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Children's Lung Function and Antioxidant Vitamin, Fruit, Juice, and Vegetable Intake

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The authors investigated the relation between children's pulmonary function and intake of fruits, vegetables, juices, and vitamins A, C, and E by examining cross-sectional data from 2,566 children in the Children's Health Study collected during 1997–1998. Low total vitamin C intake (≤10th percentile) was associated with deficits in forced vital capacity for both boys and girls and with deficits in flows that were larger in girls (forced expiratory volume in 1 second (FEV_1), –3.3%, 95% confidence interval (CI): –6.0, –0.5; forced expiratory flow between 25% and 75% of forced vital capacity ($FEF_{25–75}$), –5.5%, 95% CI: –10.5, –0.3) compared with boys (FEV_1, –2.3%, 95% CI: –4.8, 0.3; $FEF_{25–75}$, –2.4%, 95% CI: –7.4, 2.8). Low dietary vitamin E intake was associated with lower $FEF_{25–75}$ (boys: $FEF_{25–75}$, –8.9%, 95% CI: –14.2, –3.3; girls: $FEF_{25–75}$, –2.5%, 95% CI: –8.3, 3.7). Deficits in $FEF_{25–75}$ were associated with low dietary vitamin A intake in girls ($FEF_{25–75}$, –7.9%, 95% CI: –12.7, –2.8) and with low total vitamin A intake in boys with asthma ($FEF_{25–75}$, –15.6%, 95% CI: –27.6, –1.6). Low intakes of orange and other fruit juices, which were the largest source of vitamin C, were associated with deficits in forced vital capacity and FEV_1 in boys. In summary, lung function levels were lower in children with inadequate dietary antioxidant vitamin intake.

antioxidants; ascorbic acid; child; diet; respiratory function tests; vitamin A; vitamin E

Abbreviations: CI, confidence interval; $FEF_{25–75}$, forced expiratory flow between 25 and 75 percent of forced vital capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

A substantial body of evidence indicates that nutrition influences respiratory health (1–19). Much of the nutrition research has focused on the intake of fruits, vegetables, and antioxidant micronutrients, because the lung is subject to a wide range of oxidant insults and because antioxidant defenses play an important role in protecting the lung from damage. A growing, but as yet inconsistent, body of evidence indicates that a low dietary intake of fruits and antioxidants, including vitamins A, C, and E, is associated with obstructive airway conditions and with deficits in adult lung function assessed by spirometric measurements of forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) (11, 16, 17, 20). In recent population-based studies, decreased lung function was associated with low levels of antioxidant intake and serum levels of antioxidants (10–12, 20). If causal, the associations of low antioxidant intake with adult lung function level may arise from a steeper decline of lung function during adulthood, reversible acute effects, and/or long-term effects of inadequate intake during the period of childhood growth and development.

Few population-based studies have investigated the relation between intake of antioxidants and lung function during childhood (3, 14, 21). The existing evidence among children is consistent with the findings in adults, but it suggests that the assessment of the source of antioxidant intake may be important in defining the role of specific antioxidant vitamins, including vitamin C. In a cross-sectional study of 2,650 school-age children in England and Wales, the level of FEV_1 was positively associated with the frequency of fresh fruit consumption and more weakly associated with green vegetables and salad consumption (3). However, FEV_1 was not associated with serum levels of vitamin C, suggesting that other micronutrients in fruit were important. Studies that consider dietary and total nutrient intake that include intake from food and vitamin supplements may be informative for determining whether consumption of the package of antioxi-

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dants in whole foods or of specific vitamins is important. Using the evidence available for adults and children, we hypothesized that a low intake of fruits, vegetables, and juices, as well as an inadequate daily total intake of antioxidant vitamins A, C, and E, is associated with deficits in childhood FVC, FEV_1, and forced expiratory flow between 25 and 75 percent of forced vital capacity (FEF_{25-75}) (22). The Children's Health Study offered an opportunity to investigate the role of inadequate dietary and total antioxidant vitamin, fruit, vegetable, and juice intake on children's lung function (23, 24).

