

## Research and Professional Briefs

Almonds in the Diet Simultaneously Improve Plasma  $\alpha$ -Tocopherol Concentrations and Reduce Plasma Lipids

PERA R. JAMBAZIAN, DrPH; ELLA HADDAD, DrPH, RD; SUJATHA RAJARAM, PhD; JAY TANZMAN; JOAN SABATÉ, MD, DrPH

## ABSTRACT

The objective of this study was to assess the dose-response effect of almond intake on plasma and red blood cell tocopherol concentrations in healthy adults enrolled in a randomized, crossover feeding trial. Participants were 16 healthy men and women, aged  $41 \pm 13$  years. After a 2-week run-in period, participants were fed three diets for 4 weeks each: a control diet, a low-almond diet, and a high-almond diet, in which almonds contributed 0%, 10%, and 20% of total energy, respectively. Changes in blood tocopherol levels were assayed by high pressure liquid chromatography. Incorporating almonds into the diet helped meet the revised Recommended Dietary Allowance of 15 mg/day  $\alpha$ -tocopherol and increased lipid-adjusted plasma and red blood cell  $\alpha$ -tocopherol concentrations. A significant dose-response effect was observed between percent energy in the diet from almonds and plasma ratio of  $\alpha$ -tocopherol to total cholesterol.

*J Am Diet Assoc. 2005;105:449-454.*

There is increasing concern about the dietary adequacy of vitamin E, a potent lipophilic antioxidant and stabilizer of membranes (1,2). In 2000, the Food and Nutrition Board of the Institute of Medicine defined vitamin E as  $\alpha$ -tocopherol and increased the Recommended Dietary Allowance for the vitamin from only 10 mg/day  $\alpha$ -tocopherol equivalents to 15 mg  $\alpha$ -tocopherol per day for adult men and women (3). This is substantially more than what is usually obtained in US diets. The

Third National Health and Nutrition Examination Survey reported a median vitamin E intake of 9 mg  $\alpha$ -tocopherol equivalents or approximately 7 mg  $\alpha$ -tocopherol per day (4,5). Analysis of data from the 1994 to 1996 Continuing Survey of Food Intakes by Individuals found that only 8.0% of men and 2.4% of women in the United States met the new Estimated Average Requirement of 12 mg  $\alpha$ -tocopherol per day from foods alone (6).

The challenge to dietetics professionals is to design diets with the recommended amounts of this important nutrient. The main unfortified dietary sources are vegetable fats and oils and foods containing vegetable oils. However, the more commonly used oils such as corn and soy contain substantially more  $\gamma$ - than  $\alpha$ -tocopherol. Foods rich in  $\alpha$ -tocopherol are sunflower seeds, almonds, hazelnuts, wheat germ, and sunflower, safflower, and cottonseed oils (6). What is not known yet is whether the daily consumption of a food rich in  $\alpha$ -tocopherol contributes to vitamin status assessed by blood levels of the nutrient.

Almonds rank high as a source for vitamin E because they contain 7.4 mg  $\alpha$ -tocopherol per 28 g (1 oz) (7). The objective of this study was to measure the change in plasma and red blood cell (RBC)  $\alpha$ -tocopherol concentrations with the incorporation of two increasing amounts of almonds in the diet. Because almond consumption affects serum lipids and plasma vitamin E levels are known to correlate strongly with serum lipid concentrations (4), we noted changes in blood lipids examined in a prior study (8). We hypothesized that the addition of a single food high in  $\alpha$ -tocopherol has the ability to raise lipid-adjusted plasma and RBC  $\alpha$ -tocopherol levels.

## METHODS

Sixteen subjects were selected from those participating in a randomized feeding trial investigating lipid responses to graded almond intakes (8). Those selected were male (n=8) and female (n=8) participants not taking multivitamins, vitamin E, or other dietary supplements before and during the study. Pertinent characteristics were age ( $41 \pm 13$  years), body weight ( $71 \pm 2.7$  kg), and body mass index (calculated as  $\text{kg}/\text{m}^2$ )  $25.2 \pm 3.6$ . The Institutional Review Board of Loma Linda University approved the study.

