Serum Concentrations of Retinol, α-Tocopherol and the Carotenoids Are Influenced by Diet, Race and Obesity in a Sample of Healthy Adolescents

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ABSTRACT An important part of understanding the functions of vitamin A, vitamin E and the carotenoids in nutritional status assessment, health promotion and disease prevention is knowledge of factors that influence their distribution in human tissues. Our objective was to examine serum concentrations of these nutrients and compounds in a sample of 285 healthy participants, 12–17 y old, from three U.S. cities. Pearson correlations between diet measured with a food frequency questionnaire and serum nutrient concentrations among these adolescents (adjusted for total serum cholesterol, age, sex, race and body mass index) were as follows: retinol, 0.23; α-tocopherol, 0.16; α-carotene, 0.31; β-carotene, 0.15; β-cryptoxanthin, 0.38; lycopene, 0.08; and lutein + zeaxanthin, 0.25. Multivariate linear regression modeled associations of demographic, dietary and physiologic variables with serum concentrations of these nutrients. African-American participants had significantly lower concentrations of serum retinol (P < 0.001), α-tocopherol (P < 0.01) and α-carotene (P < 0.02), but higher concentrations of lutein + zeaxanthin (P = 0.001) compared with Caucasians. Obese participants had serum nutrient concentrations that were 2–10% (P < 0.05) lower than normal weight participants. Dietary intake was a significant predictor of all serum analytes (P < 0.01) except lycopene. These models explained 20% of the variability in serum retinol, 28% of the variability in serum α-tocopherol, and 14–24% of the variability in serum carotenoids. J. Nutr. 131: 2184–2191, 2001.

KEY WORDS: • retinol • α-tocopherol • carotenoids • humans • adolescents • dietary assessment

Epidemiologic studies have consistently shown that higher intakes of vitamin A, vitamin E and the carotenoids are associated with reduced risk of several chronic diseases, including cardiovascular disease, age-related macular degeneration and some cancers (1–4). These micronutrients exhibit multiple biological actions that may protect against disease. For example, vitamin E is a chain breaking antioxidant that protects cell membranes from damage caused by lipid peroxidation and also inhibits cell proliferation, platelet adhesion and formation of N-nitroso compounds (5). Both the carotenoids and vitamin E stimulate cell-mediated and humoral immunity (6,7). Retinol and its precursors (e.g., α-carotene and β-carotene) are essential for differentiation of epithelial cells and maintenance of cell signaling and communication.

Other potential benefits of these nutrients have been reviewed previously (4,8–13).

An important part of understanding the role of vitamin A, vitamin E and the carotenoids in nutritional status assessment and their function in disease prevention is knowledge of factors that influence their absorption and distribution in human tissues. Several published reports have identified dietary, demographic and lifestyle variables that affect serum concentrations of these nutrients in adults (14–18). However, there are fewer data of this nature published from child and adolescent populations. Four reports have used National Health and Nutrition Examination Survey (NHANES) II and HHANES data to examine relationships of age or race/ethnicity with serum concentrations of vitamins A and E in children and adolescents (19–22) and one investigation using NHANES III data showed that obese, 6- to 19-y-old children had significantly lower serum concentrations of α-tocopherol and β-car-
otene than nonobese children (23). Other studies have fo-

cused on the risk of inadequate vitamin E, vitamin A or
carotenoid status among newborn infants (24), children with
dehnatic diseases (e.g., cystic fibrosis, malaria, renal disease)
and low income or malnourished children (25–27).

In 2000, the Panel on Dietary Antioxidants and Related
Compounds (National Academy of Sciences, Institute of Medi-
cine) published NHANES III (1998–1994) data, which pro-
vided distributions of serum vitamin E and the carotenoids
among a representative sample of the U. S. population, in-
cluding adolescents (9). The Panel on Micronutrients released
similar data for serum vitamin A (retinol) in 2001 (13). These
NHANES III data are important because they provide current
reference values for this group of important nutrients, but they
do not include any information on factors that may influence
these distributions, such as diet or other physiologic or lifestyle
variables. There are at least two reasons that identification of
determinants of these serum nutrient concentrations in adoles-
cents would be of interest. First, these data would be published.
First, this information would provide additional details about
nutritional status in this population subgroup and would iden-
tify health or lifestyle factors (e.g., obesity) that might place
individuals at risk of nutrient inadequacy. Second, scientists
conducting research to investigate associations of serum vita-
m E, vitamin A and the carotenoids with growth, develop-
ment and other health outcomes among adolescents must be
aware of these potentially confounding variables. These influ-
encing factors should be carefully considered during analysis
and interpretation of data and subsequent conclusions about
diet/health relationships. To investigate these issues, we con-
ducted a comprehensive examination of serum concentrations
of retinol, a-tocopherol and the carotenoids among a group of
healthy U. S. adolescents who were participants in a study of
diet and health. Specifically, we examined associations of age,
sex, race, body mass index (BMI) and other physiologic and
lifestyle variables, together with usual dietary intake of vita-
m E, vitamin A, vitamin E, a-carotene, b-carotene, a-\(\beta\)-cryptoxanthin,
lycopene and lutein + zeaxanthin with their respective serum
concentrations.

