

TOP Journal Club

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Fish consumption and omega-3 fatty acid status and determinants in long-term hemodialysis.

Am J Kidney Dis. 2006 Jun;47(6):1064-71

BACKGROUND: Blood levels of the anti-inflammatory and cardioprotective omega-3 eicosapentaenoic (EPA) and docosahexaenoic (DHA) fatty acids are determined primarily by dietary consumption. There is reason to believe that hemodialysis patients are at risk for inadequate omega-3 intake and, consequently, low blood levels. **METHODS:** This question was tested in 75 long-term hemodialysis patients and 25 matched controls by measuring fasting, predialysis plasma and red blood cell (RBC) fatty acid levels using gas chromatography and performing a fish-consumption survey. **RESULTS:** Sixty-seven percent of patients did not meet American Heart Association fish-consumption guidelines for healthy persons. Compared with controls, patients had lower plasma omega-3 levels (mean % wt: DHA, 1.33 +/- 0.38 [SD] versus 1.51 +/- 0.36; P = 0.0370; omega-3 index [ie, EPA plus DHA], 1.67 +/- 0.49 versus 1.92 +/- 0.40; P = 0.0249). RBC levels, which estimate more long-term consumption, showed mixed results (EPA, 0.29 +/- 0.08 versus 0.33 +/- 0.11; P = 0.0816; DHA, 4.65 +/- 0.92 versus 3.16 +/- 1.15; P < 0.0001; omega-3 index, 4.95 +/- 0.95 versus 3.49 +/- 1.22; P < 0.0001). RBC omega-3 levels in patients roughly reflected fish consumption. Independent predictors of plasma and RBC omega-3 levels at the 0.05 level of significance included age, race, sex, alcohol use, and fish servings. **CONCLUSION:** Hemodialysis patients consumed fish in quantities far below current American Heart Association recommendations and manifested suboptimal omega-3 levels given their high heart disease risk. These results identify a potentially modifiable cardiovascular risk factor.

Omega-3 fatty acid eicosapentaenoic acid. A new treatment for psychiatric and neurodegenerative diseases: a review of clinical investigations.

Expert Opin Investig Drugs. 2007 Oct;16(10):1627-38.

Decreased n-3 fatty acid levels have been reported in patients with depression, schizophrenia or Alzheimer's disease. Recently, eicosapentaenoic acid (EPA) has been used to treat several psychiatric and neurodegenerative diseases due to its anti-inflammatory and neuroprotective effects. A total of six out of seven clinical trials have shown that EPA significantly improved depressive symptoms when compared with the placebo-treated populations. Several investigations have also reported that EPA could effectively treat schizophrenia. A case report and a clinical trial have shown that EPA was beneficial for the management of most symptoms of Huntington's disease, while a more extensive clinical investigation has demonstrated that EPA could only improve motor functions. Further clinical studies are required to fully explore the effects of EPA on other neurodegenerative diseases. The limitations of previous studies and further research directions have also been discussed.

Omega-3 polyunsaturated fatty acid intake and islet autoimmunity in children at increased risk for type 1 diabetes.

JAMA. 2007 Sep 26;298(12):1420-8.

CONTEXT: Cod liver oil supplements in infancy have been associated with a decreased risk of type 1 diabetes mellitus in a retrospective study. **OBJECTIVE:** To examine whether intakes of omega-3 and omega-6 fatty acids are associated with the development of islet autoimmunity (IA) in children. **DESIGN, SETTING, AND PARTICIPANTS:** A longitudinal, observational study, the Diabetes Autoimmunity Study in the Young (DAISY), conducted in Denver, Colorado, between January 1994 and November 2006, of 1770 children at increased risk for type 1 diabetes, defined as either possession of a high diabetes risk HLA genotype or having a sibling or parent with type 1 diabetes. The mean age at follow-up was 6.2 years. Islet autoimmunity was assessed in association with reported dietary intake of polyunsaturated fatty acids starting at age 1 year. A case-cohort study