A detailed outline of study design and diets has been published elsewhere (8). Briefly, the study was a  $3 \times 3$  crossover complete Latin Square design that, after a 2-week initial stabilization period, ran in three consecutive 4-week cycles. Participants were randomized to six

*P. R. Jambazian is associate professor, School of Kinesiology and Nutritional Science, California State University, Los Angeles. E. Haddad is associate professor, S. Rajaram is assistant professor, and J. Sabaté is chair and professor, all with the Department of Nutrition, School of Public Health, Loma Linda University, Loma Linda, CA. J. Tanzman is with the School of Public Health, Loma Linda University, Loma Linda, CA.*

*Address correspondence to: Ella Haddad, DrPH, RD, Department of Nutrition, School of Public Health, Loma Linda University, Loma Linda, CA 92350. E-mail: ehaddad@sph.llu.edu*

*Copyright © 2005 by the American Dietetic Association.*

*0002-8223/05/10503-0018\$30.00/0*

*doi: 10.1016/j.jada.2004.12.002*

**Table 1.** Plasma and red blood cell tocopherol and serum lipid levels of subjects following 4 weeks of eating a diet with 0% of energy from almonds, 10% of energy from almonds, and 20% of energy from almonds (N=16)<sup>a</sup>

	Control	Low almond	High almond	P <sup>c</sup>
<b>Plasma tocopherol (μmol/L)<sup>b</sup></b>	← $\chi^2 \pm \text{standard error}$ →			
α-tocopherol	26.27 ± 1.07	29.88 ± 1.07 <sup>u</sup>	31.19 ± 1.09 <sup>u</sup>	<.01
γ-tocopherol	3.06 ± 0.17	1.04 ± 0.18 <sup>u</sup>	1.89 ± 0.18 <sup>u</sup>	<.001
β-tocopherol	0.50 ± 0.04	0.49 ± 0.04 <sup>u</sup>	0.43 ± 0.04 <sup>uy</sup>	<.001
<b>Red blood cell tocopherol (μmol/L)<sup>b</sup></b>				
α-tocopherol	3.54 ± 0.24	4.23 ± 0.23 <sup>w</sup>	4.55 ± 0.23 <sup>u</sup>	<.001
γ-tocopherol	0.51 ± 0.05	0.52 ± 0.05	0.36 ± 0.00 <sup>ux</sup>	<.001
β-tocopherol	0.08 ± 0.01	0.10 ± 0.01	0.07 ± 0.01	.39
<b>Serum lipids</b>				
Total cholesterol (mmol/L) <sup>d</sup>	5.50 ± 0.26	5.49 ± 0.26	5.25 ± 0.26 <sup>vy</sup>	<.01
Low-density lipoprotein (mmol/L) <sup>d</sup>	3.81 ± 0.30	3.79 ± 0.30	3.54 ± 0.30 <sup>vy</sup>	<.001
High-density lipoprotein (mmol/L) <sup>d</sup>	1.21 ± 0.06	1.21 ± 0.06	1.23 ± 0.06	.18
Triglycerides (mmol/L) <sup>e</sup>	1.30 ± 0.22	1.42 ± 0.22	1.29 ± 0.22	.91
<b>Tocopherol:cholesterol (mmol/L::mol/L)</b>				
α-tocopherol/total cholesterol	48.21 ± 1.94	54.20 ± 1.95 <sup>u</sup>	56.39 ± 1.98 <sup>u</sup>	
γ-tocopherol/total cholesterol	5.72 ± 0.34	4.60 ± 0.35 <sup>u</sup>	3.55 ± 0.35 <sup>ux</sup>	
β-tocopherol/total cholesterol	0.91 ± 0.07	0.84 ± 0.07 <sup>y</sup>	0.78 ± 0.07 <sup>uz</sup>	