SUBJECTS AND METHODS

Study design and subjects. Data are from the Olestra Post-
Marketing Surveillance Study (OPMSS); this project was designed to
monitor the adoption of olestra-containing foods and to examine
associations of olestra consumption with serum concentrations of
fat-soluble vitamins and carotenoids in representative samples of the
U. S. population. The design of OPMSS offers a unique opportunity
to examine a large number of serum nutrients and their correlates in the
diets of population subgroups, such as adolescents. Details of the design of OPMSS and baseline results of adults in the study have been
reported previously (15,28,29). Briefly, the first phase of OPMSS is a
list-assisted random-digit-dial telephone survey conducted by
WESTAT, Inc. (Rockville, MD). Adults 18 y of age and older in four
U. S. cities (Indianapolis, Baltimore, Minneapolis and San Diego)
and their surrounding suburbs and unincorporated areas were re-
cruited to complete a telephone survey with a focus on beliefs and
attitudes about health and usual dietary intake of fruit, vegetables and
sauory snacks. A random sample of participants who completed the
telephone survey was invited to attend a clinic visit. If the household
contained a child 7–17 y old, then the child was invited to join the
study. In households with more than one child, the one with the
closest birthday to the phone call date was selected as the participant.
The participation rate for the data presented in this report (number of participants 12–17 y old who completed clinic visits divided by the
number households with completed telephone interviews and at least
one adolescent child) was 63.8%. Individuals with medical condi-
tions (e.g., cystic fibrosis, kidney disease requiring dialysis, short
bowel syndrome) that would interfere with accurate measurements of the
serum analytes under investigation were excluded (30). Clinic
visits were conducted between October 1997 and April 1998, before
the introduction of olestra products in Baltimore, Minneapolis and
San Diego. Because slightly different data collection instruments were
used at the Indianapolis clinic, those results are not included in this
report. The institutional review boards of all the participating insti-
tutions approved procedures for this study, and written informed
consent was obtained from all participants and a consenting adult.

Measures. All study participants completed a self-administered
122-item food frequency questionnaire (FFQ) at home, which was
reviewed for completeness by staff during the clinic visit. The refer-
ence period for the FFQ was in the past month. This FFQ is divided
into three sections: 1) adjustment questions; 2) foods and food groups;
and 3) summary questions. The 19 adjustment questions permit
refined analysis of fat intake by asking detailed questions about foods
preparation practices and fats added in cooking and at the table. The
main section of the FFQ is 122 foods or food groups, with questions
on the usual frequency of intake (from “never or less than once a
month” to “2+ per day” for foods and “6+ per day” for beverages and
portion size (small, medium or large compared with the stated me-
dium portion size). These line items include 13 fruit and fruit juice
line items, 19 vegetable and vegetable juice line items and 12 mixed
foods with vegetables (e.g., pizza, stew) line items. Finally, the four
summary questions ask about usual intake of fruits, vegetables and fat
added to foods and used in cooking (31). The nutrient database for
the FFQ was derived from the University of Minnesota Nutrition
Coordinating Center (NCC) nutrient database (32) and included the
most recent U. S. Department of Agriculture-NCC Carotenoid Data-
base for U. S. Foods (33). This carotenoid database is an important
resource for investigators conducting research on carotenoids because
it contains carotenoid content for 215 foods, including mixed dishes
(e.g., pizza and stew) (33). Our approach to analyzing food frequency
questionnaires and the algorithms for analysis are described in details
elsewhere (34).

