Association of Smoking With Serum and Dietary Levels of Antioxidants in Adults: NHANES III, 1988–1994

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A B S T R A C T

Objectives. This study examined the association of smoking with serum levels and dietary intakes of antioxidants in a nationally representative sample.

Methods. This study classified 7873 apparently healthy adults aged 17 to 50 years from National Health and Nutrition Examination Survey III (NHANES III) data as nonsmokers or as smokers if their serum cotinine levels were either lower than 14 ng/mL or 14 ng/mL or greater, respectively. SUDAAN software was used for the statistical analysis.

Results. Smokers of both sexes had significantly ($P<.001$) lower serum levels of vitamin C, α-carotene, β-carotene, β-cryptoxanthin, and lutein/zeaxanthin. Reduction in the serum vitamin E, lycopene, and selenium levels in smokers was slight. Smokers also had significantly lower dietary intakes of vitamin C and β-carotene. A significant ($P<.001$) inverse relation was found between serum vitamin C and β-carotene levels and cotinine levels independent of diet effect, and a positive relation ($P<.001$) was found between serum levels and dietary intakes.

Conclusions. Antioxidants appear to have differing declines in serum levels as a result of reduced dietary intakes and the effects of smoking. (*Am J Public Health.* 2001;91:258–264)

Smoking has long been accepted as a risk factor for many chronic diseases, including cardiovascular diseases, respiratory diseases, cancers, ulcers, and osteoporosis. In the United States alone, tobacco use resulted in more than 430 000 deaths each year, or 20% of total annual deaths, from 1990 to 1994.[1,2] Tobacco smoke contains many oxidants and free radicals that can cause damage to lipids, proteins, DNA, carbohydrates, and other biomolecules.[3] In vivo, antioxidant nutrients, including vitamin C, vitamin E, carotenoids, and selenium, play crucial roles in defending against oxidant damage.[4] Epidemiologic studies have shown strong protective effects of antioxidants against cancers and cardiovascular diseases, and the higher incidences of these diseases among smokers are partially attributed to lower intakes and serum levels of antioxidants in this population.[5–10]

Carotenoids are lipid-soluble pigments found in plant foods that function as vitamin A precursors and as antioxidants. The 5 major serum carotenoids are lycopene, lutein/zeaxanthin, β-carotene, β-cryptoxanthin, and α-carotene and account for more than 90% of the circulating carotenoids in humans.[11] The association of smoking with lower serum and dietary levels of β-carotene has been consistently reported in the literature.[12,13] However, findings on the association of smoking with the other carotenoids are limited and inconsistent.[14–17]

Cotinine is a principal metabolite of nicotine, with a half-life of approximately 20 hours.[18] Serum cotinine, which is directly proportional to the absorbed nicotine, has been used to measure tobacco exposure in epidemiologic studies. Serum cotinine is considered a better marker of smoking status than self-reported tobacco use, because self-reports underestimate smoking prevalence in certain populations. Nicotine inhalation among smokers may differ depending on the types and brands of tobacco products and on smoking habits.[19–23]

Few studies have examined the association between smoking and the antioxidant nutrient status of US adults in large-scale surveys. Likewise, few studies have used serum cotinine as the metabolic indicator of smoking in a population study. In this study, using data from the National Health and Nutrition Examination Survey III (NHANES III), we investigated the associations between smoking and serum concentrations and dietary intakes of vitamin C, vitamin E, 5 major carotenoids, and selenium in the adult US population aged 17 to 50 years.

Methods

Study Population and Design

The data used in this study were a subsample of NHANES III data.[24] NHANES III was conducted from 1988 to 1994 to examine the health and nutritional status of the civilian noninstitutionalized US population 2 months and older. The survey used "complex, multistage, stratified and clustered samples."[24(p20)] Of the 39 695 persons selected from across the United States, 33 994 (86%) were interviewed in their homes; 30 818 (78%) also were examined in the mobile examination centers. The survey collected information on socioeconomic demography, health behavior, lifestyle, personal and family health, biochemical measures, food frequency, and 24-hour dietary recall.

This study included apparently healthy adults aged 17 to 50 years whose serum cotinine measurements were available. We ex-

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cluded pregnant and lactating women; adults with chronic diseases, including cardiovascular diseases, stroke, diabetes, cancers, thyroid disease, goiter, lupus, gout, and respiratory diseases; and persons with hypertension that required dietary intervention. Selected subjects were classified as nonsmokers or as smokers if their serum cotinine levels were lower than 14 ng/mL or 14 ng/mL or greater, respectively.