MATERIALS AND METHODS

Study design

The Children's Health Study is a 10-year longitudinal study of respiratory health in schoolchildren who reside in 12 communities within a 200-mile (321.9-km) radius of Los Angeles, California. Details on the design, site selection, subject recruitment, and assessment of health effects are reported elsewhere (23, 24). This report focuses on cross-sectional analyses using the initial dietary intake data and lung function measurements collected during 1997–1998. At study entry in early 1993, parents or guardians of 3,681 participating children provided written informed consents and completed self-administered questionnaires on demographics, medical and family health histories, indoor air exposures, and household characteristics. In the spring of 1993, pulmonary function testing was conducted, and in each subsequent year of the ongoing study, each child completed a follow-up questionnaire and repeated the pulmonary function testing. In the fall of 1995, a second group of 2,081 fourth grade students was recruited and completed the same baseline and follow-up questionnaires and pulmonary function testing as the group enrolled in 1993. Beginning in the 1997–1998 school year, dietary data were collected using a validated food frequency questionnaire; these questionnaires were completed by 2,895 children who ranged in age from 11 to 19 years and who were enrolled in schools in the participating communities during the 1997–1998 school year.

Pulmonary function testing

Maximum forced expiratory flow-volume maneuvers were recorded using rolling-seal spirometers (Spiroflow; P. K. Morgan, Ltd., Gillingham, United Kingdom). Spirometer calibrations and room temperatures were measured just before, during, and just after each testing session using flow-volume syringes (Jones Medical Instrument Co., Oak Brook, Illinois), and lung function measures were corrected for changes in calibration or internal temperature. Testing and data management procedures have been reported previously (25).

Dietary information

Dietary intake was assessed using the Youth/Adolescent Questionnaire, a validated food frequency questionnaire developed by Rockett et al. in 1997 for use in older children and adolescents (26, 27). The questionnaire has 131 food items including snacks and is a modified version of the validated Nurses' Health Study food frequency questionnaire (28). Nutrient intake was estimated for diet without supplements and diet plus supplements, and total energy intake was quantified for each individual. Of the 2,633 children who completed both the food frequency questionnaire and lung function tests, 67 children with a total energy intake below 500 calories or above 5,000 calories were excluded from analyses, resulting in a final sample size of 2,566 children aged 11–19 years. Because vitamin intake depended on gender and total caloric intake, we used sex-specific means and deciles for descriptive analyses of antioxidant vitamin intake. On the basis of our hypotheses that the effects of antioxidant vitamin intake on lung function result from an inadequately low intake, we compared a low intake (≤10th percentile) with a higher intake (>10th percentile) in the models. Fruits and vegetables were examined as servings per day of individual items and grouped by summing the intake per day of individual members of each group. Food frequency questionnaire items assessed orange juice and other juices including apple juice. Juices were categorized as any intake of juice, intake of either category of juice, or no intake of juices. Total juice intake summed the daily servings of orange, apple, and other juices. Magnesium intake was also assessed using the food frequency questionnaire and categorized into quintiles of intake.

Sociodemographic, medical history, and exposure data

The Children's Health Study questionnaires provided information on sociodemographic factors, history of respiratory illness and associated risk factors, exposure to environmental tobacco smoke, and maternal smoking history during pregnancy. Ethnicity was defined as non-Hispanic White, Hispanic, African American, Asian, and other/mixed ethnicity, on the basis of self-report. Health insurance was defined as any insurance coverage reported for the participant's family. Self-report of physician-diagnosed asthma during follow-up lung function testing sessions was used to categorize children's asthma status at the time of food frequency questionnaire completion. Personal smoking was defined as a history of the participant's reporting having ever smoked more than 100 cigarettes.