Data on vitamin supplement use over the past month were ob-
tained from all participants, using a validated inventory procedure
(35) that was modified to collect detailed dosage information on
vitamin A, vitamin E and b-carotene (the only carotenoid available in
supplements at the time). Total micronutrient intakes used in
analyses included sources from all supplements plus food. Trained
staff measured height and weight of all participants using a standard-
zeized protocol and BMI was calculated as weight (kg)/height (m)2.
Staff members also collected information on medical history, age, sex,
race/ethnicity, household income and alcohol and tobacco use.

Blood collection and processing. Phlebotomists collected non-
fasting blood samples by venipuncture into 13-mL serum separating
tubes, which were protected from heat and light throughout handling
and processing. Serum was stored at –20°C for no longer than four
days, shipped to the study’s Coordinating Center on dry ice and then
stored at –70°C until analysis. All assays were conducted at Quintiles
Laboratories (Atlanta, GA). Details on laboratory analysis and pro-
cedures are given elsewhere (15). Serum retinol, a-tocopherol and
the carotenoids were analyzed using reversed-phase HPLC method-
ology. The inter assay coefficients of variation for individual analytes
ranged from 1.9% to 9.8%. Total serum cholesterol was analyzed
using enzymatic methods. Precision was evaluated using packaged
reagents, pooled human serum and control serum; both interassay
precision and bias were <3%.

Statistical analysis. We excluded from analyses participants who
were pregnant (n = 2) at the time of the clinic visit because of the
profound changes in serum nutrient concentrations that can occur
during pregnancy (36). For participants whose serum values were
undetectable by laboratory methods (10% undetectable for \(\alpha\)-caro-
tene, <1% undetectable for all other carotenoids and \(\alpha\)-tocopherol),
we replaced the missing values with the midpoint between zero and
the laboratory’s minimum detectable value. The minimum detectable
concentrations were as follows (\(\mu\)mol/L): \(\alpha\)-tocopherol, 1.163; \(\alpha\)-caro-
tene, 0.003; \(\beta\)-carotene, \(\beta\)-\(\alpha\)-cryptoxanthin and lycopene, 0.011; lu-
tein, 0.004; and zeaxanthin, 0.01. The interpretation of data and our
conclusions were not changed by these analytic decisions. We ex-
cluded from analysis data from 34 (10.6%) FFQ because the energy
TABLE 1
Demographic characteristics of adolescents in three U.S. cities (n = 285)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>153</td>
<td>53.7</td>
</tr>
<tr>
<td>Female</td>
<td>132</td>
<td>46.3</td>
</tr>
<tr>
<td>Age, y (mean ± sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>14.7</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>162</td>
<td>57.7</td>
</tr>
<tr>
<td>African-American</td>
<td>64</td>
<td>22.8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>33</td>
<td>11.7</td>
</tr>
<tr>
<td>Other1</td>
<td>22</td>
<td>7.8</td>
</tr>
<tr>
<td>Yearly household income,1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25,000</td>
<td>39</td>
<td>14.0</td>
</tr>
<tr>
<td>25–50,000</td>
<td>120</td>
<td>43.0</td>
</tr>
<tr>
<td>&gt;50,000</td>
<td>120</td>
<td>43.0</td>
</tr>
<tr>
<td>Geographic location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baltimore</td>
<td>107</td>
<td>37.5</td>
</tr>
<tr>
<td>Minneapolis</td>
<td>102</td>
<td>35.8</td>
</tr>
<tr>
<td>San Diego</td>
<td>76</td>
<td>26.7</td>
</tr>
<tr>
<td>BMI,3 kg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>190</td>
<td>66.7</td>
</tr>
<tr>
<td>Overweight</td>
<td>56</td>
<td>19.6</td>
</tr>
<tr>
<td>Obese</td>
<td>39</td>
<td>13.7</td>
</tr>
</tbody>
</table>

1 Cell sizes may vary slightly due to missing values.
2 Includes Asian-American, Native American and mixed race.
3 BMI (kg/m²): male: normal < 23.2; overweight 23.2–27.2; obese ≥ 27.2 female: normal < 23.9; overweight 23.9–28.1; obese ≥ 28.1.