NHANES III Database on Dietary Intakes and Blood Values

In NHANES III, 24-hour dietary recalls were used as the principal methodology to obtain quantitative information on food and nutrient intakes of the US population.[24] The University of Minnesota Nutrition Coordinating Center nutrient database was used for the dietary nutrient intake analysis. Of the antioxidants of interest in our study, intake data on vitamin C, vitamin E, β-carotene, and selenium were available in the database. NHANES III collected and analyzed blood samples by the designated laboratories.[25] Serum cotinine levels were measured with high-performance liquid chromatography and atmospheric-pressure chemical ionization tandem mass spectrometry. Serum levels of vitamin E, vitamin C, and carotenoids were measured with isocratic high-performance liquid chromatography. The serum selenium content was determined by atomic absorption spectrophotometry.

Statistical Analysis

The statistical analysis was carried out with SUDAAN, a statistical computer program that takes into account the complex, stratified, multistage survey design and sample weights of NHANES III.[26] In this study, we analyzed the arithmetic means and medians of serum levels and dietary intakes of antioxidants. The differences between smokers and nonsmokers for crude values and adjusted values were tested with 2-tailed *t* tests or analysis of variance. Means adjusted for social factors, dietary intakes, or serum cotinine levels were calculated with multiple regression models. A *P* value of less than .05 was regarded as indicating statistical significance.

Results

Study Population

Among the 10 771 persons aged 17 to 50 years who were interviewed, 3972 men and 3901 women were included in this analysis according to the study design. Among men, 1484 (37.4%) were smokers based on their serum cotinine levels, and among women, 1007 (25.8%) were smokers. The mean ± SEM values of serum cotinine were 0.77 ± 0.05 and 0.63 ± 0.05 ng/mL in male and female nonsmokers, respectively, and 242.45 ± 6.35 and 224.93 ± 5.44 ng/mL in male and female smokers, respectively. There were differences in race/ethnicity between smokers and nonsmokers as well as between men and women (Table 1). Smokers of both sexes had lower education levels, annual incomes, and frequency of leisure time physical activity than did nonsmokers but consumed more alcohol. In addition, a smaller percentage of smokers, compared with nonsmokers, took vitamin or mineral supplements. Mean age, height, and weight did not differ in smokers and nonsmokers.

Serum Levels and Dietary Intakes of Antioxidants

Table 2 shows the mean and median serum levels and dietary intakes of antioxidants in nonsmokers and smokers of both sexes. Male and female smokers, compared with nonsmokers, had significantly lower serum concentrations of vitamin C, vitamin E, α-carotene, β-carotene, β-cryptoxanthin, and lutein/zeaxanthin. Serum levels of vitamin E in smokers were reduced by about 5%, but when the values were adjusted for social factors, no difference was found between smokers and nonsmokers. Serum levels of lycopene in male smokers were reduced by 6% ($P < .05$), but when the values were adjusted for social factors, the resulting difference was not statistically significant. The depression effect of smoking on serum levels of selenium was slight (4%), although statistically significant. No difference was found in serum lycopene or serum selenium levels between female smokers and nonsmokers. In addition, sex differences were found for some measures. Regardless of smoking status, males had significantly lower mean serum levels of vitamin C ($P = .01$), α-carotene ($P = .003$), and β-carotene ($P < .001$). On the other hand, no sex differences were seen in the serum levels of vitamin E, β-cryptoxanthin, lutein/zeaxanthin, lycopene, and selenium.

Male and female smokers, compared with nonsmokers, had significantly lower dietary intakes of vitamin C and β-carotene. Although vitamin E intake did not differ by

TABLE 1—Characteristics[a] of Adult Nonsmokers and Smokers Aged 17 to 50 Years: NHANES III, 1988–1994

