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# Serum carotenoid concentrations in US children and adolescents<sup>1,2</sup>

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# **ABSTRACT**

**Background:** Carotenoids, a class of phytochemicals, may affect the risk of several chronic conditions.

**Objective:** Our objective was to describe the distributions and correlates of serum carotenoid concentrations in US children and adolescents. **Design:** Using data from the third National Health and Nutrition Examination Survey (1988–1994), a cross-sectional study, we examined the distributions of serum concentrations of  $\alpha$ -carotene,  $\beta$ -carotene,  $\beta$ -cryptoxanthin, lutein and zeaxanthin, and lycopene among 4231 persons aged 6–16 y.

Results: After adjustment for age, sex, race or ethnicity, povertyincome ratio, body mass index status, HDL- and non-HDL-cholesterol concentrations, C-reactive protein concentration, and cotinine concentration, only HDL-cholesterol (P < 0.001) and non-HDLcholesterol (P < 0.001) concentrations were directly related to all carotenoid concentrations. Age (P < 0.001) and body mass index status (P < 0.001) were inversely related to all carotenoid concentrations except those of lycopene. Young males had slightly higher carotenoid concentrations than did young females, but the differences were significant only for lycopene concentrations (P = 0.029). African American children and adolescents had significantly higher \( \beta \)-cryptoxanthin (P < 0.001), lutein and zeaxanthin (P < 0.001), and lycopene (P = 0.006) concentrations but lower  $\alpha$ -carotene (P < 0.001) concentrations than did white children and adolescents. Mexican American children and adolescents had higher  $\alpha$ -carotene (P < 0.001),  $\beta$ -cryptoxanthin (P < 0.001), and lutein and zeaxanthin (P < 0.001) concentrations but lower lycopene (P = 0.001) concentrations than did white children and adolescents. C-reactive protein concentrations were inversely related to  $\beta$ -carotene (P < 0.001), lutein and zeaxanthin (P < 0.001), and lycopene (P = 0.023) concentrations. Cotinine concentrations were inversely related to  $\alpha$ -carotene (P = 0.002),  $\beta$ -carotene (P < 0.001), and  $\beta$ -cryptoxanthin (P < 0.001) concentrations.

**Conclusion:** These data show significant variations in serum carotenoid concentrations among US children and adolescents and may be valuable as reference ranges for this population. *Am J Clin Nutr* 2002;76:818–27.

**KEY WORDS** Antioxidants,  $\beta$ -carotene, carotene, carotenoids, children, adolescents, C-reactive protein, ethnic groups, health surveys, sex distribution, third National Health and Nutrition Examination Survey

# INTRODUCTION

The benefits of consuming an adequate amount of fruit and vegetables are well known, although which of their numerous phytochemicals account for their health benefits remains unresolved. Fruit and vegetable intake is inversely related to cardiovascular

disease (1, 2), cancer (3, 4), diabetes (5), and other conditions. Despite these benefits, fruit and vegetable intake in the US population is inadequate (6, 7).

Carotenoids, a prominent class of phytochemicals, are compounds with vitamin A–like chemical structures that are found mostly in plants (8). Many carotenoids have been described, but 5— $\alpha$ -carotene,  $\beta$ -carotene,  $\beta$ -cryptoxanthin, lutein and zeaxanthin, and lycopene—account for most of the concentrations of carotenoids found in humans. Their health benefits are not conclusively established, but epidemiologic studies suggest that carotenoid intake or circulating concentrations are inversely related to all-cause mortality (9), cardiovascular disease (10–17), various cancers (18), insulin resistance (19, 20), and other chronic conditions. The antioxidant potential of carotenoids is thought to account for their health benefits, but other mechanisms have been proposed as well (21).

Because of the possible health benefits of carotenoids, knowing the population distribution of their concentrations and identifying subgroups with low concentrations, who might be at increased risk of future disease, are of considerable interest. Recently, significant differences in carotenoid concentrations by sex and ethnicity were reported for the adult US population (22), but few population-based data about the distribution of carotenoid concentrations in children and adolescents are available. Furthermore, it is important to examine predictors of carotenoid concentrations to identify potentially modifiable determinants of these concentrations and to identify possible confounders for epidemiologic studies of carotenoids. Therefore, we examined the distributions and determinants of the concentrations of 5 carotenoids—  $\alpha$ -carotene,  $\beta$ -carotene,  $\beta$ -cryptoxanthin, lutein and zeaxanthin, and lycopene—for children and adolescents who participated in the third National Health and Nutrition Examination Survey (NHANES III).

### SUBJECTS AND METHODS

NHANES III was started in 1988 and completed in 1994. A representative sample of the US population, selected using a multistage sampling design, was contacted and asked to participate.

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The American Journal of Clinical Nutrition

TABLE 1 Distribution of serum  $\alpha$ -carotene concentrations among children and adolescents aged 6–16 y who participated in the third National Health and Nutrition Examination Survey, 1988–1994