RESULTS
Table 1 gives the demographic characteristics of the study population. Fifty-four percent of participants were male and the mean age was 14 3/4 y of age. Twenty-three percent of participants were African-American, nearly 12% were Hispanic, and 7.8% were Asian-American or of mixed-race/ethnicity. The mean BMI was 22.7 (sd ± 4.5); 19.6% of participants were overweight and nearly 14% were obese, which was defined as the 85th and 95th percentiles, respectively, of the NHANES II distribution (38,39). Twenty-four percent of participants used a dietary supplement, such as multivitamins, at least three times per week. Eight percent were smokers and 20% reported use of alcohol within the previous month (data not shown). On average, these adolescents ate two servings of fruit and vegetables per day. The estimated mean intake of vitamin A was 960 (sd ± 7) RE/d for females, and estimated mean vitamin intakes were 10 (sd ± 7) for males and 752 (sd ± 517) RE/d for females, and estimated mean vitamin intakes were 10 (sd ± 7) and 8 (sd ± 7) mg/dL, respectively (data not shown). These estimated dietary intakes are very close to the RDA for vitamin A (13), but 50–67% below the RDA for vitamin E (9). We note the wide variability in the estimated intakes of these vitamins, indicating that some participants in our study may have had marginal nutrient intakes.

TABLE 2
Distribution of serum cholesterol, retinol, tocopherol and carotenoid concentrations in adolescents aged 12–17 y

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Mean1 ± SD</th>
<th>Percentiles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol, mmol/L</td>
<td>2.91 ± 0.74</td>
<td>10% 50% 90%</td>
</tr>
<tr>
<td>Retinol, µmol/L</td>
<td>1.06 ± 0.21</td>
<td>10% 50% 90%</td>
</tr>
<tr>
<td>α-Tocopherol, µmol/L</td>
<td>12.76 ± 2.75</td>
<td>10% 50% 90%</td>
</tr>
<tr>
<td>β-Carotene, µmol/L</td>
<td>0.08 ± 0.20</td>
<td>10% 50% 90%</td>
</tr>
<tr>
<td>β-Cryptoxanthin, µmol/L</td>
<td>0.06 ± 0.12</td>
<td>10% 50% 90%</td>
</tr>
<tr>
<td>Lutein, µmol/L</td>
<td>0.08 ± 0.14</td>
<td>10% 50% 90%</td>
</tr>
<tr>
<td>Lycopene, µmol/L</td>
<td>0.03 ± 0.03</td>
<td>10% 50% 90%</td>
</tr>
<tr>
<td>Zeaxanthin, µmol/L</td>
<td>0.03 ± 0.06</td>
<td>10% 50% 90%</td>
</tr>
</tbody>
</table>

1 Geometric mean.


TABLE 3

Pearson correlation coefficients between serum retinol, α-tocopherol and carotenoid concentrations and respective dietary intakes in healthy adolescents aged 12–17 y (n = 285)

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Crude1</th>
<th>Adjusted2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinol</td>
<td>0.24***</td>
<td>0.23***</td>
</tr>
<tr>
<td>α-Tocopherol</td>
<td>0.12*</td>
<td>0.16**</td>
</tr>
<tr>
<td>α-Carotene</td>
<td>0.27</td>
<td>0.31**</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>0.14*</td>
<td>0.15*</td>
</tr>
<tr>
<td>β-Cryptoxanthin</td>
<td>0.36***</td>
<td>0.38***</td>
</tr>
<tr>
<td>Lycopene</td>
<td>0.05</td>
<td>0.08</td>
</tr>
<tr>
<td>Lutein-zeaxanthin</td>
<td>0.18**</td>
<td>0.25***</td>
</tr>
</tbody>
</table>

1 Correlations between serum nutrient concentrations and their respective dietary intakes.
2 Correlations are adjusted for serum cholesterol, age, sex, race, energy intake and BMI.

The distributions of serum concentrations of cholesterol, retinol, α-tocopherol and six carotenoids in males and females in the study sample are given in Table 2. There were no differences in mean concentrations of any nutrient by sex. Pearson correlations between dietary intake of each nutrient and the corresponding serum concentrations in adolescents are shown in Table 3. There were modest associations of dietary vitamin A, α-carotene and β-cryptoxanthin with their serum concentrations (r = 0.24, 0.27 and 0.36, respectively, all P < 0.001), which changed only slightly after adjustment for factors known to affect serum concentrations of these nutrients, including total serum cholesterol concentration, age, race, energy intake and BMI. The crude correlation of diet with serum lutein-zeaxanthin was 0.18, which improved to 0.25 (P < 0.01) after the statistical adjustments. There were weak associations of dietary α-tocopherol (r = 0.16, P < 0.05) and β-carotene (r = 0.15, P < 0.05) with their respective adjusted serum concentrations, and no association of dietary and serum lycopene even after adjustment for confounding variables (r = 0.08, P = 0.34).