	Men		Women	
	Nonsmokers (n = 2488)	Smokers (n = 1484)	Nonsmokers (n = 2894)	Smokers (n = 1007)
Age, y	31.8 ± 0.4	32.4 ± 0.4	33.0 ± 0.3	31.8 ± 0.4
Ethnicity, %				
White[b]	71	76	68	80
Black[b]	10	11	12	13
Mexican[c]	9	5	7	3
Other	10	8	13	4
Education, y	13.3 ± 0.1	12.0 ± 0.1	12.9 ± 0.1	12.0 ± 0.1
Family annual income ≥$20 000, %	78.8	64.7	74.6	61.2
Leisure physical activity, times/mo	32.4 ± 1.0	26.6 ± 1.6	22.6 ± 1.1	20.9 ± 1.6
Take vitamin/mineral supplement, %	36.1	27.2	44.3	34.0
Drink alcohol, g/d	11.2 ± 1.1	27.0 ± 2.3	5.6 ± 0.7	9.6 ± 1.1
Height, cm	176.3 ± 0.2	176.7 ± 0.3	162.8 ± 0.2	163.4 ± 0.2
Weight, kg	80.9 ± 0.5	79.7 ± 0.7	66.6 ± 0.6	67.1 ± 0.7
Body mass index, kg/m^2	26.0 ± 0.1	25.5 ± 0.2	25.1 ± 0.2	25.1 ± 0.2

Note. NHANES III = National Health and Nutrition Examination Survey III.
[a]Values are mean ± SE or percentage.
[b]Non-Hispanic.
[c]Mexican American.

TABLE 2—Serum Levels and Daily Dietary Intakes of Antioxidants Among US Adult Nonsmokers and Smokers Aged 17 to 50 Years: NHANES III, 1988–1994

	Men					Women				
	Nonsmokers		Smokers		Smokers/	Nonsmokers		Smokers		Smokers/
Antioxidant Level	Mean ± SEM	Median	Mean ± SEM	Median	Nonsmokers[a]	Mean ± SEM	Median	Mean ± SEM	Median	Nonsmokers[a]
Serum vitamin C, mg/dL										
Crude	0.75 ± 0.02	0.75	0.51 ± 0.02***	0.39	68%	0.85 ± 0.02	0.85	0.61 ± 0.03***	0.50	72%
Adjusted[b]	0.73 ± 0.02		0.54 ± 0.03***		74%	0.84 ± 0.02		0.65 ± 0.03***		77%
Serum vitamin E, μg/dL										
Crude	1045 ± 20	964	980 ± 15**	911	94%	1005 ± 12	939	954 ± 15**	873	95%
Adjusted[b]	1034 ± 13		1003 ± 17		97%	992 ± 9		995 ± 14		100%
Serum α-carotene, μg/dL										
Crude	4.5 ± 0.2	3.2	2.7 ± 0.1***	1.3	60%	5.6 ± 0.2	3.9	3.2 ± 0.2***	1.9	56%
Adjusted[b]	4.4 ± 0.2		2.9 ± 0.1***		65%	5.3 ± 0.2		3.8 ± 0.2***		71%
Serum β-carotene, μg/dL										
Crude	17.7 ± 0.7	12.8	11.0 ± 0.4***	8.3	62%	21.9 ± 0.7	16.6	14.2 ± 0.8***	10.4	65%
Adjusted[b]	17.3 ± 0.6		11.9 ± 0.5***		69%	21.1 ± 0.6		15.9 ± 0.8***		75%
Serum β-cryptoxanthin, μg/dL										
Crude	10.0 ± 0.2	7.8	6.9 ± 0.2***	5.3	68%	10.1 ± 0.2	7.7	6.5 ± 0.1***	5.1	65%
Adjusted[b]	9.7 ± 0.2		7.4 ± 0.2***		76%	9.7 ± 0.2		7.2 ± 0.2***		74%
Serum lutein/zeaxanthin, μg/dL										
Crude	21.8 ± 0.5	19.0	17.5 ± 0.4***	15.5	80%	21.6 ± 0.5	18.8	16.9 ± 0.3***	15.2	79%
Adjusted[b]	21.5 ± 0.4		18.1 ± 0.4***		84%	21.0 ± 0.5		18.1 ± 0.4***		86%
Serum lycopene, μg/dL										
Crude	27.4 ± 0.6	25.6	25.7 ± 0.6*	23.9	94%	23.8 ± 0.4	22.2	23.5 ± 0.5	21.5	99%
Adjusted[b]	27.3 ± 0.5		26.1 ± 0.7		96%	23.9 ± 0.4		23.4 ± 0.5		98%
Serum selenium, ng/mL										
Crude	129 ± 1	127	124 ± 1***	122	96%	124 ± 1	121	122 ± 1	120	99%
Adjusted[b]	129 ± 1		124 ± 1***		96%	124 ± 1		122 ± 1		99%
Dietary vitamin C intake, mg/d										
Crude	112 ± 3	77	83 ± 3***	53	73%	82 ± 3	54	66 ± 4**	36	81%
Adjusted[b]	111 ± 3		88 ± 4***		79%	80 ± 2		70 ± 4*		88%
Dietary vitamin E[c] intake, mg/d										
Crude	13.0 ± 0.5	10.3	11.5 ± 0.5*	9.8	89%	8.9 ± 0.4	7.2	8.5 ± 0.4	6.8	96%
Adjusted[b]	12.8 ± 0.3		11.7 ± 0.3		91%	8.8 ± 0.3		8.7 ± 0.4		99%
Dietary β-carotene intake, μg/d										
Crude	3175 ± 228	1597	2412 ± 181*	1144	76%	2669 ± 148	1052	1852 ± 119***	836	69%
Adjusted[b]	3095 ± 249		2575 ± 208		83%	2553 ± 150		2074 ± 133*		81%