(N = 244) was also conducted in which risk of IA by polyunsaturated fatty acid content of erythrocyte membranes (as a percentage of total lipids) was examined. MAIN OUTCOME MEASURE: Risk of IA, defined as being positive for insulin, glutamic acid decarboxylase, or insulinoma-associated antigen-2 autoantibodies on 2 consecutive visits and still autoantibody positive or having diabetes at last follow-up visit. RESULTS: Fifty-eight children developed IA. Adjusting for HLA genotype, family history of type 1 diabetes, caloric intake, and omega-6 fatty acid intake, omega-3 fatty acid intake was inversely associated with risk of IA (hazard ratio [HR], 0.45; 95% confidence interval [CI], 0.21-0.96; P = .04). The association was strengthened when the definition of the outcome was limited to those positive for 2 or more autoantibodies (HR, 0.23; 95% CI, 0.09-0.58; P = .002). In the case-cohort study, omega-3 fatty acid content of erythrocyte membranes was also inversely associated with IA risk (HR, 0.63; 95% CI, 0.41-0.96; P = .03). CONCLUSION: Dietary intake of omega-3 fatty acids is associated with reduced risk of IA in children at increased genetic risk for type 1 diabetes.

Modulation of enzymatic activities by n-3 polyunsaturated fatty acids to support cardiovascular health.

J Nutr Biochem. 2007 Sep 26

Epidemiological evidence from Greenland Eskimos and Japanese fishing villages suggests that eating fish oil and marine animals can prevent coronary heart disease. Dietary studies from various laboratories have similarly indicated that regular fish oil intake affects several humoral and cellular factors involved in atherogenesis and may prevent atherosclerosis, arrhythmia, thrombosis, cardiac hypertrophy and sudden cardiac death. The beneficial effects of fish oil are attributed to their n-3 polyunsaturated fatty acid (PUFA; also known as omega-3 fatty acids) content, particularly eicosapentaenoic acid (EPA; 20:5, n-3) and docosahexaenoic acid (DHA; 22:6, n-3). Dietary supplementation of DHA and EPA influences the fatty acid composition of plasma phospholipids that, in turn, may affect cardiac cell functions in vivo. Recent studies have demonstrated that long-chain omega-3 fatty acids may exert beneficial effects by affecting a wide variety of cellular signaling mechanisms. Pathways involved in calcium homeostasis in the heart may be of particular importance. L-type calcium channels, the Na(+)-Ca(2+) exchanger and mobilization of calcium from intracellular stores are the most obvious key signaling pathways affecting the cardiovascular system; however, recent studies now suggest that other signaling pathways involving activation of phospholipases, synthesis of eicosanoids, regulation of receptor-associated enzymes and protein kinases also play very important roles in mediating n-3 PUFA effects on cardiovascular health. This review is therefore focused on the molecular targets and signaling pathways that are regulated by n-3 PUFAs in relation to their cardioprotective effects.

Beyond lipids: the role of omega-3 fatty acids from fish oil in the prevention of coronary heart disease.

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Omega-3 fatty acid therapy shows great promise in the secondary prevention of coronary artery disease. A meta-analysis of recent omega-3 trials shows reductions of coronary heart disease mortality of 36% (95% CI, 20%-50%; P<0.001) and total mortality of 17% (95% CI, 0%-32%; P=0.046). Some of the potential mechanisms for cardiovascular protection include a reduction in cardiac arrhythmias and plaque stabilization. Since the publication of the landmark GISSI-Prevenzione trial, there have been three major intermediate cardiovascular endpoint studies in patients with implantable cardioverter defibrillators (ICDs) and one large trial, the Japan EPA Lipid Interventional Study (JELIS) trial, which involved 18,645 Japanese patients in primary and secondary prevention. The three studies with ICD patients have been mixed, with favorable trends toward reduction in the incidence of ventricular arrhythmias in some but not all of the studies. Results of the recent JELIS trial in a Japanese population already consuming a high intake of omega-3 fatty acids showed a 19% risk reduction in major coronary events. Most of the reductions were in unstable angina and nonfatal coronary events, but not in sudden death and cardiovascular mortality. The totality of evidence suggests greater benefits with omega-3 fatty acids in secondary prevention than primary prevention and in populations consuming low amounts of omega-3 fatty acids.