					Percentile					
	$\overline{x} \pm SE$	5th	15th	25th	50th	75th	85th	95th	Minimum	Maximum
	μmol/L				μmol/L				μmol/L	μmol/L
Total $(n = 4231)$	$0.0698 \pm 0.0026$	0.0118	0.0160	0.0204	0.0524	0.0745	0.0969	0.1580	0.0100	0.8800
Non-Hispanic white $(n = 1158)$	$0.0694 \pm 0.0032$	0.0117	0.0157	0.0197	0.0525	0.0765	0.0978	0.1601	0.0100	0.6900
Non-Hispanic black ( $n = 1442$ )	$0.0500 \pm 0.0013$	0.0112	0.0141	0.0170	0.0325	0.0575	0.0666	0.1047	0.0100	0.7300
Mexican American $(n = 1433)$	$0.0717 \pm 0.0030$	0.0127	0.0184	0.0296	0.0568	0.0754	0.0971	0.1533	0.0100	0.4100
Other $(n = 198)$	$0.1019 \pm 0.0097$	0.0171	0.0430	0.0548	0.0673	0.1007	0.1234	0.2258	0.0100	0.8800
Male $(n = 2115)$	$0.0703 \pm 0.0033$	0.0118	0.0160	0.0206	0.0523	0.0757	0.0976	0.1475	0.0100	0.8800
Non-Hispanic white $(n = 578)$	$0.0683 \pm 0.0033$	0.0116	0.0156	0.0196	0.0510	0.0773	0.0983	0.1441	0.0100	0.6900
Non-Hispanic black ( $n = 726$ )	$0.0527 \pm 0.0017$	0.0114	0.0146	0.0177	0.0364	0.0607	0.0677	0.1132	0.0100	0.6100
Mexican American $(n = 710)$	$0.0692 \pm 0.0024$	0.0128	0.0184	0.0293	0.0559	0.0747	0.0934	0.1491	0.0100	0.3900
Other $(n = 101)$	$0.1139 \pm 0.0203$	0.0169	0.0464	0.0594	0.0686	0.1008	0.1227	0.2255	0.0100	0.8800
Female ( $n = 2116$ )	$0.0693 \pm 0.0027$	0.0119	0.0160	0.0202	0.0526	0.0731	0.0960	0.1668	0.0100	0.7300
Non-Hispanic white $(n = 580)$	$0.0706 \pm 0.0039$	0.0119	0.0159	0.0199	0.0542	0.7570	0.0971	0.1767	0.0100	0.4500
Non-Hispanic black ( $n = 716$ )	$0.0473 \pm 0.0019$	0.0110	0.0137	0.0164	0.0291	0.5340	0.6480	0.9790	0.0100	0.7300
Mexican American $(n = 723)$	$0.0743 \pm 0.0048$	0.0126	0.0184	0.0300	0.0577	0.0763	0.1010	0.1577	0.0100	0.4100
Other $(n = 97)$	$0.0898 \pm 0.0085$	_	0.0402	0.0510	0.0660	0.1005	0.1240	0.2049	0.0200	0.3900
Age (y)										
6-7 (n = 839)	$0.0745 \pm 0.0035$	0.0124	0.0177	0.0304	0.0613	0.0845	0.1054	0.1515	0.0100	0.6100
$8-11 \ (n=1753)$	$0.0790 \pm 0.0038$	0.0127	0.0188	0.0337	0.0607	0.0824	0.1060	0.1984	0.0100	0.6900
$12-16 \ (n=1639)$	$0.0601 \pm 0.0033$	0.0113	0.0143	0.0174	0.0388	0.0661	0.0837	0.1374	0.0100	0.8800
Poverty-income ratio										
$\leq 1.3 \ (n = 2100)$	$0.0619 \pm 0.0027$	0.0115	0.0150	0.0184	0.0459	0.0683	0.0889	0.1355	0.0100	0.6100
>1.3-3.5 ( $n=1704$ )	$0.0702 \pm 0.0038$	0.0117	0.0158	0.0199	0.0511	0.0734	0.0950	0.1541	0.0100	0.8800
>3.5 (n = 427)	$0.0808 \pm 0.0059$	0.0131	0.0193	0.0362	0.0622	0.0874	0.1086	0.2098	0.0100	0.3500
BMI (percentile)										
$\leq 15 \ (n = 378)$	$0.0756 \pm 0.0034$	0.0124	0.0210	0.0389	0.0623	0.0831	0.1121	0.1448	0.0100	0.3900
$16-84 \ (n=2645)$	$0.0740 \pm 0.0034$	0.0121	0.0168	0.0245	0.0550	0.0779	0.1000	0.1831	0.0100	0.8800
85–94 ( <i>n</i> = 629)	$0.0641 \pm 0.0035$	0.0117	0.0152	0.0187	0.0516	0.0704	0.0882	0.1419	0.0100	0.7300
$\geq$ 95 ( $n$ = 579)	$0.0483 \pm 0.0037$	0.0110	0.0132	0.0154	0.0250	0.0549	0.0679	0.1226	0.0100	0.2600

Participants, who were interviewed at home, were asked to come to the mobile examination center for additional tests and to complete additional questionnaires. For most participants a blood sample was drawn during the examination, but for those who could not attend, a blood sample was requested during the original home interview. To provide more stable estimates, children aged 2 mo to 5 y, African Americans, and Mexican Americans were oversampled. More detailed information about the survey is available elsewhere (23, 24).

Participants attended a morning, afternoon, or evening examination session. Those who attended morning sessions were asked to fast for 12 h, and those who attended afternoon or evening sessions were asked to fast for 6 h. Five carotenoids were assayed at the NHANES laboratory at the Centers for Disease Control and Prevention:  $\alpha$ -carotene,  $\beta$ -carotene,  $\beta$ -cryptoxanthin, lutein and zeaxanthin, and lycopene. Detailed procedures for these assays were published elsewhere (25). Reversed-phase HPLC with multiwavelength detection was used to quantify the concentrations of these carotenoids (26). Because a longer run time is needed to measure concentrations of lutein and zeaxanthin separately, the decision was made to measure them together for practical reasons. Total carotenoid concentrations were calculated by summing the concentrations of the individual carotenoid concentrations.

We included the following covariates: age, sex, race or ethnicity, poverty-income ratio, body mass index, serum HDL- and non-HDL-cholesterol concentrations, C-reactive protein concentration, supplement use, cotinine concentration, physical activity,

and fruit and vegetable intake. As discussed below, associations between these variables and carotenoid concentrations have been examined in adults. Four racial or ethnic groups were created: white, African American, Mexican American, and other. Because the last group was small, we excluded it from some analyses. The poverty-income ratio represents reported family income divided by the poverty threshold produced annually by the Census Bureau and adjusted for changes caused by inflation. Body mass index (in kg/m<sup>2</sup>) was calculated from measured heights and weights. Using the body mass index growth charts recently released by the Centers for Disease Control and Prevention, body mass index was divided into the following categories by age- and sex-specific percentiles: <15th, 15th to <85th, 85th to <95th, and  $\ge95$ th (27). Serum concentrations of total and HDL cholesterol (after precipitation with a heparin-manganese chloride solution) were measured enzymatically with a Hitachi 704 analyzer (Boehringer Mannheim Diagnostics, Indianapolis). We calculated the non-HDL-cholesterol concentration by subtracting the concentration of HDL cholesterol from that of total cholesterol. C-reactive protein concentrations were measured by using latex-enhanced nephelometry. The lower detection limit was 3.0 mg/L. Participants with a concentration below the lower detection limit were assigned a value of 2.1 mg/L (3.0 mg/L divided by the square root of 2). C-reactive protein concentrations were divided into 2 categories: ≤2.1 and > 2.1 mg/L. Serum cotinine concentrations were determined by using HPLC with atmospheric pressure chemical ionization tandem mass spectrometry. The number of times per