Note. NHANES III = National Health and Nutrition Examination Survey III.
[a]Comparison of means.
[b]Values were adjusted for age, race/ethnicity, education level, family annual income, leisure physical activity, vitamin/mineral supplement intake, and body mass index.
[c]Total α-tocopherol equivalents.
*P < .05; **P < .01; ***P < .001, smokers compared with nonsmokers (within each sex).

smoking status in females, it was lower in male smokers than in male nonsmokers (P < .05). However, the difference in vitamin E intake by smoking status did not remain statistically significant when adjustment was made for social factors.

Serum Antioxidant Levels Affected by Cotinine Levels or Dietary Intake Levels

The decrease in serum levels of antioxidants in relation to the metabolic effects of smoking was studied (by cotinine levels [Table 3] or by dietary intake levels [Table 4]). Subjects were classified as nonsmokers (cotinine level < 14 ng/mL), light smokers (cotinine level = 14–100 ng/mL), moderate smokers (cotinine level = 100–200 ng/mL), or heavy smokers (cotinine level > 200 ng/mL). Dietary levels were divided into 4 groups: 25th percentile or less, 26th to 50th percentiles, 51st to 75th percentiles, and 76th percentile or greater. Inverse and generally linear relations were found between serum levels and cotinine levels for vitamins C and E and β-carotene in both sexes. However, differential declines were noted for vitamin C and β-carotene (P < .001) and vitamin E (not statistically significant). The linear relation was clearer for vitamin C than for β-carotene. For β-carotene in both sexes, the biggest decrease in serum levels was noted between nonsmokers and light smokers. Increase in smoking intensity did not show statistically significant decreases in serum levels of β-carotene. The inverse association persisted after adjustment for dietary intake of a corresponding nutrient.

Table 4 shows the association of smoking with dietary intakes and serum levels of antioxidants. Relations between serum levels of antioxidants and dietary intakes were positive and generally linear in both sexes. Adjustment for cotinine levels did not influence the overall relation between dietary intake and serum level of a specific nutrient. The linearity was clearer for vitamin C (P < .001) than for β-carotene (P < .001) or for vitamin E (not significant).

TABLE 3—Serum Levels of Antioxidant Nutrients,[a] by Cotinine Levels: NHANES III, 1988–1994