<sup>a</sup>Superscripts indicate significant difference from control diet (<sup>u</sup>P<.001, <sup>v</sup>P<.01, <sup>w</sup>P<.05) and significant difference from low-almond diet (<sup>x</sup>P<.001, <sup>y</sup>P<.01, <sup>z</sup>P<.05).  
<sup>b</sup>To convert μmol/L α-, β-, γ-tocopherol to mg/dL, multiply μmol/L by 0.0431, 0.0417, and 0.0417, respectively.  
<sup>c</sup>Analysis of covariance test for trend, using percent of energy from almonds as the covariate.  
<sup>d</sup>To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.026. Cholesterol of 5.00 mmol/L=193 mg/dL.  
<sup>e</sup>To convert mmol/L triglycerides to mg/dL, multiply mmol/L by 88.6. To convert mg/dL triglycerides to mmol/L, multiply mg/dL by 0.0113. Triglycerides of 1.80 mmol/L=159 mg/dL.

possible diet sequences for the study period. The isocaloric test diets were control, low almond, and high almond, with 0%, 10%, and 20% of energy provided by almonds, respectively. All food items of the control diet were reduced by 10% or 20% of energy to accommodate the almonds. The amount of α-tocopherol in the diets per 8,368 kJ/day (2,000 kcal) increased from 7.96 mg α-tocopherol in the control diet to 15.87 mg and 24.77 mg in the low-almond (10%) and high-almond (20%) diets, respectively.

Blood samples were collected in sterile blood collection tubes after an overnight fast at the end of each diet period. Plasma and RBC tocopherol was extracted using the method of Mino and colleagues (9) and separated into tocopherol fractions by high performance liquid chromatography using a method described by Kramer and colleagues (10).

Statistical analyses were performed using the Statistical Analysis System (version 8.0, 1999, SAS Institute Inc, Cary, NC) and data are presented as least-squares means ± standard error. Changes in plasma tocopherol levels and tocopherol to cholesterol ratios were determined by analysis of variance using mixed linear models that included a random-effect term for participants and fixed-effect term for diet and period. Models of plasma tocopherols also included a covariate to adjust for serum cholesterol. A test for a linear dose-response effect of the amount of almonds in the diet on the α-tocopherol to total cholesterol ratio was conducted by analyses of covariance by replacing the diet variable in the previously described model with a continuous variable representing the percent energy in the diet contributed by almonds.

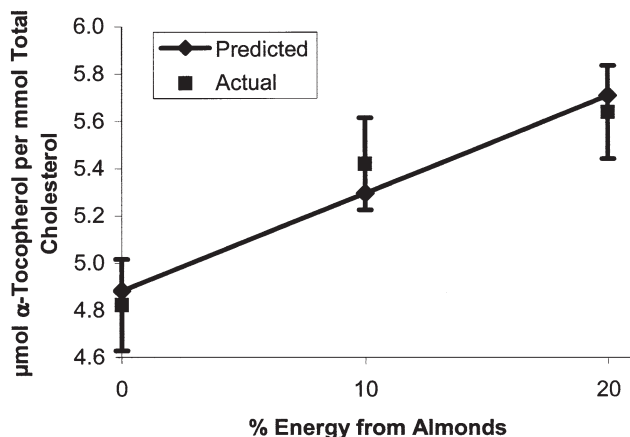
## RESULTS

Our study demonstrates that incorporation of almonds into the diet both increases blood α-tocopherol levels and decreases cholesterol levels. Table 1 shows plasma, RBC tocopherols, and serum lipids at the end of each dietary treatment. Compared with the control diet, plasma α-tocopherol concentrations increased significantly on the low- and high-almond diets. Mean plasma γ- and β-tocopherol concentrations decreased with the low- and high-almond diets in both plasma and RBCs. The ratio of α-tocopherol to total cholesterol was significantly higher, and those of γ- and β-tocopherol to total cholesterol lower on the almond diets.