Participants' height and weight were measured using a standardized protocol, and any respiratory infection within 1 month of testing and exercising within 30 minutes of testing were documented by trained field staff immediately prior to lung function testing. Body mass index was calculated as weight (kg)/height $(m)^2$ and categorized into age- and sex-specific quintiles.

Statistical analyses

We assessed the effect of low vitamin, fruit, vegetable, and juice intakes on lung function by using regression splines to capture the nonlinear relation among pulmonary function, age, and height (29–33). Initially, a knot was placed at each integer age. The final models were fit by using knots at the ages of 13 and 17 years, leading to a more parsimonious model with essentially the same results.

All models were fit separately for males and females, because their smoothed shapes for the relation between lung function and age are different. The gender-specific regression model is

$$E\{\log(\text{PFT})\} = \mu + S_1\,(\text{AGE}) + S_2\,(\text{AGE}) \times \log(\text{HT}) + \mathbf{X}\beta,$$

where "PFT" is a pulmonary function test such as the FVC or FEV_1, "μ" is the overall mean, "AGE" is age at visit, "HT" is the residual of height at visit after smoothing height on age, and "**X**" is a vector of covariates including vitamin intake or food group of interest and a set of adjustment variables including cohort, community, technician, spirometer, race/ethnicity, barometric pressure, and other possible confounders (34). We used natural cubic splines that impose the additional constraint that the function be linear beyond the boundary knots. Flexible models were fitted that included servings of fruit and vegetable groups and sex-specific deciles of dietary and total vitamin intake and variables for cohort, community, ethnicity, spirometer, spirometer temperature, technician, and barometric pressure. Note that the models are additive on the log scale, and the results are presented as the differences in percentage from the reference curve, at the mean age. The primary parameters of interest are the main effects for low vitamin or food group intake, which characterize a parallel difference in percentage in pulmonary function compared with the baseline group of high vitamin intake. Separate models were fitted for dietary intake with and without vitamin supplements. All models were adjusted for total energy intake. We assessed parental education, household income, body mass index, age- and sex-specific quintiles, insurance status, personal smoking, environmental tobacco smoke exposure, and respiratory illness at lung function testing as potential confounders. Covariates were included in models if the adjusted estimates for intake changed by 10 percent or more compared with the unadjusted estimates. Because the lung function level is associated with magnesium intake, which is contained in foods with antioxidant vitamins, we conducted sensitivity analyses to assess the independent effects of each vitamin by adjusting for magnesium intake. We also fit multinutrient models to assess the joint effects of vitamin intake. Subjects with missing data for a given covariate were excluded from the analyses involving that covariate.

To assess the modifying effect of asthma on the relation between low vitamin and lung functions, we conducted gender-specific stratified analyses for children with and without asthma. We tested the statistical significance of interaction terms between asthma status and vitamin intake (or food groups) using likelihood ratio tests. All analyses were conducted by using generalized linear models in the S-Plus statistical software package (35).

RESULTS

Selected characteristics of participants who completed both a food frequency questionnaire and lung function testing during 1997–1998 are shown in table 1. Participants ranged in age from 11 to 19 years. The majority of participants were non-Hispanic White and from middle-class families with health insurance.

TABLE 1. Selected characteristics of participants with dietary assessment and lung function tests, Children's Health Study, 1997–1998

	No.	%
All	2,566	100.0
Sex		
Girls	1,389	54.1
Boys	1,177	45.9
Age (years)		
11–<14	1,090	42.5
14–<16	617	24.0
≥16	859	33.5
Race/ethnicity		
Non-Hispanic White	1,481	57.9
Hispanic	678	26.5
Black (African American)	112	4.4
Asian	149	5.8
Others	137	5.4
Parental education		
Some graduate school	349	14.1
College	269	10.9
Some college	1,100	44.5
12 grades	466	18.9
<12 grades	286	11.6
Income ($)		
≥100,000	152	7.0
50,000–99,999	794	36.5
30,000–49,999	597	27.4
15,000–29,999	332	15.2
7,500–14,999	193	8.9
<7,500	110	5.1
Insurance		
Yes	2,136	85.4
Respiratory illness at lung function test		
Yes	429	18.2
In utero exposure to maternal smoking		
Yes	377	15.3
Current environmental tobacco smoke exposure		
Yes	848	33.1
Personal smoking		
Yes	197	7.7
Ever asthma		
Yes	579	23.0