Serum Levels	Cotinine Levels, ng/mL <14 (Nonsmokers)	14–100 (Light Smokers)	100–200 (Moderate Smokers)	>200 (Heavy Smokers)	ANOVA
		Men			
Vitamin C, mg/dL					
Crude	0.75 ± 0.02^{x}	0.65 ± 0.04^{y}	0.50 ± 0.03^{z}	0.46 ± 0.02^{z}	***
Diet-adjusted[b]	0.74 ± 0.02^{x}	0.65 ± 0.04^{x}	0.51 ± 0.03^{y}	0.50 ± 0.03^{y}	***
Vitamin E, μg/dL					
Crude	1045 ± 20	1033 ± 38	975 ± 33	963 ± 16	
Diet-adjusted[c]	1047 ± 20	1038 ± 38	977 ± 33	970 ± 17	
β-Carotene, μg/dL					
Crude	17.7 ± 0.7^{x}	13.2 ± 0.8^{y}	10.7 ± 0.6^{y}	10.4 ± 0.4^{y}	***
Diet-adjusted[d]	17.7 ± 0.7^{x}	13.1 ± 0.9^{y}	10.7 ± 0.6^{y}	10.9 ± 0.5^{y}	***
		Women			
Vitamin C, mg/dL					
Crude	0.85 ± 0.02^{x}	0.84 ± 0.05^{x}	0.60 ± 0.05^{y}	0.54 ± 0.04^{y}	***
Diet-adjusted[b]	0.85 ± 0.02^{x}	0.83 ± 0.04^{x}	0.61 ± 0.05^{y}	0.55 ± 0.04^{y}	***
Vitamin E, μg/dL					
Crude	1005 ± 12	969 ± 43	966 ± 29	944 ± 21	
Diet-adjusted[c]	1005 ± 12	970 ± 43	967 ± 30	942 ± 23	
β-Carotene, μg/dL					
Crude	21.9 ± 0.7^{x}	14.2 ± 1.2^{y}	13.0 ± 0.9^{y}	14.7 ± 1.2^{y}	***
Diet-adjusted[d]	21.7 ± 0.7^{x}	14.6 ± 1.0^{y}	13.3 ± 0.9^{y}	15.0 ± 1.1^{y}	***

Note. NHANES III = National Health and Nutrition Examination Survey III; ANOVA = analysis of variance. Means within a row with different superscript letters (x–z) are significantly different, $P \leq .05$ (Newman-Keuls test).
[a]Mean ± SE.
[b]Adjusted for daily dietary vitamin C.
[c]Adjusted for daily dietary vitamin E.
[d]Adjusted for daily dietary β-carotene.
***$P < .001$.

TABLE 4—Serum Levels of Antioxidant Nutrients,[a] by Dietary Intake Levels: NHANES III, 1988–1994

Serum Levels	Dietary Levels ≤25th Percentile	26th–50th Percentile	51st–75th Percentile	>75th Percentile	ANOVA
		Men			
Vitamin C, mg/dL					
Crude	0.50 ± 0.02^{w}	0.58 ± 0.03^{x}	0.69 ± 0.02^{y}	0.84 ± 0.02^{z}	***
Cotinine-adjusted	0.52 ± 0.02^{w}	0.59 ± 0.03^{x}	0.69 ± 0.02^{y}	0.81 ± 0.02^{z}	***
Vitamin E, μg/dL					
Crude	997 ± 20	1022 ± 20	1017 ± 23	1052 ± 23	
Cotinine-adjusted	1003 ± 20	1020 ± 20	1017 ± 23	1049 ± 23	
β-Carotene, μg/dL					
Crude	10.8 ± 0.4^{x}	14.2 ± 0.7^{y}	16.9 ± 1.2^{z}	18.4 ± 0.9^{z}	***
Cotinine-adjusted	11.3 ± 0.4^{x}	14.6 ± 0.7^{y}	16.6 ± 1.2^{z}	18.0 ± 0.8^{z}	***
		Women			
Vitamin C, mg/dL					
Crude	0.60 ± 0.03^{x}	0.68 ± 0.03^{x}	0.85 ± 0.02^{y}	0.98 ± 0.03^{z}	***
Cotinine-adjusted	0.62 ± 0.03^{x}	0.70 ± 0.03^{x}	0.84 ± 0.02^{y}	0.96 ± 0.03^{z}	***
Vitamin E, μg/dL					
Crude	968 ± 18	982 ± 14	986 ± 22	1019 ± 22	
Cotinine-adjusted	971 ± 18	983 ± 14	984 ± 22	1018 ± 22	
β-Carotene, μg/dL					
Crude	14.8 ± 0.8^{x}	18.5 ± 1.1^{y}	17.7 ± 0.5^{y}	27.4 ± 1.3^{z}	***
Cotinine-adjusted	15.3 ± 0.8^{x}	18.4 ± 1.1^{y}	17.6 ± 0.5^{y}	27.1 ± 1.3^{z}	***

Note. NHANES III = National Health and Nutrition Examination Survey III; ANOVA = analysis of variance. Means within a row with different superscript letters (w–z) are significantly different, $P \leq .05$ (Newman-Keuls test). Vitamin C—25th, 50th, 75th percentile (mg/day): men, 30, 67, 132, respectively; women, 22, 49, 103, respectively. Vitamin E—25th, 50th, 75th percentile (mg/day): men, 6.6, 10.1, 15.3, respectively; women, 4.5, 7.1, 10.5, respectively. β-Carotene—25th, 50th, 75th percentile (μg/day): men, 697, 1367, 2978, respectively; women, 487, 995, 2543, respectively.
[a]Mean ± SE.
***$P < .001$.