The Figure compares the observed mean ratio of α-tocopherol to total cholesterol following each diet with that predicted from a linear dose-response model based on the percent energy in the diet contributed by almonds. For each diet, the predicted value falls within the standard error of the observed mean, suggesting that the percent energy in the diet from almonds affects the ratio of α-tocopherol to total cholesterol in a linear dose-response fashion.

## DISCUSSION

According to current recommendations (3), the only physiologically pertinent form of vitamin E is α-tocopherol. Although all vitamin E forms are absorbed and transported by chylomicrons from the intestine to the liver, the liver preferentially secretes α-tocopherol into the circulation. This is regulated by the hepatic α-tocopherol transfer protein (11,12). Consequently, although γ-tocopherol accounts for as much as 70% of total intake of tocopherols



**Figure.** Change in the ratio of  $\alpha$ -tocopherol to total cholesterol in response to almonds. The molar ratio of plasma  $\alpha$ -tocopherol to total cholesterol increased by  $0.15 \mu\text{mol/L}^a$  for every 1% energy increase from almonds. <sup>a</sup>To convert  $\mu\text{mol/L}$  vitamin E to  $\text{mg/dL}$ , multiply  $\mu\text{mol/L}$  by 0.04307. To convert  $\text{mg/dL}$  vitamin E to  $\mu\text{mol/L}$ , multiply  $\text{mg/dL}$  by 23.2. Vitamin E of  $30 \mu\text{mol/L} = 1.3 \text{ mg/dL}$ .

in the United States, plasma  $\alpha$ -tocopherol levels are about 10-fold higher than  $\gamma$ -tocopherol with  $\beta$ -tocopherol levels lower still (13).

Almonds contain little  $\gamma$ - or  $\beta$ -tocopherol, and isocaloric incorporation of almonds reduced the  $\gamma$ - and  $\beta$ -tocopherol content of the experimental diets and of the participants' blood. Previous studies reported a negative correlation between  $\alpha$ - and  $\gamma$ -tocopherol levels and suppression of plasma  $\gamma$ - and  $\beta$ -tocopherols by supplemental doses of  $\alpha$ -tocopherol (14,15). The relatively high levels of  $\alpha$ -tocopherol of the almond diets in our study may have had a similar effect.

This is the first randomized controlled feeding trial to demonstrate dose-response enrichment of blood  $\alpha$ -tocopherol levels through the ingestion of increasing amounts of a single  $\alpha$ -tocopherol-rich food. Previously, blood  $\alpha$ -tocopherol concentrations were observed to have a positive correlation to diets rich in the vitamin (16,17). The importance of the delivery vehicle in enhancing uptake was demonstrated in a study showing that fortifying milk with a microdispersion of vitamin E increased the molar ratio of plasma tocopherol to cholesterol more dramatically than did fortifying orange juice or the use of vitamin E capsules (18).

Observational studies have shown  $\alpha$ -tocopherol is protective against conditions such as cardiovascular disease, cancer, diabetes, hypertension, and cognitive decline (3,6,19-22). In contrast, prospective, randomized, placebo-controlled studies have failed to verify a consistent benefit from vitamin E supplementation (23-25). Supplemental vitamin E is considered safe even at relatively high doses; an upper tolerable level has been set at 1,000  $\text{mg/day}$  (1,100 IU all-*rac*- or 1,500 IU RRR- $\alpha$ -tocopherol) by the Food and Nutrition Board (3). However, recent evidence suggests that under certain conditions, pharmacological doses of vitamin E may cause detrimental interactions. Vitamin E supplementation (800 IU/day) increased in vivo lipid oxidation in smokers consuming diets high in polyunsaturated fatty acids (26). A supple-

ment containing vitamin E, vitamin C, beta carotene, and selenium was shown to blunt favorable responses of high-density lipoprotein cholesterol to simvastatin-niacin therapy (27). In the Women's Angiographic Vitamin Estrogen trial, all-cause mortality increased in postmenopausal women receiving hormone replacement therapy who were assigned to the group receiving the antioxidant vitamins E (800 IU) and C (1,000 mg) (28). These unexpected reactions raise questions regarding the safety of supplemental doses, especially in association with smoking or drug therapies.