The total antioxidant intake, including supplements and dietary intake without supplements, varied according to the

TABLE 2. Daily average intakes of vitamins A, C, and E among boys and girls by age, Children's Health Study, 1997–1998

	Age (years)	Boys (*n* = 1,177)						Girls (*n* = 1,389)					
		Without supplements			With supplements			Without supplements			With supplements		
		Mean	SD*	Lowest decile	Mean	SD	Lowest decile	Mean	SD	Lowest decile	Mean	SD	Lowest decile
Vitamin C (mg/day)	11–<14	130	86	42	140	90	45	122	80	40	131	82	41
	14–<16	121	77	37	131	84	41	119	74	43	132	79	49
	≥16	129	84	43	140	90	46	135	86	47	144	59	49
	Overall	127	83	41	138	89	44	126†	81	41	136	54	44
Vitamin E (mg/day)	11–<14	6.5	3.1	3.1	9.0	5.9	3.3	6.0	3.2	2.8	8.2	5.2	3.1
	14–<16	6.3	3.1	3.0	8.8	6.1	3.1	5.8	3.0	2.7	9.0	6.6	3.1
	≥16	7.1	5.3	3.3	9.9	9.0	3.5	6.0	2.7	3.1	8.5	6.7	3.2
	Overall	6.6†	4.0	3.1	9.3	7.1	3.3	6.0	3.0	2.9	8.5	6.1	3.2
Vitamin A (IU/day)	11–<14	8,118	5,528	2,960	8,827	5,849	3,307	7,767	5,337	2,477	8,364	5,553	2,817
	14–<16	7,700	5,218	2,634	8,391	5,557	2,694	7,660	4,876	2,661	8,535	5,216	3,090
	≥16	7,935	5,502	2,829	8,651	6,062	2,896	7,912	5,485	2,795	8,542	5,757	2,893
	Overall	7,959	5,445	2,730	8,666	5,850	2,979	7,790	5,278	2,675	8,466	5,541	2,893

* SD, standard deviation.

† *F* test for difference among three age groups: $p < 0.01$.

participant's age and sex (table 2). Total and dietary intakes of vitamins A, C, and E were higher for boys than for girls in all age groups combined and varied among age groups for dietary vitamin E in boys and dietary vitamin C in girls. The lowest decile of total vitamin C intake (44 mg/day) was below the recommended daily allowance for both boys (45 mg/day for ages 9–13 years and 75 mg/day for ages 14–18 years) and girls (45 mg/day for ages 9–13 years and 65 mg/day for ages 14–18 years) (36). The mean and the 10th decile for total and dietary intakes of vitamin E were less than the recommended daily allowance for α-tocopherol (11 mg/day for ages 9–13 years and 15 mg/day for ages 14–18 years) (36). Based on approximate conversion of international untits to retinol activity equivalency, the lowest decile of total and dietary vitamin A intakes slightly exceeded the recommended daily allowance for retinol activity equivalency (37).

For vitamin C, the major dietary contributors were mixed fruit juice drinks, orange juice, oranges, cereal, and multivitamins. In contrast, supplements were the leading contributor for intake of vitamin E, followed by turkey and peanut butter and jelly sandwiches, added fat, and cereal. The leading sources for vitamin A intake in descending order were carrots, liver, mixed vegetables, cereal, yams, and multivitamins.

Fruit, juice, and vegetable intakes were relatively low among Children's Health Study participants compared with recommendations for five servings of fruit and vegetables per day (table 3). On average, boys and girls consumed 1.5–2 servings of vegetables per day, about one serving of fruit per day, and 0.8 servings of fruit juice per day. On average, boys and girls consumed 3.2 and 3.5 servings per day of fruits, vegetables, and juices combined, respectively.