Table 4 gives results from the multivariate regression analyses predicting serum concentrations of retinol, α-tocopherol and the carotenoids. The determinants and the strength of association of the predictor variables varied across the serum nutrients. Serum cholesterol concentration was a consistent positive predictor of all analytes examined. For each 10% increase in serum cholesterol, there was a statistically significant increase in the serum nutrient concentrations, which ranged from 0.3% for α-carotene to 4.1% for α-tocopherol. Dietary intake was positively associated with serum concentrations of all nutrients except lycopene, but the magnitude varied across nutrients. For example, for each 10% increase in dietary vitamin A, vitamin E, α-carotene, β-carotene, β-cryptoxanthin and lutein + zeaxanthin, there was a 0.08–0.6% increase in the serum concentrations. Associations of percentage of energy from fat with serum analytes were inconsistent; percentage of energy from fat was inversely associated with serum concentrations of retinol and α-tocopherol but was not predictive of any serum carotenoids.

Race had independent effects on serum nutrient concentrations. Participants who were African-American had serum retinol, α-tocopherol and α-carotene concentrations that were 2–11% lower than Caucasian participants, but lutein + zeaxanthin concentrations were 4% higher in African-Americans compared with Caucasians. Asian-American, Hispanic and mixed race participants had α-tocopherol concentrations that were ~7% lower than Caucasians. In a univariate analysis, we found that African-American participants had significant lower intakes of vitamin A, α-carotene, β-cryptoxanthin and lycopene compared with Caucasians (data not shown), which may partly explain these findings. Obese participants had consistently lower serum concentrations of all nutrients examined, except serum retinol and lutein-zeaxanthin. For example, serum α-tocopherol concentration was 10% lower, and serum carotenoid concentrations, with the exception of lutein-zeaxanthin, were 2–9% lower among obese participants compared with normal weight participants. Univariate analyses showed that obese participants consumed significantly fewer fruits and vegetables (and their associated nutrients) per day compared with normal weight participants (data not shown). Age had inconsistent effects on serum nutrients. For each year increase in age, there was a 1.5%, 0.2% and 0.3% increase in serum retinol, α-tocopherol and α-carotene concentration, respectively; a 0.2% decrease per year for β-carotene, β-cryptoxanthin and lycopene; and a 0.3% decrease per year for serum lutein + zeaxanthin. These multivariate models explained 20% of the variance in serum retinol, 28% of the variance in serum α-tocopherol and 14–24% of the variance in serum carotenoid concentrations.

**DISCUSSION**

In this study of healthy adolescents from three U. S. cities, the distributions of serum retinol, α-tocopherol and the carotenoids were very similar to results from NHANES III, a large nationally representative sample (9,13). The mean concentrations of serum retinol in our sample were slightly lower than those for males and females aged 14–18 y in NHANES III. We note, however, that serum retinol for NHANES III participants aged 9–13 y was 1.43 μmol/L for males and 1.40 μmol/L for females; the lower portion of our age distribution overlaps with the NHANES III 9- to 13-y-old group (13), which may explain the slightly lower mean values for our entire sample. Similar age-related changes in serum retinol concentrations were recognized in NHANES II (19). Mean serum β-carotene and all other carotenoid concentrations in our sample were very similar to those for males and females aged 14–18 y in NHANES III. Overall, we found that the predominant carotenoids in our sample of healthy adolescents were serum lycopene and β-carotene. Apgar and colleagues (40) observed that the predominant circulating carotenoids were lutein and β-carotene among 493 healthy children in Belize. Variations in dietary patterns, such as higher consumption of lycopene-rich condiments and pizza, among American children, may explain these differences.

