

# NONPRESCRIPTION MEDICINES DIGEST



May, 2005

Welcome to the May quarterly issue of the *NMA Newsletter*. The announcement last year from the National Board of Pharmacy regarding their desire to increase assessment of dietary supplements is reflected in this month's topic choices. The first article provides an overview of omega-3 fatty acids and includes a reminder of possible adverse effects. The second article reviews vitamin E use in heart failure. The third is an announcement from Procter & Gamble regarding how P&G is helping to address the growing concerns about using pseudoephedrine in the manufacture of methamphetamine.

The *NMA Newsletters* are now in the process of being archived. In case you have missed an issue, you can find the archives [here](#).

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## Fish Oils for Alzheimer's Disease

**Seena Zierler-Brown, Pharm.D.**

Fish oils, particularly omega-3 fatty acids, have been cited in several studies as providing beneficial effects in comorbid conditions such as type 2 diabetes, coronary artery disease, and dementia. A diet high in fatty acids such as docosahexaenoic acid (DHA) and/or eicosapentaenoic (EPA) has shown promise in slowing the progression of Alzheimer's disease in animal subjects. DHA is a long chain n-3 polyunsaturated fatty acid that is found most abundantly in cod liver oil or cold-water fish such as salmon, sardines, herring, tuna, mackerel, and halibut. Other natural sources include almonds, walnuts, soy, and fortified eggs.

Progression of Alzheimer's disease is caused by an overproduction and accumulation of insoluble beta-amyloid proteins, which contribute to plaque formation in the brain. These free radicals or oxidants can lead to cumulative damage to brain cells. Long-chain polyunsaturated fatty acids make up a third of all lipids in brain grey matter, which is important for neural development. DHA and related fatty acids are fortified in infant formulas to promote brain development. In Japan, the diet is low in fat with frequent consumption of fish and the prevalence of

Alzheimer's disease is less than in the United States. The typical American diet is higher in consumption of omega-6 fats, which come from sources such as corn, soy, canola, safflower, and sunflower oils. The Food and Drug Administration (FDA) has approved a qualified health claim for the use of EPA and DHA omega-3 fatty acids (present in conventional foods and dietary supplements) for cardio-protection and cholesterol reduction.

Patients should be cautious in consuming grocery-store fish (such as tuna in particular), since it may be contaminated with mercury. This is especially a concern for pregnant and nursing mothers, who should limit their intake to no more than 6 ounces per week, according to the FDA. Patients should also check to be sure fish oil or cod liver oil supplements have therapeutic levels of DHA and EPA.

The antithrombotic activity of fish oils results from an increase in prostacyclin synthesis coupled with a reduction in platelet count and adhesiveness. Doses exceeding three grams may decrease coagulation, leading to an increased risk of bleeding; other potential side effects include nausea, loose stools, and belching. The FDA's office of Dietary Supplements is collaborating with the NIH and other agencies to develop research agendas focusing on the use of omega-3 fatty acids in the prevention of Alzheimer's disease since reliable evidence is needed regarding safety and efficacy.

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## Long-Term Vitamin E and Heart Failure

**Seena Zierler-Brown, Pharm.D.**

Vitamin E has been publicized for its antioxidant benefits in cardiovascular disease. Approximately 22% of United States adults older than the age of 55 take vitamin E, making it the most widely used antioxidant. Vitamin E can be found in wheat germ, almonds, peanuts, walnuts, vegetable oils, and green leafy vegetables. Vitamin E is a fat-soluble vitamin that is sequestered in adipose tissue until activated, and prevents the formation of free radicals involved in the oxidation of LDL cholesterol and plaque formation. It aids in the formation of red blood cells and facilitates the activation of trace mineral selenium and vitamins A and K.