We found that both lung volume and measures of flow showed deficits associated with low vitamin C intake among girls (table 4). Among boys, low total vitamin C intake was associated with deficits in lung function compared with those with higher vitamin C intake that were significant for FVC. FEV$_1$ and FEF$_{25-75}$ were significantly lower in girls who had intake in the lowest decile compared with higher vitamin C intake. We did not observe a statistically significant relation between increasing vitamin C intake and lung function deficits (data not shown). For example, FVC increased 0.5 percent (95 percent confidence interval (CI): –0.1, 1.1) per quintile of vitamin C intake among boys, and FEV$_1$ increased 0.3 percent (95 percent CI: –0.4, 1.0) per quintile among girls. The effect estimates for low vitamin C intake were reduced by 10–15 percent by adjustment for magnesium (data not shown). Adjustment for magnesium had little effect on the vitamin C effects. The effects of low vitamin C intake showed no substantial difference in children with or without asthma (data not shown).

Boys with low vitamin E intake showed deficits in FEF$_{25-75}$. To further investigate the effects of vitamin E on air flows, we assessed the FEV$_1$/FVC ratio and peak expiratory flow rates and found deficits of –2.3 percent (95 percent CI: –4.1, –0.4) and –5.1 percent (95 percent CI: –8.7, –1.4), respectively, in boys with a low total vitamin E intake. Among girls, the estimates for the effect of low intake on FEF$_{25-75}$ and peak expiratory flow rates were negative but not statistically significant. The magnitude of the lung function deficits did not increase with increasing vitamin E intake above the 10th decile (data not shown). Again, adjustment for magnesium intake had little effect on the vitamin E associations. There was little variation in the effects of low vitamin E intake in either boys or girls with or without asthma (data not shown).

Low dietary vitamin A intake was associated with a substantial reduction in FEF$_{25-75}$ in girls. Overall, vitamin A intake was not strongly associated with lung function in boys; however, boys with asthma who had low intake showed deficits in airflows, especially FEF$_{25-75}$, that were

TABLE 3. Daily average intake of vegetables, fruits, and juices (servings/day) among boys and girls by age, Children's Health Study, 1997–1998

Intake	Age (years)	Boys		Girls	
		Mean	SD*	Mean	SD
Vegetables	11–<14	1.5	1.3	1.5	1.2
	14–<16	1.5	1.3	1.6	1.3
	≥16	1.6	1.2	1.9	1.3
	Overall	1.6	1.3	1.7†	1.3
Fruits	11–<14	1.0	0.8	1.1	0.9
	14–<16	0.8	0.8	0.9	0.7
	≥16	0.9	0.8	1.1	0.9
	Overall	0.9†	0.8	1.0	0.8
All juices	11–<14	0.8	0.9	0.8	0.9
	14–<16	0.8	0.8	0.8	0.8
	≥16	0.8	0.9	0.8	0.9
	Overall	0.8	0.9	0.8	0.9
Orange juice	11–<14	0.4	0.5	0.4	0.5
	14–<16	0.4	0.5	0.4	0.5
	≥16	0.3	0.5	0.4	0.5
	Overall	0.4	0.5	0.4	0.5
Other juices	11–<14	0.4	0.5	0.4	0.5
	14–<16	0.4	0.5	0.4	0.5
	≥16	0.4	0.5	0.5	0.6
	Overall	0.4	0.5	0.4	0.5

* SD, standard deviation.

