

POLYUNSATURATED FATTY ACID-INDUCED ANTIOXIDANT INSUFFICIENCY

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The consumption of essential fatty acid dietary supplements has risen sharply in recent years due to increasing awareness of epidemic deficiencies and a rising tide of scientific evidence of adverse clinical effects caused by deficiency. However, just as the development of essential fatty acid deficiency is an insidious process, so is the free radical pathology induced by excessive intake of polyunsaturated fatty acids (PUFAs). Quantitative concentration determinations of arachidonic acid (AA) and eicosapentaenoic acid (EPA) in plasma, malondialdehyde, and thiobarbituric acid-reactive substances (TBARS), and vitamin E in serum were made on 478 individuals. Serum TBARS values of .90, 1.07, and 1.28 nmol/mL were found for populations in low, middle, and high quartiles of plasma AA and EPA. Evidence is presented for a strong linear relationship of lipid peroxide (LPO) values and the AA and EPA sum. The elevation of LPO is found even when serum vitamin E is normal. Five cases with widely varying medical histories illustrate slight to extreme elevations of LPO when either AA or docosahexaenoic acid (DHA) is elevated. We conclude that PUFA-induced lipid peroxidation is common among patients who supplement flax and fish oils with inadequate antioxidant protection. Clinical management of fatty acid and antioxidant supplementation is aided by testing for fatty acid balance and measuring markers of oxidant damage.

Animal models have clearly shown the potential for increased oxidative damage from vitamin E deficiency induced by high polyunsaturated fatty acid (PUFA) intake. Muscle weakness due to necrotizing myopathy is a characteristic sign of increased tissue peroxidation, but there are many other risks.¹ A substantial body of evidence has demonstrated the toxic potentiation of arachidonic acid (AA) under certain conditions. In cells expressing cytochrome P4502E1, AA produces depletion

of cellular glutathione and marked elevation of malondialdehyde and 4-hydroxy-2-nonenal. This concentration-dependent, toxic effect of AA is prevented by the addition of antioxidants.² Potential toxic effects of AA are especially of concern in alcoholic liver injury where salicylates have been shown to enhance the resulting mitochondrial damage.³ Diets high in AA induce liver injury in alcoholics by inducing a mitochondrial membrane permeability transition. Such effects are related to the ease of oxidation of PUFAs and the tendency to deplete tissue antioxidant status. The mechanism is similar for all classes of PUFAs, but it is of most concern for the 20-carbon eicosanoid precursor fatty acids, AA, and eicosapentaenoic acid (EPA), because the concentrations of these members, of all fatty acids with more than 2 double bonds, are generally the highest in both depot fat and cell membrane phosphatides of most tissues. Diet and dietary supplements of fatty acids also are most likely to have effects on these fatty acids.

Discussions of excessive PUFA consumption have centered on the potential for vitamin A overdosing with high-dose cod liver oil supplementation.⁴ Many studies of high-dose fish oil supplementation have shown beneficial short-term effects. Arthritic patients who took 130 mg/kg/d of fish oils had fewer tender joints, and some were able to discontinue nonsteroidal anti-inflammatory drugs.⁵ For the average 70 kg person, this intake of 9 g/d is high enough to raise plasma EPA levels significantly. Antioxidant status was not evaluated in this study. EPA levels also may be raised by supplementation