820 FORD ET AL

TABLE 2
Distribution of serum  $\beta$ -carotene concentrations among children and adolescents aged 6–16 y who participated in the third National Health and Nutrition Examination Survey, 1988–1994

					Percentile					
	$\overline{x} \pm SE$	5th	15th	25th	50th	75th	85th	95th	Minimum	Maximum
	μmol/L				μmol/L				μmol/L	μmol/L
Total $(n = 4231)$	$0.3023 \pm 0.0052$	0.1038	0.1409	0.1754	0.2529	0.3550	0.4384	0.5994	0.0200	1.7700
Non-Hispanic white $(n = 1158)$	$0.3007 \pm 0.0073$	0.1026	0.1390	0.1733	0.2513	0.3564	0.4366	0.5909	0.0400	1.5300
Non-Hispanic black ( $n = 1442$ )	$0.2920 \pm 0.0046$	0.0986	0.1360	0.1705	0.2505	0.3460	0.4059	0.5954	0.0400	1.7700
Mexican American $(n = 1433)$	$0.2964 \pm 0.0072$	0.0952	0.1370	0.1727	0.2477	0.3480	0.4239	0.6261	0.0200	1.4500
Other $(n = 198)$	$0.3356 \pm 0.0169$	0.1236	0.1648	0.1946	0.2716	0.4135	0.4902	0.6657	0.0900	1.3800
Male $(n = 2115)$	$0.3046 \pm 0.0070$	0.0990	0.1428	0.1767	0.2568	0.3552	0.4416	0.6032	0.0400	1.7700
Non-Hispanic white $(n = 578)$	$0.2988 \pm 0.0090$	0.0967	0.1382	0.1713	0.2530	0.3554	0.4409	0.5745	0.0400	1.4200
Non-Hispanic black ( $n = 726$ )	$0.3029 \pm 0.0084$	0.1018	0.1426	0.1801	0.2622	0.3475	0.4111	0.6062	0.0600	1.7700
Mexican American $(n = 710)$	$0.2992 \pm 0.0092$	0.0902	0.1334	0.1725	0.2460	0.3565	0.4290	0.5996	0.0600	1.4500
Other $(n = 101)$	$0.3566 \pm 0.0289$	0.1518	0.1800	0.2061	0.2896	0.4033	0.4666	0.6874	0.0900	1.3800
Female $(n = 2116)$	$0.2998 \pm 0.0068$	0.1102	0.1392	0.1739	0.2476	0.3547	0.4324	0.5969	0.0200	1.6200
Non-Hispanic white $(n = 580)$	$0.3027 \pm 0.0092$	0.1106	0.1400	0.1759	0.2489	0.3575	0.4270	0.5963	0.0700	1.5300
Non-Hispanic black ( $n = 716$ )	$0.2809 \pm 0.0063$	0.0960	0.1306	0.1626	0.2362	0.3443	0.3990	0.5750	0.0400	1.6200
Mexican American $(n = 723)$	$0.2937 \pm 0.0111$	0.1026	0.1397	0.1729	0.2493	0.3445	0.4134	0.6525	0.0200	1.3600
Other $(n = 97)$	$0.3143 \pm 0.0319$	0.1189	0.1474	0.1888	0.2567	0.4172	0.5133	0.5991	0.0900	0.8400
Age (y)										
6-7 (n = 839)	$0.3410 \pm 0.0116$	0.1240	0.1754	0.2062	0.2848	0.4199	0.4764	0.6633	0.0700	1.4500
$8-11 \ (n=1753)$	$0.3267 \pm 0.0076$	0.1193	0.1637	0.1986	0.2847	0.3891	0.4607	0.6485	0.0400	1.7700
$12-16 \ (n=1639)$	$0.2664 \pm 0.0078$	0.0908	0.1212	0.1492	0.2168	0.3075	0.3687	0.5443	0.0200	1.5300
Poverty-income ratio										
$\leq 1.3 \ (n = 2100)$	$0.2848 \pm 0.0081$	0.1020	0.1392	0.1685	0.2381	0.3338	0.4157	0.5584	0.0200	1.4500
>1.3-3.5 (n = 1704)	$0.3034 \pm 0.0074$	0.0995	0.1387	0.1724	0.2512	0.3665	0.4463	0.6017	0.0400	1.3800
>3.5 (n = 427)	$0.3262 \pm 0.0144$	0.1128	0.1530	0.1958	0.2746	0.3703	0.4520	0.6643	0.0600	1.7700
BMI (percentile)										
$\leq 15 \ (n = 378)$	$0.3286 \pm 0.0106$	0.1198	0.1767	0.2116	0.3019	0.3934	0.4589	0.5775	0.0400	1.3400
$16-84 \ (n=2645)$	$0.3185 \pm 0.0072$	0.1144	0.1520	0.1891	0.2634	0.3684	0.4562	0.6624	0.0600	1.7700
$85-94 \ (n=629)$	$0.2788 \pm 0.0117$	0.0958	0.1336	0.1634	0.2369	0.3384	0.4164	0.5117	0.0200	1.1600
$\geq$ 95 ( $n = 579$ )	$0.2173 \pm 0.0086$	0.0688	0.1002	0.1215	0.1753	0.2524	0.3275	0.4539	0.0400	1.3200

month that children and adolescents aged 12–16 y consumed fruit and vegetables was estimated from 18 questions on a food-frequency questionnaire.

A total of 4231 males and nonpregnant females aged 6-16 y with complete data on serum carotenoid concentrations, body mass index, and poverty-income ratio were used to examine the distributions of these compounds. Additional exclusions for missing values for independent variables reduced the number of participants for multiple linear regression models to 3828. Differences in carotenoid concentrations for continuous variables that were categorized into more than 2 levels were assessed with a test for linear trend. Differences in concentrations for categorical variables with 2 or more levels were tested with a t test or analysis of variance, respectively. To examine the independent relations between carotenoid concentrations and the study variables, we log transformed the carotenoid concentrations before running multiple linear regression analyses. Analyses were performed with the statistical software SUDAAN to account for the complex sampling design of the survey and produce valid variance estimates (28).