Food sources are a preferable method of obtaining needed nutrients. Epidemiologic studies suggest frequent nut consumption is beneficial for cardiovascular health (28-31) and intervention studies have examined the inclusion of nuts into diets in free-living (32-34) and controlled conditions (8,35-38).

Dietary advice often cautions that it may not be possible to plan daily meals with needed amounts of vitamin E (39). However, we demonstrated that incorporating almonds at 10% of energy (approximately 28 g [1 oz] or about 24 almonds and 165 kcal) in a 1,650-kcal diet provides 7.4 mg  $\alpha$ -tocopherol and is a practical method of substantially increasing intake and of achieving the vitamin E requirement for most persons. Other readily available foods that may contribute substantial amounts of vitamin E to the diet include sunflower, safflower, and cottonseed oils, peanuts, peanut butter, soybeans, mayonnaise, salad dressings, fortified cereals and breads, wheat germ, and broccoli. Planning a diet with a variety of these foods daily may also help achieve vitamin E recommendations (see Table 2).

This study examined the dose-response effect of almond consumption on vitamin E status. We found that an  $\alpha$ -tocopherol-rich food like almonds was a vehicle for enriching both the diet and blood with  $\alpha$ -tocopherol. The almond diets resulted in higher plasma and RBC levels of  $\alpha$ -tocopherol and higher  $\alpha$ -tocopherol to cholesterol ratios in healthy adults.

## CONCLUSIONS

- The recommended dietary allowance for vitamin E has been increased to 15  $\text{mg/day}$   $\alpha$ -tocopherol for both men and women. The typical US diet is low in  $\alpha$ -tocopherol. One ounce of almonds (165 kcal) can be isocalorically substituted for white bread, crackers, chips, and similar refined products to provide 7.4  $\text{mg}$   $\alpha$ -tocopherol.
- Other than almonds, foods that provide  $>4 \text{ mg}$   $\alpha$ -tocopherol in a typical serving are sunflower seeds, hazelnuts, wheat germ, wheat germ oil, sunflower oil, cottonseed oil, and safflower oil (6). Other important sources are green vegetables, tomato sauce, avocado, mango, and papaya. Dietetics professionals and nutrition educators can encourage the public to consume foods as opposed to dietary supplements that in addition to  $\alpha$ -tocopherol contain important nutrients and bioactive substances (40).
- Incorporating almonds into a diet may not be feasible for some persons due to personal preference, allergies, or economic factors. A limiting factor of our study is that only one food could be tested at a time to determine its ability to increase plasma vitamin E concentrations.

**Table 2.** Sample study menus for control, low-almond, and high-almond diets based on a 1,800-kcal/day<sup>a</sup> diet<sup>b</sup>

	Control	Low almond	High almond
<b>Sample menu 1</b>			
<b>Breakfast</b>			
Egg	41	37	33
Hash browns	68	60	47
Wheat bread	1 slice	1 slice	1 slice
Butter	8	—	—
Almond butter	—	11	23
Jam	19	17	15
Yogurt, flavored	113	101	90
Orange juice	0	0	0
<b>Lunch</b>			
Cheese sandwich	0.75 each	0.75 each	0.5 each
Corn chips	21	19	17
Black bean dip	21	19	17
Trail mix	38	34	30
Cranberry juice	6-oz can	6-oz can	6-oz can
Whole almonds	—	—	23
<b>Dinner</b>			
Baked chicken breast	98	89	79
Baked potato	113	101	90
Green beans	75	68	60
Green salad	Small	Small	Small
Tomato wedges	26	24	21
Olive oil	8	7	6
Lemon juice dressing	1 tsp	1 tsp	1 tsp
Cornbread	21	19	17
Honey	11	10	9
Butter	8	7	6
Fresh fruit cup	116	105	93
Slivered almonds	—	11	15
<b>Sample menu 2</b>			
<b>Breakfast</b>			
Corn flakes	21	19	17
Waffles	60	54	48
Syrup	23	20	18
Butter	4	4	3
Milk (2%)	139	125	111
Orange juice	0	0	0
Sliced almonds	0	9	19
<b>Lunch</b>			
Meatless sandwich patty	1 each	1 each	.75 each
Hamburger bun	1 each	1 each	1 each
Lettuce	2 pieces	2 pieces	2 pieces
Tomato	2 slices	2 slices	2 slices
Onions	2 slices	2 slices	2 slices
Ranch dressing	5	5	5
Ketchup	15	14	12
Potato chips	21	19	17
Celery stalk	3 pieces	3 pieces	3 pieces
Granola bar	20	—	—
Almond granola bar	—	19	28
Orange, medium	1 each	1 each	1 each
Cranberry juice	6-oz can	6-oz can	6-oz can
Baby carrots	60	54	48