† *F* test for difference among three age groups: $p < 0.05$.

significantly larger than the deficits in boys without asthma (table 5). Girls with asthma and low vitamin A intake had larger deficits than girls without asthma, but the difference in deficits was not statistically significant (data not shown). The magnitude of the lung function deficits did not increase with increasing vitamin A intake above the 10th decile (data

TABLE 4. Change in lung function level associated with low* daily dietary and total intakes of vitamins A, C, and E, Children's Health Study, 1997–1998†

	Lung function test	Boys (n = 1,177)				Girls (n = 1,389)			
		Low intake without supplements		Low intake with supplements		Low intake without supplements		Low intake with supplements	
		% change	95% CI‡	% change	95% CI	% change	95% CI	% change	95% CI
Vitamin C	FVC‡	–1.8	–4.2, 0.8	–2.6	–5.1, –0.2	–3.1	–5.6, –0.6	–2.7	–5.2, –0.1
	FEV$_1$‡	–1.0	–3.6, 1.7	–2.3	–4.8, 0.3	–3.5	–6.2, –0.8	–3.3	–6.0, –0.5
	FEF$_{25–75}$‡	0.6	–4.5, 6.1	–2.4	–7.4, 2.8	–4.9	–9.9, 0.3	–5.5	–10.5, –0.3
Vitamin E	FVC	0.7	–2.2, 3.7	0.8	–2.0, 3.6	0.8	–2.1, 3.9	1.5	–1.4, 4.4
	FEV$_1$	–1.5	–4.5, 1.5	–0.9	–3.7, 2.1	0.5	–2.8, 3.8	1.2	–1.9, 4.4
	FEF$_{25–75}$	–8.9	–14.2, –3.3	–6.5	–11.8, –1.0	–2.5	–8.3, 3.7	–1.0	–6.7, 5.0
Vitamin A	FVC	–1.2	–3.7, 1.3	–0.5	–3.0, 2.1	–0.7	–3.3, 1.9	0.2	–2.4, 2.8
	FEV$_1$	–0.5	–3.1, 2.2	–0.4	–3.2, 2.3	–2.6	–5.3, 0.3	–0.8	–3.5, 2.1
	FEF$_{25–75}$	0.4	–4.7, 5.9	–0.7	–5.8, 4.7	–7.9	–12.7, –2.8	–4.2	–9.2, 1.1

* Low intake is defined as less than or equal to the gender-specific lowest decile. The reference group for % change is intake greater than the lowest decile.

† Models are adjusted for community, grade, spirometer, technician, pressure, log (height), age, race, asthma, respiratory illness at pulmonary function test, in utero exposure to maternal smoke, current environmental tobacco smoke exposure, and total energy intake.

‡ CI, confidence interval; FVC, forced vital capacity; FEV$_1$, forced expiratory volume in 1 second; FEF$_{25–75}$, forced expiratory flow between 25% and 75% of forced vital capacity.

TABLE 5. Change in lung function associated with low* daily dietary and total vitamin A intakes in boys with and without asthma, Children's Health Study, 1997–1998†

Lung function test	Low intake without supplements				Low intake with supplements			
	Nonasthmatics		Asthmatics		Nonasthmatics		Asthmatics	
	% change	95% CI‡	% change	95% CI	% change	95% CI	% change	95% CI
FVC‡	–0.1	–2.8, 2.7	–6.1§	–11.6, –0.2	–0.2	–2.9, 2.6	–1.8	–7.5, 4.2
FEV_1‡	1.1	–1.7, 4.0	–6.5¶	–12.8, 0.2	1.4	–1.5, 4.3	–6.3¶	–12.4, 0.3
FEF_{25-75}‡	3.4	–2.0, 9.2	–9.1¶	–22.4, 6.6	4.3	–1.3, 10.1	–15.6¶	–27.6, –1.6

* Low intake is defined as less than or equal to the gender-specific lowest decile. The reference group for % change is intake greater than the lowest decile.

† Models are adjusted for community, grade, spirometer, technician, pressure, log (height), age, race, respiratory illness at pulmonary function test, in utero exposure to maternal smoke, current environmental tobacco smoke exposure, and total energy intake.

‡ CI, confidence interval; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; FEF_{25-75}, forced expiratory flow between 25% and 75% of forced vital capacity.

§ Test for interaction of intake and asthma: $p < 0.05$.