## RESULTS

The young males had slightly higher mean and median concentrations of all carotenoid concentrations than did the young females, but the differences were not significant (Tables 1-5). Age was inversely related to the concentrations of all carotenoids ( $P \le$ 0.001) except lycopene (P = 0.584). African American children and adolescents had the highest mean and median total serum carotenoid concentrations, and white children and adolescents had the lowest (P < 0.001). Of the 3 major race or ethnic groups, African American children and adolescents had the highest mean and median concentrations of lutein and zeaxanthin and lycopene, Mexican American children and adolescents had the highest concentrations of  $\alpha$ -carotene (but not significantly higher than those of white children and adolescents) and β-cryptoxanthin, and white children and adolescents had the highest concentrations of β-carotene although race or ethnicity was not significantly associated with β-carotene concentrations. The poverty-income ratio was positively associated with  $\alpha$ -carotene (P = 0.005) and  $\beta$ -carotene (P = 0.022) concentrations and inversely associated with lutein and zeaxanthin (P = 0.018) concentrations. Body mass index percentiles were inversely associated with the concentrations of all carotenoids ( $P \le 0.001$ ) except lycopene.

We also examined the distributions of carotenoid concentrations among 2554 children and adolescents after excluding from the full sample of 4231 those who reported having had a cold, flu, diarrhea, vomiting, pneumonia, or ear infection in the past 4 wk; those who were thought by the examining clinician to have a possible active infection; those with a C-reactive protein concentration



TABLE 3

Distribution of serum β-cryptoxanthin concentrations among children and adolescents aged 6–16 y who participated in the third National Health and Nutrition Examination Survey, 1988–1994

					Percentile					
	$\overline{x} \pm SE$	5th	15th	25th	50th	75th	85th	95th	Minimum	Maximum
	μmol/L				$\mu mol/L$				$\mu mol/L$	$\mu mol/L$
Total $(n = 4231)$	$0.1907 \pm 0.0026$	0.0659	0.0930	0.1114	0.1527	0.2298	0.2724	0.3799	0.0200	1.9500
Non-Hispanic white $(n = 1158)$	$0.1775 \pm 0.0035$	0.0611	0.0874	0.1041	0.1382	0.2108	0.2486	0.3506	0.0200	1.2700
Non-Hispanic black ( $n = 1442$ )	$0.2104 \pm 0.0044$	0.0811	0.1132	0.1323	0.1788	0.2443	0.2940	0.4076	0.0200	0.8700
Mexican American $(n = 1433)$	$0.2517 \pm 0.0062$	0.0915	0.1271	0.1476	0.2180	0.3037	0.3610	0.4951	0.0400	1.9500
Other $(n = 198)$	$0.2034 \pm 0.0097$	0.0720	0.0982	0.1187	0.1735	0.2416	0.3163	0.3658	0.0500	0.9600
Male $(n = 2115)$	$0.1923 \pm 0.0033$	0.0632	0.0937	0.1118	0.1534	0.2308	0.2823	0.3848	0.0200	1.9500
Non-Hispanic white $(n = 578)$	$0.1775 \pm 0.0045$	0.0577	0.0873	0.1040	0.1381	0.2112	0.2493	0.3474	0.0200	1.2700
Non-Hispanic black ( $n = 726$ )	$0.2139 \pm 0.0056$	0.0809	0.1139	0.1327	0.1835	0.2452	0.3023	0.4231	0.0200	0.8700
Mexican American $(n = 710)$	$0.2540 \pm 0.0080$	0.0891	0.1227	0.1460	0.2115	0.3137	0.3659	0.5152	0.0400	1.9500
Other $(n = 101)$	$0.2189 \pm 0.0112$	0.0853	0.1073	0.1405	0.1750	0.2666	0.3348	0.3962	0.0500	0.9200
Female ( $n = 2116$ )	$0.1890 \pm 0.0039$	0.0685	0.0922	0.1111	0.1519	0.2290	0.2636	0.3745	0.0500	0.9800
Non-Hispanic white $(n = 580)$	$0.1774 \pm 0.0047$	0.0645	0.0874	0.1042	0.1385	0.2101	0.2476	0.3565	0.0500	0.6300
Non-Hispanic black ( $n = 716$ )	$0.2067 \pm 0.0055$	0.0812	0.1125	0.1319	0.1743	0.2434	0.2863	0.3902	0.0500	0.7200
Mexican American $(n = 723)$	$0.2495 \pm 0.0078$	0.0939	0.1311	0.1491	0.2236	0.2939	0.3559	0.4568	0.0500	0.9800
Other $(n = 97)$	$0.1877 \pm 0.0129$	0.0684	0.0870	0.1096	0.1678	0.2202	0.2485	0.3422	0.0500	0.9600
Age (y)										
6-7 (n = 839)	$0.2110 \pm 0.0052$	0.0838	0.1103	0.1310	0.1796	0.2450	0.2918	0.3889	0.0500	1.0100
$8-11 \ (n=1753)$	$0.2027 \pm 0.0044$	0.0737	0.1016	0.1213	0.1691	0.2421	0.2848	0.4175	0.0200	1.9500
$12-16 \ (n=1639)$	$0.1725 \pm 0.0037$	0.0579	0.0818	0.0987	0.1352	0.1970	0.2474	0.3460	0.0400	1.2700
Poverty-income ratio										
$\leq 1.3 \ (n = 2100)$	$0.1943 \pm 0.0053$	0.0689	0.0943	0.1146	0.1579	0.2309	0.2888	0.3849	0.0500	1.0100
>1.3-3.5 ( $n=1704$ )	$0.1841 \pm 0.0032$	0.0645	0.0918	0.1079	0.1503	0.2217	0.2539	0.3501	0.0200	1.9500
>3.5 (n = 427)	$0.2007 \pm 0.0092$	0.0643	0.0950	0.1145	0.1512	0.2436	0.3149	0.4236	0.0400	1.2700
BMI (percentile)										
$\leq 15 \ (n = 378)$	$0.2142 \pm 0.0077$	0.0741	0.1119	0.1311	0.1904	0.2483	0.2982	0.3631	0.0200	1.9500
$16-84 \ (n=2645)$	$0.1985 \pm 0.0033$	0.0710	0.0973	0.1171	0.1606	0.2400	0.2840	0.3946	0.0200	1.2700
85–94 ( <i>n</i> = 629)	$0.1703 \pm 0.0054$	0.0661	0.0859	0.1006	0.1352	0.1896	0.2401	0.3624	0.0500	0.7800
$\geq 95 \ (n = 579)$	$0.1532 \pm 0.0054$	0.0499	0.0724	0.0924	0.1262	0.1677	0.2185	0.3099	0.0400	0.8500

> 10 mg/L; and those with liver enzymes > 2 times the upper normal limit. With few exceptions, the differences between the median concentrations of this sample and those of the full sample were < 5% (data not shown).

