 2005;201:713-722. Paterson JR, Lawrence JR. Salicylic acid: a link between aspirin, diet and the prevention of colorectal cancer. *Quarterly Journal of Medicine*, 2001;94:445-448. □

Perspectives...

And Now...12 Food Pyramids!?!

The original food pyramid, devised by the US Department of Agriculture in 1982, was a well-meaning effort. But its design has always been counter-intuitive – we tend to think of the top of a pyramid as being the cherished pinnacle, not the foods to avoid eating. The pyramid also appeased too many food industries – can you imagine how fat we would all be if we actually ate 6 to 11 servings of grains a day! And it also gave some poor advice – such as by failing to distinguish refined from unrefined grains and good fats from bad fats.

In April, the USDA released its latest food pyramid – or rather, 12 food pyramids. Simplicity seems to elude the USDA. We live in a country in which two-thirds of adults are overweight or obese, and people don't regularly read or understand food labels. Instead of streamlining dietary guidelines, the USDA made them virtually impossible to decipher.

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Prudent nutrition advice could be distilled into a few basic recommendations: eat a lot of high-fiber and nonstarchy fruits and veggies; some fish, chicken, and lean meats; a few nuts, seeds, and legumes; some good fats; go easy on most everything else; and avoid sugars, refined grains, and trans fats.

For years, I have recommended turning the food pyramid on its side, adding a few curves, and calling it a food cornucopia. I may not be a USDA scientist, but that strikes me as being much more intuitive. We would eat more of the foods (veggies) in the wider section of the cornucopia, a little less of those in the middle (fish, chicken), and virtually none of those at the tip (sugars, fats).

If you wonder why people need clear and simple dietary advice, just read the next report. *–JC*

Most People Don't Do What They Should to Stay Healthy and Lower Disease Risk

Just how many Americans follow all of the dietary and lifestyle recommendations to stay healthy and lower their risk of disease?

Only 3 percent, according to a study by researchers at Michigan State University.

Mathew J. Reeves, PhD, and Ann P. Rafferty, PhD, analyzed dietary and lifestyle data from 153,000 adults. Three-fourths of them were nonsmokers, which was good, but only two-thirds maintained a healthy weight. Just under one-fourth ate five servings of fruits and vegetables daily, and about the same number engaged in regular physical activity. Only 3 percent followed all four "healthy lifestyle characteristics," according to the researchers.

According to Reeves and Rafferty, "no subgroup followed this combination to a level remotely consistent with clinical or public health recommendations." They concluded by stating that there is a "need...to increase healthy lifestyles and to reduce the prevalence of chronic disease risk factors..."

Reference: Reeves MJ, Rafferty AP. Healthy lifestyle characteristics among adults in the United States, 2000. *Archives of Internal Medicine*, 2005; 165:854-857. □

Supplements of Coenzyme Q10 Reduce Frequency, Severity of Migraines

A study has confirmed that supplements of coenzyme Q10 can significantly reduce the frequency and duration of migraine headaches.

Peter S. Sandor, MD, of University Hospital, Zurich, Switzerland, and his colleagues treated 42 patients who had a history of migraine headaches. About half of the patients received 100 mg of CoQ10 three times daily, and the others received placebos.

By the end of the third month of treatment, almost 48 percent of patients taking CoQ10 improved, compared with only about 14 percent of those taking placebos. On average, patients taking CoQ10 had a decrease from four migraine attacks to three per month.

In addition, the length of migraine headaches decreased significantly, as did the number of days with headaches and the number of days with headache-related nausea.

CoQ10 plays a key role in cellular oxygen metabolism, the researchers suggested that impaired oxygen metabolism in the brain might play a role in migraine headaches. That would also explain why vitamin B2 is also helpful in preventing migraine headaches. The vitamin is also involved in oxygen metabolism.

Reference: Sandor PS, Clemente D, Coppola G, et al. Efficacy of coenzyme Q10 in migraine prophylaxis: a randomized control trial. *Neurology*, 2005; 64:713-715. □

Vitamin Supplements Improve Cognitive Function in Elderly

Frail elderly subjects who took a low-dose liquid supplement of vitamins, minerals, and antioxidants daily sharpened their thinking processes after six months.

Wendeline Wouters-Wesseling, PhD, and her colleagues tracked 67 people who took either the vitamin supplement or placebos. The subjects underwent cognitive tests at the beginning and end of the study.