The correlations between dietary intake of vitamin A, vitamin E and the carotenoids, as measured by the food frequency questionnaire, and the serum nutrient concentrations, differed somewhat from previously published reports in adults. For example, in the Framingham Study, adjusted correlations of diet and serum carotenoids ranged from 0.14 to 0.45 (16). The Nurses’ Health Study and the Health Professionals’ Follow-Up Study reported diet-serum carotenoid correlations of 0.21–0.48 for women and 0.35–0.47 for men (41), compared with our reported range of 0.08–0.38. We found a very weak correlation between diet and serum lycopene (0.08), which is
similar to results from Campbell et al. (42), who found a diet-serum lycopene correlation of 0.11, but is lower than the 0.20 reported by Casso et al. (43). We propose two reasons for this weak dietary lycopene-serum association. First, the primary sources of dietary lycopene are tomatoes and tomato products, such as catsup, tomato sauce and salsa. Because catsup may be a substantial source of lycopene in the adolescent diet, and there is no specific line item for catsup on the food frequency questionnaire, dietary intake of lycopene is likely measured with error, thus reducing the ability to explain variance in serum lycopene. Second, reliable estimates of lycopene content of foods are limited. Although the U. S. Department of Agriculture-NCC Carotenoid Database for U. S. Foods contains recent food carotenoid data for 215 foods (including mixed foods), only 2% of the foods analyzed have been given a confidence code of A, meaning the user can have considerable confidence in the mean carotenoid estimates for that food (33). Moreover, data for many of the carotenoids are incomplete; there are lycopene values for 79 foods, and zeaxanthin values for only 22 foods (33). Correlates of dietary and serum carotenoids will improve as the U. S. Department of Agriculture-NCC Carotenoid Database continues their extensive and ongoing research program and adds new and improved values to the dietary database. Results from the Women’s Health Initiative were very similar to our findings for serum α-tocopherol. The partial correlation for diet and serum α-tocopherol was only 0.11 among nonsupplement users in a sample of 1047 women drawn from this large study of diet and health (44), which is similar in magnitude to our adjusted correlation of 0.16. These weak correlations are likely due to the fact that only 24% of the adolescents in our study used vitamin E-containing multivitamins and none used single supplements; these dietary supplements are very strong predictors of circulating α-tocopherol (15,44).

The value of using serum analytes as nutritional biomarkers depends in part on an understanding of physiologic and lifestyle factors that influence their circulating concentrations (15). An interesting finding from this study was that the determinants of serum retinol, α-tocopherol and the carotenoids among adolescents were very similar to the factors that influence serum concentrations of these nutrients in adults. The strongest and most consistent predictor of all serum fat-soluble nutrients was serum cholesterol, a finding that agrees with results from studies conducted in adults (15,17,44) and one study of 309 French children aged 10–15 y (45). Because the carotenoids and vitamin E are carried by the cholesterol-rich lipoproteins, this consistent physiologic association is expected. Dietary intake, when measured as a specific intake variable, was a statistically significant predictor of all analytes except serum lycopene. These results are in agreement with studies conducted in adult populations, which have shown that intakes of fat-soluble vitamins and individual carotenoids are important predictors of plasma carotenoids (15,16,41,42).

Similar to findings in adults, we found an inverse association of both energy intake and percentage of energy from fat with serum concentrations of most fat-soluble nutrients (15,46). Although vitamin A, vitamin E and the carotenoids are fat-soluble and require some dietary fat for absorption, the amount required is small (3–5 g/meal) and excessive fat intake does not further increase bioavailability (47). In addition, it has been noted in many studies that dietary patterns that are high in fat and energy are frequently low in fruits and vegetables (48).