In multiple linear regression analyses of log-transformed carotenoid concentrations among children and adolescents aged 6-16 y that included age, sex, race or ethnicity, poverty-income ratio, body mass index status, HDL- and non-HDL-cholesterol concentrations, and C-reactive protein concentration, only HDLand non-HDL-cholesterol concentrations were directly related to all carotenoid concentrations (Table 6). Age and body mass index status were inversely related to the concentrations of all carotenoids except lycopene. African American children and adolescents had significantly lower α-carotene and significantly higher β-cryptoxanthin, lutein and zeaxanthin, and lycopene concentrations than did white children and adolescents. Mexican American children and adolescents had significantly higher α-carotene, β-cryptoxanthin, and lutein and zeaxanthin concentrations but significantly lower lycopene concentrations than did white children. The poverty-income ratio was directly associated with α-carotene concentrations. C-reactive protein concentrations were inversely related to β-carotene, lutein and zeaxanthin, and lycopene concentrations. Cotinine concentrations were inversely related to  $\alpha$ -carotene,  $\beta$ -carotene, and  $\beta$ -cryptoxanthin concentrations.

To further explore the associations between cotinine concentrations and carotenoid concentrations, we restricted analyses

to children with a cotinine concentration < 15 ng/mL, which is the concentration considered to separate people who smoke from those who are exposed to environmental tobacco smoke only (n = 3699). In multiple linear regression models with cotinine entered as a continuous variable, significant inverse associations were noted for  $\beta$ -carotene and  $\beta$ -cryptoxanthin concentrations ( $\alpha$ -carotene:  $\beta = -0.01734$ , P = 0.099;  $\beta$ -carotene:  $\beta = -0.02352$ , P < 0.001;  $\beta$ -cryptoxanthin:  $\beta = -0.02480$ , P = 0.002; lutein and zeaxanthin:  $\beta = 0.00699$ , P = 0.335; and lycopene:  $\beta = -0.0651$ , P = 0.348). Similar results were found when quartiles of cotinine concentration were entered in these models.

Information about fruit and vegetable intake was requested only from the children and adolescents aged 12–16 y. Using multiple linear regression models that included the same set of covariates listed in Table 6, as well as physical activity and fruit and vegetable intake (n=1415), we found significant positive associations between fruit and vegetable intake and the concentrations of all carotenoids except lycopene ( $\alpha$ -carotene:  $\beta=0.00532$ , P=0.007;  $\beta$ -carotene:  $\beta=0.00469$ , P<0.001;  $\beta$ -cryptoxanthin:  $\beta=0.00496$ , P<0.001; lutein and zeaxanthin:  $\beta=0.00304$ , P<0.001; and lycopene:  $\beta=-0.0032$ , P=0.667). Because tomatoes are a rich source of lycopene, we examined the association between the frequency of tomato consumption during the previous 30 d and lycopene concentrations (n=1427) and found no significant relations in univariate and multivariate linear regression models.



TABLE 4
Distribution of serum lutein and zeaxanthin concentrations among children and adolescents aged 6–16 y who participated in the third National Health and Nutrition Examination Survey, 1988–1994

					Percentile					
	$\overline{x} \pm SE$	5th	15th	25th	50th	75th	85th	95th	Minimum	Maximum
	μmol/L				μmol/L				μmol/L	μmol/L
Total $(n = 4231)$	$0.3122 \pm 0.0055$	0.1396	0.1837	0.2097	0.2801	0.3682	0.4143	0.5479	0.0700	1.7400
Non-Hispanic white $(n = 1158)$	$0.2911 \pm 0.0058$	0.1313	0.1758	0.1944	0.2586	0.3381	0.3912	0.5113	0.0700	1.0200
Non-Hispanic black ( $n = 1442$ )	$0.3894 \pm 0.0072$	0.1864	0.2387	0.2728	0.3565	0.4517	0.5176	0.6856	0.1100	1.7400
Mexican American $(n = 1433)$	$0.3294 \pm 0.0083$	0.1546	0.1970	0.2310	0.3000	0.3869	0.4543	0.5670	0.0900	0.9700
Other $(n = 198)$	$0.3318 \pm 0.0192$	0.1810	0.2140	0.2402	0.3107	0.3934	0.4421	0.5386	0.1100	0.8300
Male $(n = 2115)$	$0.3160 \pm 0.0054$	0.1391	0.1834	0.2087	0.2796	0.3742	0.4250	0.5841	0.0700	1.7400
Non-Hispanic white $(n = 578)$	$0.2933 \pm 0.0066$	0.1310	0.1750	0.1929	0.2567	0.3412	0.3939	0.5262	0.0700	1.0200
Non-Hispanic black ( $n = 726$ )	$0.3900 \pm 0.0078$	0.1818	0.2370	0.2721	0.3569	0.4474	0.5146	0.6918	0.1200	1.7400
Mexican American $(n = 710)$	$0.3376 \pm 0.0089$	0.1516	0.2042	0.2366	0.3020	0.3998	0.4745	0.5736	0.0900	0.9700
Other $(n = 101)$	$0.3568 \pm 0.0166$	0.1876	0.2174	0.2472	0.3236	0.4391	0.4818	0.5778	0.1100	0.8300
Female ( $n = 2116$ )	$0.3080 \pm 0.0071$	0.1404	0.1841	0.2108	0.2807	0.3612	0.4044	0.5295	0.0900	1.1600
Non-Hispanic white $(n = 580)$	$0.2886 \pm 0.0070$	0.1316	0.1767	0.1960	0.2622	0.3346	0.3859	0.4866	0.0900	0.9300
Non-Hispanic black ( $n = 716$ )	$0.3888 \pm 0.0086$	0.1928	0.2400	0.2736	0.3561	0.4558	0.5198	0.6673	0.1100	1.1600
Mexican American $(n = 723)$	$0.3213 \pm 0.0090$	0.1594	0.1910	0.2252	0.2971	0.3765	0.4215	0.5565	0.1100	0.8600
Other $(n = 97)$	$0.3065 \pm 0.0236$	0.1578	0.2025	0.2380	0.2825	0.3569	0.4035	0.4516	0.1200	0.5800
Age (y)										
6-7 (n = 839)	$0.3357 \pm 0.0075$	0.1777	0.2000	0.2384	0.3031	0.3958	0.4548	0.5752	0.1100	1.0500
$8-11 \ (n=1753)$	$0.3412 \pm 0.0072$	0.1684	0.2010	0.2441	0.3153	0.3940	0.4571	0.5937	0.0900	1.7400
12-16 (n = 1639)	$0.2783 \pm 0.0057$	0.1235	0.1649	0.1864	0.2477	0.3267	0.3784	0.4725	0.0700	1.1800
Poverty-income ratio										
$\leq 1.3 \ (n = 2100)$	$0.3295 \pm 0.0077$	0.1504	0.1902	0.2270	0.2944	0.3900	0.4518	0.5984	0.0900	1.7400
>1.3-3.5 ( $n=1704$ )	$0.3052 \pm 0.0055$	0.1340	0.1801	0.2039	0.2743	0.3603	0.4043	0.5330	0.0700	1.0700
>3.5 (n = 427)	$0.3025 \pm 0.0111$	0.1374	0.1840	0.2026	0.2719	0.3535	0.3980	0.5117	0.0900	0.9300
BMI (percentile)										
$\leq 15 \ (n = 378)$	$0.3350 \pm 0.0124$	0.1396	0.2029	0.2437	0.3131	0.4000	0.4360	0.5753	0.0900	0.9000
$16-84 \ (n=2645)$	$0.3164 \pm 0.0059$	0.1470	0.1866	0.2154	0.2846	0.3679	0.4162	0.5665	0.0700	1.2000
$85-94 \ (n = 629)$	$0.2970 \pm 0.0079$	0.1194	0.1752	0.1892	0.2690	0.3578	0.3990	0.5127	0.0900	1.7400
$\geq$ 95 (n = 579)	$0.2896 \pm 0.0082$	0.1251	0.1684	0.1902	0.2540	0.3379	0.3988	0.5234	0.0900	0.8300

