Fatty acid–related functions$^{1-3}$

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ABSTRACT The first recommendations for specific nutrient quantities that must be obtained to support health were made by the US Department of Agriculture before 1939. Hazel Stiebeling was the leader of this effort and the scientific background was published in the Yearbook of Agriculture. The recommendations clearly stated that food must be available to provide the nutrients to support health. The science of nutrition in the United States is engaged in the most thorough review and reexamination of the recommended dietary allowances in at least a generation of nutrition scientists. There is a new awareness of nutrition complexity and the likelihood of identification of new essential nutrients. This meeting was devoted to the search for functional endpoints to reach quantitative estimates of dietary substances needed to support a function. Included in that concept is determining a range of individual needs and identifying factors that alter these needs. We give the rationale for endpoints of fatty acid metabolism related to platelets and the risk of thrombosis, give the rationale for the recommendation for a new nutrient, and show the necessity for including nutrient interaction in the determination of needs for two nutrients. Am J Clin Nutr 1996;63:991S–3S.

KEY WORDS Essential fatty acids, platelet function, thrombosis, linoleic acid, linolenic acid, antioxidants, hypercholesterolemia

INTRODUCTION

The recommended dietary allowances (RDAs) have been promulgated and published by the Food and Nutrition Board of the National Academy of Sciences since 1941. The 10th edition was published in 1989 (1). In fact, the first quantitative recommendations for specific nutrients were made by the US Department of Agriculture (USDA) before 1939. Hazel Stiebeling was the leader of this effort and scientists from what is currently the Agricultural Research Service and the Cooperative States Research Service of the USDA were the major contributors. The recommendations and scientific background were published in the Yearbook of Agriculture (2).

We are presently engaged in a discussion as to whether a requirement includes a health component. From the beginning, the recommendations clearly stated that the purpose of food and nutrient recommendations was to support health. Many forums are being used to reexamine the concept and add definition to the term “health.” All indicators of nutrient function are candidates for inclusion in the definition of health. Furthermore, new concepts include the possibility of identification of new nutrients. The overall subject of this meeting was the recognition of nutrition complexity. This section of the meeting was devoted to defining some of the complexity of essential fatty acids.

CLOTTING, THROMBOSIS, AND DIETARY FATS

Current death rates from acute myocardial infarction, other ischemic heart diseases, and atherosclerosis for American males (aged 45–54 y) are now ≈600% greater than those for corresponding Japanese men. These wide differences cannot be accounted for by the moderate differences in serum cholesterol concentrations between these two populations. Measurements of the ability of blood platelets to aggregate and of reactivity in human subjects were found to be useful indicators of both active coronary artery disease and the prediction of coronary events and mortality in survivors of myocardial infarction. It is becoming increasingly apparent that dietary modifications and recommendations that target nonconventional risk factors for cardiovascular disease including thromboatherogenic and hemorrhagic factors may be of considerable importance. Thus, dietary fatty acids have been shown to significantly influence various thrombogenic risk factors in the absence or presence of hypercholesterolemia.

Human studies have shown significant effects with saturated fat (eg, fat high in palmitic acid), monoensaturated fatty acids (eg, oleic acid), n–6 polyunsaturated fatty acids (PUFAs) (linoleic acid), and sources of n–3 PUFAs including vegetable oils containing α-linolenic acid and particularly fish oils containing eicosapentaenoic plus docosahexaenoic acids. Significant dietary fat–induced alterations in blood platelet aggregation and adhesion, blood viscosity, plasma fibrinogen, factor VII coagulant activity, and several other factors have been reported. In some cases, the biochemical basis (altered thromboxane A2 synthesis, transmembrane cellular signaling, etc) for these effects of dietary fat and fatty acids have been partly elucidated. Dietary fat and fatty acid modifications directed toward the attenuation of various thrombogenic risk factors could play an important role in the prevention and management

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of coronary heart disease. A test for relative risk that might be applied is the platelet aggregation response to collagen stimulation (3, 4).

DIETARY PUFAs AND HUMAN CARDIOVASCULAR FUNCTION

The idea that fish oils containing n–3 fatty acids have antiatherosclerotic properties originated from the observation that Greenlandic Eskimo had little atherosclerotic cardiovascular disease (CVD) despite being almost entirely carnivorous and consuming a higher percentage of their energy as fat than did Iowans (see reference 5 for review). Additionally, a dietary change in Norway during the Nazi occupation led to a sharp increase in fish consumption, a decrease in total fat intake, and a precipitous drop in CVD death rates within a few months (6). Similar findings emerged from the Diet and Reinfarction Trial in Wales conducted in > 2000 male myocardial infarction survivors encouraged to increase their fiber intake, decrease their total fat, or increase oily fish intake (7).

Although n–3 PUFAs may have antiatherosclerotic properties, their short-term effects on myocardial infarction survival and CVD death rates may be more likely to relate to antithrombotic effects or an enhanced ability to lyse an occluding thrombus in the area around an infarct. Several observations suggested that members of populations consuming high amounts of marine lipids had lesser degrees of coronary atherosclerosis at autopsy than did subjects who habitually consumed diets based on foods containing predominantly n–6 fatty acids.

Because eicosanoids are made from PUFAs and exert many effects that are important in blood pressure regulation, it is often assumed that changes seen with altered dietary PUFA intakes come about through changes in the endogenous production of eicosanoids. Knapp (8) found changes in the types and amounts of prostacyclins being produced during n–3 ingestion. Prostacyclin is known to increase baroreceptor sensitivity and Knapp found that baroreceptor function was also up-regulated during n–3 PUFA supplementation.