Vitamin E is composed of two compounds called tocopherols and tocotrienols. Tocopherols are primarily seen over the counter in the alpha, beta, delta, and gamma forms; however, the alpha-tocopherol form is the only form thought to be therapeutically useful. Newer formulations contain a combination, which includes tocotrienols, since they have recently been identified as having heart-healthy benefits. Additional reported benefits of supplementing with vitamin E include improvement in endometriosis, cholesterol, neuropathy, cognition, cancer, and joint deformities. The recommended dietary intake (RDA) for alpha tocopherol is 15 mg or 23 IU daily. It is available in natural form designated with "d" and synthetic forms designated with "dl." The natural form is superior in potency to the synthetic; however, the majority of studies have assessed the synthetic form. The recommended dose for cardio-protection is 400 to 800 IU daily. Adverse events such as diarrhea and headache may occur when exceeding 1,000 IU daily (1,000 IU

synthetic or 1,500 IU natural). Recent concerns that non-healthy people who take vitamin E in doses of 400 IU/day or more might have an increased risk of mortality from all causes cloud the benefits-versus-risk discussion. Anticoagulant effects can be seen in doses exceeding 800 IU daily. The supplement can be taken with a fatty meal to avoid gastrointestinal irritation.

The Heart Outcomes Prevention Evaluation Study (HOPE) followed approximately 10,000 patients at high risk for heart disease over four years. An extension of the trial, HOPE-TOO, found similar event rates after a total of seven years in the 4,000 subjects who continued in the trial. No significant difference was seen between the vitamin E group and the placebo in rates of cancer, cancer death, major cardiovascular events (MI, stroke, or death from cardiovascular causes), or death from any cause during the extension of the trial. Patients taking 400 IU vitamin E daily did, however, have an increased risk of heart failure (13.5 percent) as compared to those taking placebo (12.1 percent). The number of patients with type 2 diabetes and obesity may answer the question as to why an increase in heart failure was found. These patients have increased small, dense LDL particles, which increase oxidative damage and progression of heart failure. The result of this trial is reflective of an older group of patients (average age of 70) with preexisting heart disease, stroke, and diabetes. Subjects were taking several medications for cardiovascular disease in addition to the supplementation. Recent evidence has suggested that vitamin E may counteract the positive effects of statins and niacin on HDL cholesterol. The conclusion of this recent study is not supported by previous studies demonstrating benefit as evident in the Cambridge Heart Antioxidant Study of 1996, which illustrated a 77 percent lower risk of subsequent nonfatal MI than placebo. Additionally several neutral prospective vitamin E trials (GISSI-IV, HPS, and HATS) reveal an absence of supporting evidence toward major protective effects through vitamin E supplementation. The Council for Responsible Nutrition believes it is too soon to conclude that the results of the HOPE-TOO trial negate the protective effects of vitamin E. Future studies are warranted to explore conclusive evidence of the effectiveness of vitamin E for cardiovascular disease and other inflammatory conditions.

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## Vicks Product Changes to Occur

The Vicks line of products manufactured by Procter & Gamble (P&G) will be changing. P&G is seriously concerned about the methamphetamine (meth) abuse problem. Unfortunately, OTC products containing pseudoephedrine (PSE) tablets have been commonly used to make illicit meth. Approximately 20 percent of the meth in the U.S. is made from OTC products in small home-based meth labs that endanger innocent children and law enforcement officers, and cost U.S. taxpayers many millions of dollars each year for environmental cleanup procedures.

Our Vicks cough/cold products are complex liquid and liquid-filled softgel products, which contain a combination of active ingredients that provide relief for multiple symptoms. Some of our products contain PSE to relieve the symptom of stuffy nose. Fortunately, Vicks cough/cold products are currently not part of the meth problem and have been exempted from new OTC shelf-access regulations in all but one

state.

Although Vicks cough/cold products are not currently a part of the meth problem and exempt from consumer shelf-access regulations in most states, the U.S. Drug Enforcement Agency (DEA) believes that liquid and liquid-filled softgel products containing PSE may become a part of the problem in the future.

As a result of this DEA position, new independent OTC product access restrictions recently implemented by several major retail outlets, and our sincere commitment to help solve the meth issue, P&G will begin offering new Vicks PSE-free cough/cold products in the U.S. this fall for the coming cough/cold season. These new Vicks PSE-free cough/cold products will not be able to be used to make meth.

Even though Vicks products containing PSE are not currently a part of the meth problem, we do not want them to become a part of the problem in the future. P&G is sincerely committed to being a part of the solution for the meth abuse problem, and we will continue to support external efforts, such as Meth Watch, that increase awareness and education concerning the meth abuse problem.

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