Discussion

Serum Cotinine as a Marker of Smoking Status

Researchers have used the serum cotinine value of 14 ng/mL as the cutoff point for nonsmokers and smokers.[21–23,27] Self-reported data misclassify or underestimate the smoking population by 1% to 4.2%.[19–22] It is well known that individuals smoke cigarettes differently from one another and may inhale very different amounts of tobacco smoke, even when smoking the same brand of cigarettes.[18] Smoking-related diseases are thought to be connected directly to the inhaled dose of tobacco smoke. Therefore, by using serum cotinine levels, we were able to investigate the association between biochemical smoke and metabolic effect more accurately than if we had based our analysis on self-reported tobacco use.

Exposure to environmental tobacco smoke (ETS), or passive smoking, has been recognized as a health hazard in association with pulmonary and cardiovascular diseases. However, no clear cutoff point distinguishes ETS exposure and non-ETS exposure among nonsmokers. Pirkle et al.[28] reported from the NHANES III data that the geometric mean serum cotinine levels of non–tobacco users with or without ETS exposure were 0.700 (95% confidence interval = 0.586, 0.835) or 0.124 (95% confidence interval = 0.111, 0.138) ng/mL, respectively. Most had serum cotinine levels below 10 ng/mL. Therefore, nonsmokers as defined in this study included people with and without ETS exposure.

Our analysis showed little overlap between serum cotinine levels for adult nonsmokers and smokers, with mean values of 0.7 ± 0.0 and 235.6 ± 4.6 ng/mL. Serum cotinine levels were mostly less than 10 ng/mL or greater than 20 ng/mL, and only 1.2% had levels between 10 and 20 ng/mL. Therefore, use of 14 ng/mL of serum cotinine as a cutoff point would not result in error in the classification of smoking status.

Because most data on smoking are based on the number of cigarettes smoked per day, it is useful to clarify the correspondence between serum cotinine levels and number of cigarettes. Smoking intensities are usually classified as nonsmoking and light, moderate, or heavy smoking according to the number of cigarettes smoked per day: 0, fewer than 10, 10 to 20, or more than 20 cigarettes, respectively.[29] These numbers generally coincide with serum cotinine levels of less than 14, 14 to 100, 100 to 200, or greater than 200 ng/mL, respectively.[23] This relation was confirmed by our own analysis of the NHANES III data, which showed that serum cotinine levels of less than 14, 14 to 100, 100 to 200, and greater than 200 ng/mL indicated the self-reported number of cigarettes per day of 0.2 ± 0.1 (mean ± SE), 6.7 ± 1.0, 14.2 ± 1.2, and 21.0 ± 0.7 in men and 0.1 ± 0.0, 6.1 ± 0.8, 15.6 ± 1.3, and 20.5 ± 0.7 in women, respectively.

Differential Decrease of Serum Antioxidant Levels by Smoking

Vitamins C and E. Researchers have consistently and clearly reported that smoking is associated with lower serum levels and lower dietary intakes of vitamin C.[30–33] Our analysis of the NHANES III data also showed that smokers had significantly ($P < .001$) lower serum levels and dietary intakes of vitamin C than did nonsmokers of both sexes. Serum levels were decreased by the increased cotinine levels, independent of dietary levels (Table 3), and also by the decreased dietary levels (Table 4), as observed in smokers. Therefore, serum levels appear to be decreased by the combined effect of smoking and lower dietary intakes in smokers.

Lower serum vitamin C levels in smokers were speculated by other researchers to be caused by impaired vitamin C absorption or increased breakdown.[34] The fact that in our analysis serum vitamin C was inversely associated with serum cotinine even after diet adjustment also indicates that declines in serum level were a metabolic effect of smoking. Studies have reported that smokers need higher vitamin C intakes to have the same serum levels as nonsmokers. Schectman et al.,[33] using NHANES II data, reported that smokers had decreased serum vitamin C levels independent of vitamin C intakes and that there was a 3-fold incidence of hypovitaminosis C (serum levels ≤ 0.2 mg/dL) among smokers. They further hypothesized that vitamin C intake of more than 200 mg daily would provide smokers the same protection as would 60 mg to nonsmokers, whereas other researchers recommended that smokers take at least 100 mg of vitamin C daily.[34]