Omega-3 fatty acids as treatments for mental illness: which disorder and which fatty acid?

ABSTRACT: BACKGROUND: A growing number of observational and epidemiological studies have suggested that mental illness, in particular mood disorders, is associated with reduced dietary intake and/or cellular abundance of omega-3 polyunsaturated fatty acids (PUFA). This has prompted researchers to test the efficacy of omega-3 PUFA in a range of different psychiatric disorders. We have critically reviewed the double blind placebo controlled clinical trials published prior to April 2007 to determine whether omega-3 PUFA are likely to be efficacious in these disorders. Most trials involved a small number of participants but were largely well designed. **RESULTS:** Omega-3 PUFA were well tolerated by both children and adults with mild gastrointestinal effects being the only consistently reported adverse effect. For schizophrenia and borderline personality disorder we found little evidence of a robust clinically relevant effect. In the case of attention deficit hyperactivity disorder and related disorders, most trials showed at most small benefits over placebo. A limited meta-analysis of these trials suggested that benefits of omega-3 PUFA supplementation may be greater in a classroom setting than at home. Some evidence indicates that omega-3 PUFA may reduce symptoms of anxiety although the data is preliminary and inconclusive. The most convincing evidence for beneficial effects of omega-3 PUFA is to be found in mood disorders. A meta-analysis of trials involving patients with major depressive disorder and bipolar disorder provided evidence that omega-3 PUFA supplementation reduces symptoms of depression. Furthermore, meta-regression analysis suggests that supplementation with eicosapentaenoic acid may be more beneficial in mood disorders than with docosahexaenoic acid, although several confounding factors prevented a definitive conclusion being made regarding which species of omega-3 PUFA is most beneficial. The mechanisms underlying the apparent efficacy of omega-3 PUFA in mood disorders compared to schizophrenia are discussed as is a rationale for the possibly greater efficacy of EPA compared to DHA. **CONCLUSIONS:** While it is not currently possible to recommend omega-3 PUFA as either mono- or adjunctive-therapy in any mental illness, the available evidence is strong enough to justify continued study, especially with regard to attentional, anxiety and mood disorders.

EPA and DHA in blood cell membranes from acute coronary syndrome patients and controls.

BACKGROUND: Increased blood levels of the omega-3 fatty acids (FA) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been inversely associated with risk for sudden cardiac death, but their relationship with acute coronary syndromes (ACS) is unclear. **OBJECTIVE:** We hypothesized that the EPA+DHA content of blood cell membranes, as a percent of total FAs, is reduced in ACS patients relative to matched controls. **METHODS:** We measured the content of EPA+DHA in 768 ACS patients and 768 age-, sex- and race-matched controls. The association with ACS case status of blood cell EPA+DHA [both by a 1unit change and by category (low, <4%; intermediate 4.1-7.9%; and high, ≥8%)] was assessed using multivariate conditional logistic regression models adjusting for matching variables and smoking status, alcohol use, diabetes, body mass index, serum lipids, education, family history of coronary artery disease, personal histories of myocardial infarction and hypertension, and statin, aspirin, and other antiplatelet drug use. **RESULTS:** The combined groups had a mean age of 61±12 years, 66% were male, and 92% were Caucasian. The EPA+DHA content was 20% lower in cases than controls (3.4±1.6 vs. 4.25±2.0%, $p<0.001$). The multivariable-adjusted odds for case status was 0.77 (95% CI 0.70 to 0.85, $p<0.001$) for a 1unit increase in EPA+DHA content. Compared with the lowest EPA+DHA group, the odds ratio for an ACS event was 0.58 (95% CI 0.42-0.80), in the intermediate EPA+DHA group and was 0.31 (95% CI 0.14-0.67; p for trend <0.0001) in the highest EPA+DHA group. **CONCLUSIONS:** Odds for ACS case status increased incrementally as the EPA+DHA content decreased suggesting that low EPA+DHA may be associated with increased risk for ACS.