# DISCUSSION

Carotenoids endow the plant world with much of its vibrancy. Fortunately, these compounds also have biological actions that may be important in maintaining health and staving off disease. Because little is known about the descriptive epidemiology of serum carotenoid concentrations in children and adolescents, we examined the serum concentrations of 5 carotenoids in a representative sample of US children and adolescents aged 6–16 y. The NHANES III data show that serum carotenoid concentrations are not uniformly distributed among children and adolescents. The highest total carotenoid concentrations occurred among African American children and adolescents, and overweight children and adolescents had the lowest concentrations. In general, the patterns among children and adolescents reported here corresponded reasonably well to those of the adults in this data set (22).

Because the carotenoid concentration distributions described in this article are the only national data to date, they could serve as reference ranges for US children and adolescents. Unfortunately, good dietary data for the younger participants were unavailable, which prevented us from examining distributions among children meeting current recommendations for fruit and vegetable intake. Examining the distributions of carotenoid concentrations among children eating sufficient quantities of fruit and vegetables would provide more optimal reference ranges.

Fruit and vegetables are the main sources of carotenoids, and it is not surprising that carotenoid concentrations were lowest in groups that are known to eat the least amount of fruit and vegetables.

In the 1989–1991 Continuing Surveys of Food Intakes by Individuals, age was inversely associated with fruit intake and directly associated with vegetable intake, sex and race or ethnicity were unrelated to fruit and vegetable intake, and socioeconomic status was directly associated with fruit intake but not vegetable intake among children and adolescents aged 2–18 y (29, 30). In the Nationwide Food Consumption Surveys of 1977–1978 and 1987–1988, fiber intake from fruit and vegetables was higher among young males than among young females, and age was directly related to vegetable intake but not fruit intake among children and adolescents aged 2–18 y (31). In a large study of children and adolescents aged 8–17 y, the sex and race or ethnicity patterns of fruit and vegetable intake varied geographically (32).

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Strauss (33) reported that concentrations of  $\alpha$ -carotene and  $\beta$ -carotene were lower among obese children and adolescents than among nonobese children and adolescents in NHANES III. Our results extend these observations to  $\beta$ -cryptoxanthin and lutein and zeaxanthin. Lycopene concentrations were not associated with body mass index, however. Although the fruit and vegetable intake of most children is less than the recommended intake, Strauss reported that obese and nonobese children and adolescents aged 12–18 y reported similar fruit and vegetable intake in NHANES III.

Studies of adults have shown relations between carotenoid concentrations, particularly  $\beta$ -carotene concentrations, and age, sex, socioeconomic status (education and income), marital status, smoking status, cholesterol concentrations, HDL-cholesterol concentrations, C-reactive protein concentrations, glucose tolerance



The American Journal of Clinical Nutrition

**TABLE 5**Distribution of serum lycopene concentrations among children and adolescents aged 6–16 y who participated in the third National Health and Nutrition Examination Survey, 1988–1994