### Table

**Predictors of serum retinol, α-tocopherol and carotenoid concentrations**

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Retinol (μmol/L)</th>
<th>% change (95% CI)</th>
<th>P value</th>
<th>α-Tocopherol (μmol/L)</th>
<th>% change (95% CI)</th>
<th>P value</th>
<th>α-Carotene (μmol/L)</th>
<th>% Change (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>−3.0 (−6.7, 0.9)</td>
<td>0.12</td>
<td></td>
<td>−2.6 (−8.1, 3.1)</td>
<td>0.36</td>
<td></td>
<td>−0.3 (−1.8, 1.0)</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td>Age (per y)</td>
<td>1.5 (0.3, 2.7)</td>
<td>0.02</td>
<td></td>
<td>0.2 (−1.5, 1.9)</td>
<td>0.82</td>
<td></td>
<td>0.3 (−0.1, 0.7)</td>
<td>0.19</td>
<td></td>
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<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
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<tr>
<td>Caucasian (reference)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>African-American¹</td>
<td>−11.0 (−15.2, −6.6)</td>
<td>&lt;0.001</td>
<td></td>
<td>−8.2 (−14.2, −1.8)</td>
<td>0.04</td>
<td></td>
<td>−2.0 (−3.7, −0.3)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Other¹,²</td>
<td>−2.3 (−7.1, 2.7)</td>
<td>0.36</td>
<td></td>
<td>−7.3 (−13.4, −0.5)</td>
<td>0.04</td>
<td></td>
<td>0.6 (1.1, 2.4)</td>
<td>0.45</td>
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<tr>
<td><strong>BMI</strong></td>
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<td></td>
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<tr>
<td>Normal (reference)</td>
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<tr>
<td>Overweight³</td>
<td>−5.3 (−11.6, 1.5)</td>
<td>0.12</td>
<td></td>
<td>−10.1 (−17.0, −2.6)</td>
<td>0.01</td>
<td></td>
<td>−2.5 (−4.4, −0.5)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Obese³</td>
<td>−11.1 (−1.5, −21.5)</td>
<td>&lt;0.001</td>
<td></td>
<td>−11.3 (−1.6, 0.0)</td>
<td>0.05</td>
<td></td>
<td>−0.4 (−0.6, −0.3)</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>Serum cholesterol concentration (per 10% increase)</td>
<td>1.4 (0.7, 2.1)</td>
<td>&lt;0.001</td>
<td></td>
<td>4.1 (3.1, 5.1)</td>
<td>&lt;0.001</td>
<td></td>
<td>0.3 (0.1, 0.5)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Energy intake (per 10% increase)</td>
<td>−0.8 (−1.6, −0.1)</td>
<td>0.02</td>
<td></td>
<td>−0.4 (−6.6, −0.3)</td>
<td>&lt;0.001</td>
<td></td>
<td>−0.4 (−6.6, −0.3)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>% energy from fat (per 5% increase)</td>
<td>−1.4 (−2.7, −0.1)</td>
<td>0.04</td>
<td></td>
<td>−2.8 (−4.7, −0.9)</td>
<td>0.01</td>
<td></td>
<td>0.08 (0.02, 0.1)</td>
<td>0.01</td>
<td></td>
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<tr>
<td>Dietary intake (per 10% increase)</td>
<td>0.5 (0.2, 0.7)</td>
<td>&lt;0.001</td>
<td></td>
<td>0.6 (0.2, 1.0)</td>
<td>0.01</td>
<td></td>
<td>0.7 (1.1, 4.4)</td>
<td>0.01</td>
<td></td>
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<tr>
<td>Use of dietary supplement</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Fruits and vegetables (servings/d)⁵</td>
<td>2.7 (1.1, 4.4)</td>
<td>0.01</td>
<td></td>
<td>2.7 (1.1, 4.4)</td>
<td>0.01</td>
<td></td>
<td></td>
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<tr>
<td>Variance explained (R²)</td>
<td>0.20</td>
<td>0.28</td>
<td></td>
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</tr>
</tbody>
</table>

¹ Compared with Caucasians.
² Hispanic, Asian-American, American Indian and mixed race; combined due to small cell size.
³ Compared with normal BMI.
⁴ Dietary intake for the nutrient represented by each analyte.
⁵ One serving of fruit is defined as 6 fluid ounces of fruit juice (−186 g), 1 medium piece of fruit (−130 g) or ½ cup of cut up fruit (−106 g). One serving of vegetables is defined as 6 fluid ounces of vegetable juice (−183 g), ½ cup of cooked vegetables (−90 g) or 1 cup of raw leafy vegetables (−65 g).

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which could explain the inverse relationships between fat and energy and most of the serum nutrients examined.

Associations of race with fat-soluble nutrients varied. We speculate that the variability in these serum nutrient concentrations across race was due to differences in dietary intake that the FFQ cannot measure with precision or other potentially confounding factors, which are difficult to assess (e.g., exercise and growth). Finally, although we did not find any association of obesity with serum retinol concentration, in contrast to results from NHANES III (23), we did show that obesity had an inverse association with the other nutrient analytes, except lutein + zeaxanthin. Our finding of an inverse association of serum α-tocopherol and most of the carotenoids with BMI agrees with results from NHANES III (23), a small study conducted in Hungary (49) and investigations conducted among adults (15,17,44). The basis for lower serum concentrations of nutrients in obese people compared with nonobese people remains speculative, but it has been suggested that dietary differences (23) and variability in body compartment size (42,44) are likely explanations.