Fish and fat intake and prevalence of allergic rhinitis in Japanese females: the Osaka Maternal and Child Health Study.

OBJECTIVE: It remains uncertain whether intake of fish or n-3 polyunsaturated fatty acids is preventive against allergic disorders. This cross-sectional study investigated the association of intake of selected high-fat foods and specific types of fatty acids with the prevalence of allergic rhinitis in Japan where intake of fish is high.

METHODS: Study subjects were 1002 Japanese pregnant females. Allergic rhinitis (including cedar pollinosis) was defined as present if subjects had received drug treatment at some point during the previous 12 months. Information on dietary factors was collected using a validated self-administered diet history questionnaire. Adjustment was made for age, gestation, parity, cigarette smoking, passive smoking at home and at work, indoor domestic pets, family history of asthma, atopic eczema, and allergic rhinitis, family income, education, mite antigen level in house dust, changes in diet in the previous month, season when data were collected, and body mass index. **RESULTS:** There was a tendency for an inverse dose-response association between fish intake and allergic rhinitis although the adjusted odds ratio for comparison of the highest with the lowest quartile was not statistically significant (p for trend = 0.09). Intake of eicosapentaenoic and docosahexaenoic acids was independently associated with a decreased prevalence of allergic rhinitis: the multivariate odds ratio for the highest quartile was 0.56 (95% confidence interval: 0.32-0.96, p for trend = 0.03). Intake of n-6 polyunsaturated fatty acids in the third quartile but not the second and fourth quartiles showed a tendency for an inverse association with the prevalence of allergic rhinitis. No measurable relationship was found between consumption of meat, eggs, dairy products, total fat, saturated, monounsaturated, and n-3 polyunsaturated fatty acids, and cholesterol or the ratio of n-3 to n-6 polyunsaturated fatty acids and allergic rhinitis. **CONCLUSION:** Our findings suggest that the intake of eicosapentaenoic and docosahexaenoic acids may be associated with a reduced prevalence of allergic rhinitis.

N-3 polyunsaturated fatty acids and atopy in Korean preschoolers.

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Atopy is a growing problem for Korean children. Since eicosapentaenoic acid is a precursor of less active inflammatory eicosanoids, n-3 polyunsaturated fatty acids (PUFA) may have a protective effect on atopy. This study was undertaken to determine whether n-3 PUFA in red blood cells (RBC) is lower in atopic than in non-atopic preschoolers. Three hundred and eight Korean children aged 4-6 years were enrolled. Total RBC fatty acid composition was measured by gas chromatography. The prevalence of atopic dermatitis, allergic rhinitis, or asthma was 29%. Total RBC n-3 PUFA were lower in preschoolers with atopy than controls (9.8 +/- 1.2 vs. 11.4 +/- 1.6%; $P < 0.05$), while n-6 PUFA (33.0 +/- 1.4 vs. 32.2 +/- 1.0%; $P < 0.05$) and n-6/n-3 PUFA ratio (3.4 +/- 0.6 vs. 2.8 +/- 0.5; $P < 0.05$) were greater. The following factors were also associated with an increase in atopy: higher saturated fatty acids (39.6 +/- 1.4 vs. 40.6 +/- 1.9; $P < 0.05$) and arachidonic acid (15.3 +/- 1.6 vs. 16.0 +/- 2.9; $P < 0.05$), and lower total PUFA (43.8 +/- 0.7 vs. 42.8 +/- 1.4; $P < 0.05$) and omega-3 index (EPA + DHA; 9.1 +/- 0.8 vs. 7.8 +/- 0.5; $P < 0.05$) in RBC. Maternal history of atopy was a significant ($P < 0.05$) risk factor, while lactation was not. The results suggest that a reduced content of n-3 PUFA in the RBC membrane could play a role in early children atopy.



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