*(continued)*

**Table 2.** Sample study menus for control, low-almond, and high-almond diets based on a 1,800-kcal/day<sup>a</sup> diet<sup>b</sup> (continued)

	Control	Low almond	High almond
<b>Dinner</b>			
Cod	64	58	51
Olive oil	10	9	8
Tartar sauce	8	7	6
Carrots	60	54	48
Green salad	Small	Small	Small
Rice	143	128	114
Canola oil	5	5	5
Lemon dressing	13	13	13
Sourdough roll	21	19	17
Butter	2	2	2
Vanilla ice cream	75	68	60
Sliced almonds	0	8	19

<sup>a</sup>Lowest energy level provided for subjects.  
<sup>b</sup>Weights are in grams unless otherwise noted.

The results suggest that consuming foods that are good sources of vitamin E may help to meet current recommendations. Public health messages can stress culturally acceptable foods that are good sources of vitamin E. Dietetics professionals can develop eating plans for groups or persons utilizing these foods.

The authors thank B. Connell, PhD, RD, K. Burke, PhD, RD, and Jack Brown for assisting with this project. This study was partially supported by a research grant from the Almond Board of California, Modesto, CA.

## References

- Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL. Beyond cholesterol. Modifications of low-density lipoprotein that increase its atherogenicity. *N Engl J Med.* 1989;320:915-924.
- Princen HMG, van Duyvenvoorde W, Buytenhek R, van der Laarse A, van Poppel G, Gevers Leuven JA, van Hinsbergh VWM. Supplementation with low doses of vitamin E protects LDL from lipid peroxidation in men and women. *Arterioscler Thromb Vasc Biol.* 1995;15:325-333.
- Institute of Medicine, Food and Nutrition Board. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids.* Washington, DC: National Academy Press; 2000.
- Ford ES, Sowell A. Serum  $\alpha$ -tocopherol status in the United States population: Findings from the Third National Health and Nutrition Examination Survey. *Am J Epidemiol.* 1999;150:290-300.
- Alaimo K, McDowell MA, Briefel RR, Bischof AM, Caughman CR, Loria CM, Johnson CL. *Dietary intake of vitamins, minerals, and fiber of persons ages 2 months and over in the United States: Third National Health and Nutrition Examination Survey, Phase 1, 1988-1991.* Hyattsville, MD: National Center for Health Statistics; 1994. Advance data from Vital and Health Statistics, No. 258.
- Maras JE, Bermudez OI, Bakun PJ, Boody-Alter EL, Tucker KL. Intake of  $\alpha$ -tocopherol is limited among US adults. *J Am Diet Assoc.* 2004;104:567-575.
- US Dept of Agriculture, Agricultural Research Service. USDA nutrient database for standard reference, release 15. Available at: <http://nal.usda.gov/fnic/foodcomp>. Accessed December 13, 2004.
- Sabaté J, Haddad E, Tanzman JS, Jambazian P, Rajaram S. Serum lipid response to a graded enrichment of a Step 1 diet with almonds: A randomized feeding trial. *Am J Clin Nutr.* 2003;77:1379-1384.
- Mino M, Kitagawa M, Nakagawa S. Red blood cell tocopherol concentration in a normal population of Japanese children and premature infants in relation to the assessment of vitamin E status. *Am J Clin Nutr.* 1985;41:631-638.
- Kramer JKG, Fouchard RC, Kallury KMR. Determination of vitamin E forms in tissues and diets by high-performance liquid chromatography using normal-phase diol column. *Methods Enzymol.* 1999;299:318-319.
- Arita M, Sato Y, Miyata A, Tanabe T, Takahashi E, Kayden HJ, Arai H, Inoue K. Human  $\alpha$ -tocopherol transfer protein cDNA cloning, expression, and chromosomal localization. *Biochem J.* 1995;306:437-443.
- Traber MG, Rader D, Acuff RV, Ramakrishnam R, Brewer HB, Kayden HJ. Vitamin E dose-response studies in humans with use of deuterated RRR- $\alpha$ -tocopherol. *Am J Clin Nutr.* 1998;68:847-853.
- Jiang Q, Christen S, Shigenaga MK, Ames BN.  $\gamma$ -tocopherol, the major form of vitamin E in the US diet, deserves more attention. *Am J Clin Nutr.* 2001;74:714-722.
- Handelman GJ, Machlin LJ, Fitch K, Weiter JJ, Dratz ED. Oral  $\alpha$ -tocopherol supplements decrease plasma  $\gamma$ -tocopherol levels in humans. *J Nutr.* 1985;115:807-813.
- Baker H, Handelman GJ, Short S, Machlin LJ, Bhagavan HN, Dratz EA, Frank O. Comparison of plasma  $\alpha$ - and  $\gamma$ -tocopherol levels following chronic oral administration of either all-rac- $\alpha$ -tocopherol ac-