					Percentile					
	$\overline{x} \pm SE$	5th	15th	25th	50th	75th	85th	95th	Minimum	Maximum
	μmol/L				μmol/L				μmol/L	μmol/L
Total $(n = 4231)$	$0.4545 \pm 0.0061$	0.1953	0.2608	0.3169	0.4202	0.5512	0.6263	0.7936	0.0200	1.7100
Non-Hispanic white $(n = 1158)$	$0.4472 \pm 0.0082$	0.1966	0.2584	0.3087	0.4114	0.5415	0.6211	0.7714	0.0200	1.4900
Non-Hispanic black ( $n = 1442$ )	$0.5140 \pm 0.0084$	0.2133	0.3087	0.3576	0.4760	0.6142	0.7087	0.9031	0.0700	1.7100
Mexican American $(n = 1433)$	$0.4063 \pm 0.0113$	0.1610	0.2212	0.2699	0.3704	0.4982	0.5679	0.7116	0.0400	1.1600
Other $(n = 198)$	$0.4582 \pm 0.0191$	0.2042	0.2689	0.3433	0.4295	0.5538	0.6064	0.7652	0.0900	1.3600
Male $(n = 2115)$	$0.4628 \pm 0.0097$	0.1968	0.2651	0.3269	0.4296	0.5606	0.6366	0.8097	0.0400	1.7100
Non-Hispanic white $(n = 578)$	$0.4563 \pm 0.0136$	0.1980	0.2604	0.3137	0.4232	0.5566	0.6326	0.8031	0.0400	1.1700
Non-Hispanic black ( $n = 726$ )	$0.5241 \pm 0.0103$	0.2240	0.3200	0.3747	0.4831	0.6161	0.7015	0.9086	0.0700	1.7100
Mexican American $(n = 710)$	$0.4197 \pm 0.0214$	0.1558	0.2295	0.2741	0.3840	0.5213	0.6000	0.7289	0.0700	1.1400
Other $(n = 101)$	$0.4556 \pm 0.0206$	0.1942	0.3189	0.3492	0.4258	0.4978	0.6078	0.7182	0.0900	1.0400
Female ( $n = 2116$ )	$0.4453 \pm 0.0058$	0.1928	0.2552	0.3088	0.4063	0.5415	0.6147	0.7807	0.0200	1.6600
Non-Hispanic white $(n = 580)$	$0.4368 \pm 0.0074$	0.1937	0.2560	0.3057	0.3987	0.5241	0.6087	0.7549	0.0200	1.4900
Non-Hispanic black ( $n = 716$ )	$0.5037 \pm 0.0107$	0.1991	0.3002	0.3450	0.4684	0.6113	0.7150	0.8899	0.1100	1.6600
Mexican American $(n = 723)$	$0.3929 \pm 0.0077$	0.1630	0.2094	0.2635	0.3579	0.4772	0.5419	0.6711	0.0400	1.1600
Other $(n = 97)$	$0.4608 \pm 0.0281$	0.2078	0.2410	0.3215	0.4242	0.5684	0.6055	0.8417	0.0900	1.3600
Age (y)										
$6-7 \ (n = 839)$	$0.4554 \pm 0.0128$	0.1671	0.2498	0.3152	0.4232	0.5563	0.6545	0.7793	0.0200	1.3600
$8-11 \ (n=1753)$	$0.4632 \pm 0.0063$	0.1972	0.2706	0.3336	0.4296	0.5562	0.6254	0.8142	0.0400	1.7100
$12-16 \ (n=1639)$	$0.4466 \pm 0.0097$	0.2000	0.2557	0.3040	0.4093	0.5446	0.6196	0.7802	0.0400	1.4900
Poverty-income ratio										
$\leq 1.3 \ (n = 2100)$	$0.4470 \pm 0.0075$	0.1916	0.2605	0.3182	0.4139	0.5289	0.6085	0.7999	0.0400	1.7100
>1.3-3.5 ( $n = 1704$ )	$0.4702 \pm 0.0096$	0.2023	0.2683	0.3253	0.4382	0.5703	0.6523	0.8231	0.0400	1.5600
>3.5 (n = 427)	$0.4286 \pm 0.0125$	0.1794	0.2375	0.3004	0.3920	0.5318	0.6097	0.7345	0.0200	0.9900
BMI (percentile)										
$\leq 15 \ (n = 378)$	$0.4486 \pm 0.0140$	0.1901	0.2539	0.3067	0.4146	0.5670	0.6057	0.7367	0.0400	1.6600
$16-84 \ (n=2645)$	$0.4583 \pm 0.0069$	0.1938	0.2600	0.3176	0.4237	0.5592	0.6430	0.8044	0.0200	1.5600
$85-94 \ (n=629)$	$0.4551 \pm 0.0136$	0.2069	0.2655	0.3255	0.4187	0.5438	0.6114	0.8035	0.0400	1.7100
$\geq$ 95 (n = 579)	$0.4355 \pm 0.0114$	0.1996	0.2634	0.3144	0.4143	0.5010	0.5909	0.7542	0.0700	1.4000

status, insulin resistance, alcohol use, body mass index, fat-free mass, physical activity, fruit and vegetable intake, and use of dietary supplements (15, 19, 22, 34-69). Little is known about such relations in children and adolescents, however. In a study of French children and adolescents aged 10-15 y (263 males and 246 females), plasma cholesterol concentrations were positively related and triacylglycerol concentrations and body fat were inversely related to plasma β-carotene concentrations (70). α-Carotene, β-carotene, β-cryptoxanthin, lutein, and lycopene concentrations were examined in 2 small studies of 10 and 50 children, respectively (71, 72). Among 97 children aged 6-10 y in Georgia, the sum of the  $\alpha$ -carotene,  $\beta$ -carotene, and  $\beta$ -cryptoxanthin concentrations was higher among the girls than among the boys, was higher among the African American children than among the white children, and increased with age (73). Among 467 Australian children, the mean B-carotene concentration was  $0.30 \mu mol/L$ , and  $\beta$ -carotene concentrations were similar in the boys and the girls (74). In a study of 70 children, African American children had higher median concentrations of β-carotene and lycopene than did white children, but only the difference in lycopene concentrations was significant (75). In an intervention study of 41 Chinese children, increased vegetable consumption favorably affected serum concentrations of several carotenoids (76). Very recently, a study of 285 children and adolescents in 3 US cities found significant associations between carotenoid concentrations and race or ethnicity, obesity, and dietary intakes that were consistent with our findings (77). The NHANES III data showed that carotenoid concentrations were related to age, race or ethnicity, poverty-income ratio, body mass index, serum lipid concentrations, C-reactive protein concentrations, cotinine concentrations, and fruit and vegetable intake in children and adolescents.

Several studies in adults have shown inverse associations between circulating concentrations of carotenoids and markers of inflammation such as C-reactive protein concentrations (68, 78–84). We believe that our results are the first to show this inverse association in a representative sample of US children and adolescents. In addition, concentrations of serum retinol and C-reactive protein are also inversely related (85). Although the directionality of associations in cross-sectional studies is difficult to discern, the more likely explanation for our findings is that underlying sources of inflammation, represented by elevated C-reactive protein concentrations, result in decreased concentrations of various circulating antioxidants including carotenoids.