This finding and those from many animal studies suggest that fish oils have favorable effects on the vasculature that decrease vasoconstriction and the tendency toward coagulation. Although n–3 fatty acids influence the types and amounts of eicosanoids formed in vivo (thromboxanes, prostacyclins, leukotrienes, etc.) and exert moderate antplatelet effects, such effects do not seem to explain completely the reduction in blood pressure and reduced pressor response seen during fish oil consumption. Epidemiologic studies have not found that populations consuming high amounts of n–3 PUFAs have lower blood pressure.

The effects of n–3 fatty acids in hyperlipidemia were studied in patients with many different diseases. The most striking and reproducible effect was a lowering of triacylglycerol in all patients. There was a marked reduction in postprandial hyperlipemia that may relate functionally to the clot-preventing or thrombolytic effects. Further clinical trials will define the usefulness of n–3 fatty acid supplements in atherosclerosis and hypercholesterolemia. Currently, such supplements do seem to be useful in reducing refractory hypertriglyceridemia at achievable doses (3–8 g/d). Overall, it is recommended that Americans eat more fish (but not fried) as a means of reducing total dietary fat and increasing polyunsaturated fat intake at the expense of saturated fat.

INFLUENCE OF DIETARY FAT ON VITAMIN E REQUIREMENTS

Vitamin E is an essential fat-soluble vitamin that includes a group of eight naturally occurring compounds in two classes with different biological activities designated as tocophersols and tocotrienols. RRR-α-Tocopherol has the highest biological activity and is the most widely available form of vitamin E in food. The other isomers (β, γ, and δ) some of which are more abundant in an average Western diet, are less biologically active than RRR-α-tocopherol. The commercially available synthetic forms of vitamin E are an approximately equal mixture of eight stereoisomeric forms of α-tocopherol. For practical purposes, 1 IU vitamin E is referred to as 1 mg of the synthetic form, all-rac-α-tocopherol acetate, and the natural form of RRR-α-tocopherol has a biological potency of vitamin E equal to 1.49 IU.

Vegetables and seed oils including soybean, safflower, corn, sunflower seed, nuts, whole grains, and wheat germ are the main sources of the tocopherols whereas animal products are generally poor sources of this vitamin. The RDAs of vitamin E for men and women are 10 and 8 mg/d, respectively. These amounts are based primarily on customary intake from food sources in the United States. The most widely accepted biological function of vitamin E is related to its antioxidant property and its prevention of the peroxidation of PUFAs. Vitamin E is the most effective lipid-soluble antioxidant and acts to break free radical chain reactions. Vitamin E protects critical cellular structures against damage from oxygen free radicals (containing an unpaired electron) and reactive products of lipid peroxidation.

Since its discovery, vitamin E has been recognized as an essential nutrient for humans and animals. Its essentiality for neurologic function, prevention of red blood cell hemolysis, and other hematologic disorders in premature infants and adults, as well as its importance in certain genetic disorders is well characterized. Beyond the deficiency, an intake higher than the RDA of vitamin E has been suggested to be important in modulating immune function and in preventing disease processes of particular public health concern, such as cardiovascular disease and cancer.

Mean intakes of dietary vitamin E in Western populations approach the level of the RDA defined to be adequate to prevent clinical vitamin E deficiency symptoms in large populations. The requirement for vitamin E increases, however, with a high intake of PUFAs and increasing degrees of unsaturation of fatty acids in the diet. Dietary guidelines from several public health organizations emphasize decreasing total fat intake to < 30% of total energy, decreasing saturated fat, and increasing monounsaturated fatty acids and PUFAs to achieve a ratio of the three of 10%:10%:10% of energy. Although foods that are high in PUFAs often contain high amounts of vitamin E, this is not always the case. Vegetable oils and margarines are relatively rich in γ-tocopherol, which has one-tenth of the biological activity of α-tocopherol; therefore, increasing PUFAs in the diet with these ingredients may
not necessarily increase total vitamin E intake to maintain a desirable ratio of > 0.4 mg RRR-α-tocopherol/g PUFA (9). Depending on the type of food, this ratio varies from 0.07 for walnuts to 1.42 for olive oil. Analysis of data from the second National Health and Nutrition Examination Survey shows that the vitamin E content of diets of most of the US population is below the RDA (69% of the RDA for men and 80% of that for women) and that mean intakes decrease with age in both sexes. The data further show that 23% of men and 15% of women had a ratio of vitamin E to PUFA of < 0.4.

The ratio of vitamin E to PUFA becomes critical in those individuals taking fish oil supplements containing PUFAs with a high degree of unsaturation. Fish oil has been claimed to have several health benefits in the prevention and treatment of age-associated diseases. Consequently, elderly populations, who have been reported to have low intakes of vitamin E from their diets, are more prone to vitamin E deficiency if they consume fish oil supplements or a high-fish diet and may require supplemental vitamin E. In controlled clinical trials, long-term fish oil supplementation or consumption of high-fish diets was shown to compromise vitamin E status and increase lipid peroxides of healthy elderly participants; accordingly, supplementation with vitamin E was recommended (10).

In defining the ideal intake of vitamin E, the interaction of vitamin E with other antioxidants, in addition to its relation to PUFA, should be considered. Laboratory experiments indicated an interaction and recycling of vitamin E with vitamin C, β-carotene, and other antioxidants. Thus, a high amount of vitamin C in the diet is suggested to decrease the vitamin E requirement. At present, the requirement and ideal intake of vitamin E are based mainly on its interaction with PUFA. However, in setting the ideal vitamin E intake for an individual, several other factors such as intake of total energy, percentage of energy from total fat and from PUFA, intake of other antioxidant nutrients, exposure to environmental pollutants, physical activity and other lifestyle habits, and age should be considered. In this regard, adopting computer modeling and compiling data from controlled studies that use functional outcomes may provide a better base to include multivariate functions and their interactions for defining ideal vitamin intake in humans.

REFERENCES