- etate or RRR- $\alpha$ -tocopheryl acetate in normal adult male subjects. *Am J Clin Nutr.* 1986;43:382-387.
16. Parfitt VJ, Rubba P, Bolton C, Marotta G, Hartog M, Mancini M. A comparison of antioxidant status and free radical peroxidation of plasma lipoproteins in healthy young persons from Naples and Bristol. *Eur Heart J.* 1994;15:871-876.
  17. Luoma PV, Nayha S, Sikkilä K, Hassi J. High serum  $\alpha$ -tocopherol, albumin, selenium, and cholesterol and low mortality from coronary heart disease in northern Finland. *J Intern Med.* 1995;237:49-54.
  18. Hayes KC, Pronczuk A, Perlman D. Vitamin E in fortified cow milk uniquely enriches human plasma lipoproteins. *Am J Clin Nutr.* 2001;74:211-218.
  19. Brigelius-Flohe R, Kelly FJ, Salonen JT, Neuzil J, Zingg JM, Azzi A. The European perspective on vitamin E: Current knowledge and future research. *Am J Clin Nutr.* 2002;76:703-716.
  20. Losonczy KG, Harris TB, Havlik RJ. Vitamin E and vitamin C supplement use and risk of all cause and coronary heart disease mortality in older persons: The Established Populations for Epidemiologic Studies of the Elderly. *Am J Clin Nutr.* 1996;64:190-196.
  21. Rimm EB, Stampfer MJ, Acherio A, Giovannucci E, Colditz GA, Willett WC. Vitamin E consumption and the risk of coronary heart disease in men. *N Engl J Med.* 1993;328:1450-1456.
  22. Stampfer MJ, Hennekens CH, Manson JE, Colitz GA, Rosner B, Willett WC. Vitamin E consumption and the risk of coronary disease in women. *N Engl J Med.* 1993;328:1444-1449.
  23. Gey KF, Puska P, Jordan P, Moser UK. Inverse correlation between plasma vitamin E and mortality from ischemic heart disease in cross-cultural epidemiology. *Am J Clin Nutr.* 1991;53(suppl 1):S326-S334.
  24. ATBC Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N Engl J Med.* 1994;330:1029-1035.
  25. Stephens NG, Parsons A, Schofield PM, Kelly F, Cheeseman K, Mitchinson MJ. Randomised controlled trial of vitamin E in patients with coronary disease: Cambridge Heart Antioxidant Study (CHAOS). *Lancet.* 1996;347:781-786.
  26. GISSI-Prevenzione Investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: Results of the GISSI-Prevenzione Trial. *Lancet.* 1999;354:447-455.
  27. Weinberg RB, VanderWerken BS, Anderson RA, Stegner JE, Thomas MJ. Pro-oxidant effect of vitamin E in cigarette smokers consuming a high polyunsaturated fat diet. *Arterioscler Thromb Vasc Biol.* 2001;21:1029-1033.
  28. Cheung MC, Zhao X-Q, Chait A, Albers JJ, Brown BC. Antioxidant supplements block the response of HDL to simvastatin-niacin therapy in patients with coronary artery disease and low HDL. *Arterioscler Thromb Vasc Biol.* 2001;21:1320-1326.