People taking the vitamin supplement were better able to remember words, as well as to name a large number of animals or professions.

Blood levels of homocysteine, a risk factor for heart attack and stroke, decreased by about one-third among the supplement takers.

Reference: Wouters-Wesseling W, Wagenaar LW, Rozendaal M, et al. Effect of an enriched drink on cognitive function in frail elderly persons. *Journal of Gerontology*, 2005;60A:265-270. □

Heal Thyself, Physician-To-Be. Vitamin D Levels Low Among Medical Residents

You don't have to look at sick patients in hospitals to find vitamin deficiencies. A study of 35 medical residents recently found vitamin D deficiencies to be embarrassingly common. Such deficiencies can reduce bone density and immune function.

Elizabeth E. Haney, MD, of Oregon Health

Sciences University, Portland, tracked vitamin D levels in residents (medical school graduates working in hospitals) between fall and spring. In northern latitudes, blood levels of vitamin D typically decline during the winter months because of reduced exposure to sunlight.

About two-thirds of the residents did not consume the recommended daily amounts of either vitamin D or calcium.

Haney reported that 74 percent of the subjects had low vitamin D in the spring compared with the preceding fall. Almost the same number had increased levels of parathyroid hormone, which reduces bone density.

Twenty-six percent had serious vitamin D deficiencies in the fall, but that number grew to 47 percent by springtime. Twenty percent had low vitamin D levels in both the fall and spring, and 51 percent were deficient at some point during the study.

"Vitamin D insufficiency is classically diagnosed among individuals with little sunlight exposure such as elderly, housebound individuals, and hospitalized individuals," Haney wrote.

Blood vitamin D levels under 20 ng/ml of blood are considered deficient. Optimal levels are 45-50 ng/ml.

Reference: Haney EM, Stadler D, Bliziotes MM. Vitamin D insufficiency in internal medicine residents. *Calcified Tissue International*, 2005;76:11-16.

Fish Oil Supplements Improve Skills and Behavior of School Children

Supplements containing omega-3 fish oils and gamma-linolenic acid (GLA) improved the reading and spelling skills, as well as the behavior, of children ages five to 12 years old. The omega-3 oils are known to be involved in brain development.

Alexandra J. Richardson, PhD, and Paul Montgomery, PhD, of Oxford University, treated 117 children diagnosed with developmental coordination disorder. Half of the children received supplements while the other half received placebos daily for three months. After this time, children in the placebo group were given supplements for another three months.

The supplements contained 80 percent fish oils and 20 percent evening primrose oil, which is rich in GLA. The daily dosage of six capsules provided 558 mg of eicosapentaenoic acid (EPA), 174 mg of docosahexaenoic acid (DHA), and 60 mg of GLA.

After three months, children taking the supplements had significant improvements in reading and spelling ability. Reading scores advanced by 9.5 months, compared with 3.3 months for those taking placebos. Spelling scores advanced by 6.6 months, compared with 1.2 months for the placebo group.

Similar improvements occurred when children in the placebo group were given supplements.

Although the researchers did not note any improvements in the children's motor skills, the supplements did lead to a 22 percent reduction in symptoms of hyperactive and impulsive behavior.

Reference: Richardson AJ, Montgomery P. The Oxford-Durham study: a randomized, controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. *Pediatrics*, 2005;115:1360-1366.

Women with Low Vitamin Intake More Likely to Develop Cataracts

Women with low intake of vitamin E and the B vitamins are more likely to develop cataracts, compared with women who consume large amounts of these nutrients. That's the finding of a study by researchers at Tufts and Harvard universities in Boston.

Paul F. Jacques, ScD, and his colleagues tracked the eye health and dietary habits of 408 women participating in the ongoing Nurses' Health Study. The women ranged from age 52 to 74 years when the study began.

Women with the lower dietary intake of vitamin E were 35 percent more likely to develop cataracts, compared with those who consumed the most. Women who never took vitamin E supplements were 42 percent more likely to develop cataracts compared with those who took supplements for at least 10 years.

Low intake of vitamin B1 increased cataract risk by 55 percent, and low consumption of vitamin B2 raised the risk of cataract by 67 percent. Similarly, low intake of vitamin B3 boosted cataract risk by 57 percent.

Reference: Jacques PF, Taylor A, Moeller S, et al. Long-term nutrient intake and 5-year change in nuclear lens opacities. *Archives of Ophthalmology*, 2005;123:517-526.