There are several strengths of this study. First, we used an effective recruitment strategy and we were able to recruit minorities and persons of lower socioeconomic status. Second, we collected detailed information about health, lifestyle and demographics; all data were collected in a uniform manner by centrally trained staff. Third, our dietary assessment tool, the FFQ, gives a more reliable estimate of usual dietary intake (37) and investigations conducted among adults (15,17,44), did not enter any of the models in our study. Less than 10% of the adolescent participants reported tobacco use, which is substantially less than nationally reported estimates of 35–50% (51), and ~20% reported alcohol use. Although parents were not present with this age group during the clinic interview, many adolescents may still hesitate to report use of alcohol or tobacco.

One of the conclusions in the report from the Panel on Dietary Antioxidants and Related Compounds (National Academy of Sciences, Institute of Medicine) was that there has been insufficient nutrition-related research conducted.

### 4

**in multivariate analyses in 285 adolescents aged 12–17 y**

<table>
<thead>
<tr>
<th></th>
<th>β-Carotene (µmol/L)</th>
<th>β-Cryptoxanthin (µmol/L)</th>
<th>Lycopene (µmol/L)</th>
<th>Lutein + Zeaxanthin (µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% change (95% CI)</td>
<td>P value</td>
<td>% change (95% CI)</td>
<td>P value</td>
<td>% change (95% CI)</td>
</tr>
<tr>
<td>−0.01 (−2.9, 3.0)</td>
<td>0.99</td>
<td>−1.0 (−3.0, 1.1)</td>
<td>0.34</td>
<td>−2.9 (−5.8, 0.2)</td>
</tr>
<tr>
<td>−0.2 (−1.0, 0.7)</td>
<td>0.66</td>
<td>−0.2 (−0.8, 0.3)</td>
<td>0.43</td>
<td>−0.2 (−1.1, 0.8)</td>
</tr>
<tr>
<td>1.7 (−1.7, 5.2)</td>
<td>0.33</td>
<td>1.1 (−1.3, 3.5)</td>
<td>0.36</td>
<td>2.9 (−0.9, 6.9)</td>
</tr>
<tr>
<td>2.5 (−1.1, 6.0)</td>
<td>0.17</td>
<td>0.7 (−1.8, 3.2)</td>
<td>0.59</td>
<td>−2.4 (−6.3, 1.6)</td>
</tr>
<tr>
<td>−2.9 (−6.2, 0.6)</td>
<td>0.10</td>
<td>0.04 (−2.4, 2.5)</td>
<td>0.97</td>
<td>3.6 (−0.3, 7.8)</td>
</tr>
<tr>
<td>−8.7 (−12.4, −4.9)</td>
<td>&lt;0.001</td>
<td>−2.7 (−5.5, 0.1)</td>
<td>0.06</td>
<td>−2.1 (−6.4, 2.4)</td>
</tr>
<tr>
<td>0.8 (−0.4, 1.3)</td>
<td>&lt;0.001</td>
<td>0.6 (0.3, 0.9)</td>
<td>&lt;0.001</td>
<td>1.4 (0.8, 1.9)</td>
</tr>
<tr>
<td>−0.4 (−0.7, −0.07)</td>
<td>0.02</td>
<td>−0.2 (−0.4, 0.02)</td>
<td>0.07</td>
<td>−0.5 (−0.7, −0.2)</td>
</tr>
<tr>
<td>0.2 (0.07, 0.4)</td>
<td>0.01</td>
<td>0.4 (0.2, 0.5)</td>
<td>&lt;0.001</td>
<td>−4.5 (−7.8, −1.0)</td>
</tr>
</tbody>
</table>

0.16 0.20 0.14 0.18
among children and adolescents (9). For this reason, the recommended levels of intakes for vitamin A and vitamin E in these life stage groups are extrapolated from adults, instead of being based on experimental data. Although the Panel did not propose a recommended intake of β-carotene or other carotenoids for any life stage or sex group, they did recommend that Americans eat foods rich in these nutrients (9). The data we have presented in this report suggest that serum concentrations of vitamin A, vitamin E and the carotenoids are influenced by similar physiologic and lifestyle factors as adults, namely serum cholesterol, diet, race and obesity. A critical need remains for continued research among children and adolescents to establish quantitative nutrient recommendations.

LITERATURE CITED