  29. Waters DD, Alderman EL, Hsia J, Howard BV, Cobb FR, Rogers WJ, Ouyang P, Thompson P, Tardif JC, Higginson L, Bittner V, Steffes M, Gordon DJ, Proschan M, Younes N, Verter JI. Effects of hormone replacement therapy and antioxidant vitamin supplements on coronary atherosclerosis in postmenopausal women: A randomized controlled trial. *JAMA.* 2002;288:2432-2440.
  30. Fraser GE, Sabaté J, Beeson WL, Strahan TM. A possible protective effect of nut consumption on risk of coronary artery disease: The Adventist Health Study. *Arch Intern Med.* 1992;152:1416-1424.
  31. Fraser GE, Shavlik DJ. Risk factors for all-cause and coronary heart disease mortality in the oldest-old. The Adventist Health Study. *Arch Intern Med.* 1997;157:2249-2258.
  32. Hu FB, Stampfer MJ, Manson JE, Rimm EB, Colditz GA, Rosner BA, Speizer FE, Hennekens CH, Willett WC. Frequent nut consumption and risk of coronary heart disease in women: Prospective cohort study. *BMJ.* 1998;317:1341-1345.
  33. Albert CM, Gaziano M, Willett WC, Manson JE. Nut consumption and decreased risk of sudden cardiac death in the Physicians' Health Study. *Arch Intern Med.* 2002;162:1382-1387.
  34. Almario RU, Vonghavaravat V, Wong R, Kasim-Karakas SE. Effects of walnut consumption on plasma fatty acids and lipoproteins in combined hyperlipidemia. *Am J Clin Nutr.* 2001;74:72-79.
  35. Spiller GA, Jenkins DAJ, Bosello O, Gates JE, Craigen LN, Bruce B. Nuts and plasma lipids: An almond-based diet lowers LDL-C while preserving HDL-C. *J Am Coll Nutr.* 1998;17:285-290.
  36. Coquhuon DM, Humphries JA, Moores D, Somerset SM. Effects of a macadamia nut-enriched diet on serum lipids and lipoproteins compared to a low-fat diet. *Food Australia.* 1996;48:216-222.
  37. Rajaram S, Burke K, Connell B, Myint T, Sabaté J. A monounsaturated fatty acid-rich pecan-enriched diet favorably alters the serum lipid profile of healthy men and women. *J Nutr.* 2001;131:2275-2279.
  38. Sabaté J, Fraser GE, Burke K, Knutsen SF, Bennett H, Linstead KD. Effects of walnuts on serum lipid levels and blood pressure in normal men. *N Engl J Med.* 1993;328:603-607.
  39. Tribble DL. AHA Science Advisory: Antioxidant consumption and risk of coronary heart disease: Emphasis on vitamin C, vitamin E and beta carotene. *Circulation.* 1999;99:591-595.
  40. Kris-Etherton PM, Yu-Poth S, Sabaté J, Ratcliffe HE, Zhao G, Etherton TD. Nuts and their bioactive constituents: Effects on serum lipids and other factors that affect disease risk. *Am J Clin Nutr.* 1999(suppl); 70:S504-S511.