Evidence of an association between tobacco smoking and vitamin E status is controversial. Some studies found that smokers had significantly lower serum levels of vitamin E,[35,36] whereas others reported no differences between smokers and nonsmokers.[13,15] However, these studies had limited sample sizes and used self-reported cigarette use as the smoking indicator, which may have led to the inconsistent results. Our use of the NHANES III data and inclusion of only apparently healthy adults as the sample prevented the confounding of factors such as disease and aging. We found a slightly inverse relation between smoking intensity and serum levels of vitamin E, but the relation was not as significant as with vitamin C and β-carotene.

Carotenoids. Of the 5 major carotenoids we analyzed, smokers had significantly ($P < .001$) reduced serum levels of α-carotene, β-carotene, β-cryptoxanthin, and lutein/zeaxanthin. Serum levels of lycopene were the exception. Statistically significant and negative associations between smoking and β-carotene have been consistently reported in the literature.[12,13] Lowered serum concentrations of β-carotene in smokers, after adjustment for dietary intakes, have been attributed in part to the enhanced turnover rate resulting from oxidative stress.[12] Similar results were reported by Margetts and Jackson,[29] who showed that at the same level of β-carotene intake, smokers were more likely to have lower circulating levels than were nonsmokers.

Fewer reports on the association of smoking with α-carotene and β-cryptoxanthin levels are available. In general, a negative association is observed. In our study, the decline of serum α-carotene and β-cryptoxanthin levels in smokers was highly significant ($P < .001$) in both men and women. From a study with African American women, Pamuk et al.[17] reported that despite the similar intakes of carotenoids, smokers had lower age-adjusted geometric mean serum concentrations of α-carotene, β-carotene, lycopene, and β-cryptoxanthin—71% to 79% of those for nonsmokers. Furthermore, women who smoked more than 10 cigarettes per day were estimated to have geometric mean serum concentrations of α-carotene, β-carotene, and lycopene of only 69%, 63%, and 67%, respectively, of those in women who had never smoked ($P < .05$).

Generally negative but statistically inconsistent associations have been reported with lutein/zeaxanthin. Our results showed clearly and significantly reduced levels in smokers. Statistically insignificant but negative associations have been reported between lycopene and smoking. Our analysis showed that male smokers had slightly reduced serum levels, but when adjustment was made for social factors, there was no difference. Female smokers and nonsmokers had similar serum lycopene levels. Lycopene was the most abundant circulating carotenoid, followed by lutein/zeaxanthin, β-carotene, β-cryptoxanthin, and α-carotene. The relative efficacies of these carotenoids as antioxidants have not been reported in the literature.

Selenium. The relation of smoking with selenium status has been examined in only a few studies.[37–41] Swanson et al.,[37] in a study of 44 adults, reported that smokers had lower serum or whole levels of blood selenium than did nonsmokers. The authors stated that the lower selenium concentrations of smokers were explained by low dietary selenium intake rather

than by smoking effect. Other researchers[39,40] reported similar results, whereas Robinson et al.[41] found no association between smoking and selenium status in New Zealand adults. Our results showed a significant reduction in serum levels of selenium in male smokers but not in female smokers. However, even though statistically significant, a 4% reduction in serum level in male smokers does not provide a clear negative association between serum level of selenium and smoking.

We found that serum concentrations of α-carotene, β-carotene, lutein/zeaxanthin, β-cryptoxanthin, and vitamin C were notably more negatively influenced by smoking than were the other antioxidants. Thus, smokers may be especially lacking in these antioxidants. Reports in the literature were inconsistent for vitamin E, α-carotene, β-cryptoxanthin, lutein/zeaxanthin, and selenium in association with smoking. It appears that the association of smoking with decreased serum levels of these antioxidants was so slight that any differences in the experimental design would have resulted in different outcomes. The differences in methodologies were noted, such as adjustment or no adjustment of serum values for various socioeconomic factors, sample size, age, sex, choice of smoking indicator as self-report or cotinine–biochemical marker, or inclusion of persons with diseases. The large sample size of NHANES III allowed a comprehensive study of the association between smoking and 8 currently important antioxidants from a national public health perspective. □

Contributors

W. Wei and Y. Kim designed the study and wrote the paper. W. Wei and N. Boudreau analyzed the data.

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