Modest Amounts of Vitamin C Can Prevent Pregnancy Complication

Taking a little extra vitamin C will reduce the risk of pregnant women "breaking their water" too early, according to a new study.

Esther Casanueva, MD, of the National Institute of Perinatology, Mexico City, and her colleagues studied 109 pregnant women. The women were given either 100 mg of vitamin C or placebos daily, starting about halfway through their pregnancy.

Women taking extra vitamin C were far less

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Quick Reviews of Recent Research

• Vitamin E helps with menstrual pain

Researchers studied 278 teenage girls suffering from painful menstrual periods and excessive bleeding. The girls were given either 200 IU of vitamin E or placebos twice daily for four months. After both two months and four months, girls taking vitamin E experienced less pain and blood loss.

Ziaei S, et al. *BJOG–International Journal of Obstetrics and Gynecology*, 2005;112:466-469.

• Nutrient deficiencies common with sinus problems

Researchers analyzed blood levels of nutrients in 14 boys and 10 girls, ranging from seven to 12 years of age, and compared them to children without chronic sinusitis. Children with chronic sinusitis had lower blood levels of vitamins E and C, zinc, and copper. All of these nutrients might control free radicals, which are believed to play a role in sinusitis.

Unal M, et al. *Journal of Trace Elements in Medicine and Biology*, 2004;18:189-192.

• Vitamin B12 may reverse some dementias

Researchers conducted neuropsychiatric evaluations of 19 elderly patients who were deficient in vitamin B12. After one year of supplemental vitamin B12, 12 of the patients had improved. Seven deteriorated, although their vitamin B12 levels had been normalized. The patients fell into two groups, based on the initial assessments. Patients who responded to vitamin B12 originally had more problems with concentration and psychotic behavior. Those who did not respond had language problems, which might have been suggestive of early signs of Alzheimer's disease when the study began.

Osimani A, et al. *Journal of Geriatric Psychiatry and Neurology*, 2005;18:33-38.

Vitamin C, Pregnancy Complication...

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likely to suffer from a premature rupture of the chorioamniotic membranes (PROM), or the placenta.

Only four (8 percent) of the 52 women taking vitamin C suffered from PROM. Among those taking placebos, 14 (25 percent) of 57 women suffered a premature rupture of the membrane.

"Because PROM may trigger approximately 40 percent of all preterm labor, supplementation could be a valuable tool in sustaining pregnancy to term," wrote Casanueva.

Reference: Casanueva E, Ripoll C, Tolentino M, et al. Vitamin C supplementation to prevent premature rupture of the chorioamniotic membranes: a randomized trial. *American Journal of Clinical Nutrition*, 2005;81:859-863. □

• Autistic children may have vitamin B6 problem

Researchers supplemented 20 autistic children with either a moderate potency multivitamin/multimineral supplement or placebos for three months. At the beginning of the study, the researchers found that the children's vitamin B6 levels were elevated, which they attributed to low activity of pyridoxyl kinase, the enzyme that converts vitamin B6 to its active form (pyridoxyl-5-phosphate). Questionnaires completed by the parents found that supplements led to improvements in sleep and a reduction in gastrointestinal problems. By the end of the study, children in the placebo group had low levels of vitamin C, whereas the supplemented children has near-average levels.

Adams JB, et al. *Journal of Alternative and Complementary Medicine*, 2004;10:1033-1039.

• Synergistic antioxidants help kill cancer cells

Using human leukemia cells, researchers found that ellagic acid, an antioxidant found in strawberries, enhanced the cancer-killing effects of quercetin, an antioxidant found in apples and onions. Both nutrients also increased the activity of p53, a key gene involved in fighting cancer.

Mertens-Talcott SU, et al. *Journal of Nutrition*, 2005;135:609-614.

• Low folic acid contributes to mental decline

Researchers investigated blood levels of B vitamins and homocysteine, as well as cognitive function among 499 people ages 70 to 79 years old over seven years. At the beginning of the study, people with high levels of homocysteine or low levels of folic acid and vitamin B6 had the poorest cognitive functioning. By the end of the study, the researchers noted that people with the lowest blood levels of folic acid were 60 percent more likely to suffer from cognitive decline during the seven years.

Kado DM, et al. *American Journal of Medicine*, 2005;118:161-167.

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