The importance for children and adolescents of having adequate body stores of carotenoids has not been shown. In adults, however, inadequate intakes or concentrations of carotenoids have been linked to increased all-cause mortality and risk of various chronic conditions. Because many of these conditions have their roots in childhood, it seems reasonable to assume that adequate carotenoid concentrations in youth, achieved mainly by sufficient consumption of fruit and vegetables, may promote better health

TABLE 6

Multiple linear regression analyses of log-transformed serum carotenoid concentrations among 3828 children and adolescents aged 6–16 y who participated in the third National Health and Nutrition Examination Survey, 1988–1994

	α-Carotene	ne ne	β-Carotene	ene	β-Cryptoxanthin	canthin	Lutein and zeaxanthin	anthin	Lycopene	ne	Total	
	$\beta \pm SE$	P Wald $\chi^{2}$	/ β ± SE	P Wald $\chi^{2}$	β ± SE	P Wald $\chi^{2}$	$\beta\pm SE$	P Wald $\chi^{2/l}$	$\beta \pm SE$	P Wald $\chi^{2,1}$	$\beta \pm SE$	P Wald $\chi^{2}$
Age (y)	$-0.04703 \pm 0.00633 < 0.001$		$-0.03746 \pm 0.00485$ <	<0.001	$-0.02615 \pm 0.00415 < 0.001$		$-0.02505 \pm 0.00361 < 0.001$	101	$0.00403 \pm 0.00390$	0.306	$-0.01905 \pm 0.00304 < 0.001$	0.001
Sex												
F (reference)												
M	$0.01065 \pm 0.03578  0.767$	0.767	$0.02141 \pm 0.02759$	0.441	$0.01224 \pm 0.02485$	0.625	$0.02524 \pm 0.02107  0.237$	37	$0.05817 \pm 0.02594$	0.029	$0.03421 \pm 0.01969$	0.089
Race or ethnicity		< 0.001		0.034		< 0.001		< 0.001		< 0.001		< 0.001
White (reference)												
African American	$-0.24840 \pm 0.04887 < 0.001$		$-0.04135 \pm 0.03328$	0.220	$0.17264 \pm 0.03445 < 0.001$	< 0.001	$0.24986 \pm 0.02383 < 0.001$	101	$0.08305 \pm 0.02872$	0.006	$0.09837 \pm 0.02187 < 0.001$	0.001
Mexican American	$0.18504 \pm 0.04873 < 0.001$	:0.001	$0.02512 \pm 0.03478$	0.474	$0.38720 \pm 0.02989 < 0.001$	< 0.001	$0.13375 \pm 0.02593 < 0.001$		$-0.11157 \pm 0.03198$	0.001	$0.07660 \pm 0.02528$	0.004
Poverty-income ratio	$0.08154 \pm 0.01686 < 0.001$	:0.001	$0.02993 \pm 0.01267$	0.022	$0.02741 \pm 0.01491  0.072$	0.072	$0.00410 \pm 0.01066$ 0.702	•	$-0.01070 \pm 0.01051$	0.314	$0.01521 \pm 0.00894$	0.095
BMI (percentile)		< 0.001		<0.001		<0.001		< 0.001		0.287		< 0.001
≤15	$0.03244 \pm 0.05147$ 0.531	0.531	$0.01411 \pm 0.04001$	0.726	$0.03310 \pm 0.04791$ 0.493		$0.02248 \pm 0.03323$ $0.502$		$-0.04835 \pm 0.03889$	ı	$-0.00882 \pm 0.02663$	0.742
16-84 (reference)												
85–94	$-0.05872 \pm 0.06011$ 0.333		$-0.07327 \pm 0.04150$	0.084	$-0.12470 \pm 0.03381$ 0.001		$-0.05444 \pm 0.02339  0.024$		$-0.00341 \pm 0.02632$	1	$-0.05422 \pm 0.02516$	0.036
≥95	$-0.40856 \pm 0.06382 < 0.001$		$-0.36092 \pm 0.03881$ <	< 0.001	$-0.29122 \pm 0.03659 < 0.001$		$-0.12093 \pm 0.02775 < 0.001$		$-0.04782 \pm 0.03359$	ı	$-0.18732 \pm 0.02423 < 0.001$	0.001
Serum HDL cholesterol	$0.36716 \pm 0.07520 < 0.001$	:0.001	$0.32565 \pm 0.05310$	< 0.001	$0.30671 \pm 0.05116 < 0.001$		$0.32303 \pm 0.02908 < 0.001$	101	$0.31865 \pm 0.04235 < 0.001$	:0.001	$0.32189 \pm 0.03344 < 0.001$	0.001
(mmol/L)												
Serum non-HDL												
cholesterol (mmol/L)	$0.15523 \pm 0.02511 < 0.001$	:0.001	$0.15522 \pm 0.02253 <$	< 0.001	$0.14440 \pm 0.01665 < 0.001$	< 0.001	$0.15695 \pm 0.01350 < 0.001$	101	$0.21460 \pm 0.01541 < 0.001$	:0.001	$0.17760 \pm 0.01394 < 0.001$	0.001
C-reactive protein (mg/L)												
≤2.1 (reference)												
>2.1	$-0.00957 \pm 0.18521$	0.959	$-0.46101 \pm 0.09611$ <	< 0.001	$-0.09654 \pm 0.08553$ 0.265		$-0.23134 \pm 0.04114 < 0.001$		$-0.18302 \pm 0.07790$	0.023	$-0.23117 \pm 0.02740 < 0.001$	0.001
Serum cotinine (ng/ml) $-0.00127 \pm 0.00038$	$-0.00127 \pm 0.00038$	0.002	$-0.00103 \pm 0.00025$ <	<0.001	$-0.00113 \pm 0.00024 < 0.001$		$-0.00034 \pm 0.00021$ 0.107	0.7	$0.00001 \pm 0.00027$	0.972	$-0.00049 \pm 0.00019$	0.011

 $^{\prime}$  P value represents the Wald  $\chi^2$  for the entire categorical variable.

in adulthood. The unique results of the present study should provide researchers and clinicians with a better understanding of the distributions and sociodemographic patterns of serum carotenoid concentrations in US children and adolescents. Furthermore, the results of the present study enabled us to identify several determinants of serum carotenoid concentrations, such as excess weight, exposure to environmental tobacco smoke, and inadequate fruit and vegetable consumption, that are amenable to clinical and public health interventions.

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826 FORD ET AL

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