¶ Test for interaction of intake and asthma: $p < 0.01$.

not shown). Adjustment for magnesium intake had little effect on the deficits associated with low vitamin A intake. We found no associations of lung function level with intake of total carotenoids.

We also assessed the joint effects of vitamins C, E, and A on lung function by including variables for each of the vitamins in a single model. The deficits in lung function associated with low intake of each vitamin did not substantially change, and the statistically significant deficits in the single nutrient models remained statistically significant after mutual adjustments.

Low intakes of all fruit juices, orange juice, and other fruit juices were associated with significant deficits in FVC and FEV_1 among boys (table 6). Among girls, the deficits were slightly smaller and did not achieve statistical significance. Low intakes of either fruits or vegetables, as well as their combined intake, were not associated with lung function level in either boys or girls. Individual food items were examined, and no consistent associations were observed for specific vegetables or fruits, including carrots and apples. We found no evidence that asthma affected the associations of fruits, vegetables, and juice intake with lung function and no confounding by family income, parents' education, health insurance status, or other sociodemographic variables. We had an insufficient number of smokers to assess interactions between food groups and smoking.

DISCUSSION

Our study indicates that a low intake of antioxidant vitamins may have adverse effects on pulmonary function in school-age children. We observed deficits in FVC, FEV_1, and FEF_{25-75} among girls with the lowest levels of dietary and total intakes of vitamin C and among boys with a low intake of fruit juices that is frequently supplemented with vitamin C. Low vitamin A intake was associated with lower FEF_{25-75} in boys with asthma and among girls independent of asthma status. We also found some evidence for an association of vitamin E with FEF_{25-75} in boys. The deficits associated with vitamins A, C, and E appeared to be independent, as the deficits remained significant when the three vitamins were mutually adjusted in a single multinutrient model. Based on the lack of statistically significant dose-response relations between antioxidant vitamin intake and lung function level, our data raise the possibility that increased intake of antioxidant vitamins above the recommended daily allowance may not provide additional protection for lung function level.

Our findings showing lung function deficits with inadequate intake of vitamin C are consistent with those of studies in adults showing that lower levels of FVC and FEV_1 are associated with a lower intake of vitamin C, but they are inconsistent with the only reported investigation of the relation between vitamin C and lung function during childhood (3, 9, 10, 12, 16, 19, 20). In the cross-sectional study of 2,650 school-age children in England and Wales, Cook et al. (3) reported that FEV_1 was positively associated with the frequency of fresh fruits, green vegetables, and salad consumption but was not associated with serum vitamin C levels, suggesting a role for other nutrients in fruit. Several studies in adults have also reported the protective effects of fruit intake on lung function or obstructive airway diseases (10). The differences in findings in the Children's Health Study may reflect variation in diet habits among the populations or diet assessment methods. In the Children's Health Study population, fruit juices, which were the leading contributor to vitamin C intake, were positively associated with lung function. Fresh fruit is also an important source of vitamin C, and the study population from the United Kingdom may have consumed more fresh fruits as a source of vitamin C than fruit juices during the period of the study; however, we could not assess this possibility because the consumption of fruit juices was not included in the published report by Cook et al. Additional information about fruit juice intake may contribute to understanding the differences between the studies. Cook et al. did not find an association between serum vitamin C levels and childhood lung function. Although dietary assessment of vitamin intake using food frequency questionnaires is imprecise, the lack of association may also be the result of a mismatch between the

TABLE 6. Effects of low intake* of vegetables, fruits, and juices on lung function in boys and girls, Children's Health Study, 1997–1998†

Food group	Lung function test	Boys		Girls	
		% change	95% CI‡	% change	95% CI
All vegetables	FVC‡	–1.1	–2.9, 0.7	–0.6	–2.4, 1.3
	FEV_1‡	–0.7	–2.6, 1.2	–0.6	–2.6, 1.4
	FEV_1/FVC ratio	0.3	–0.9, 1.5	–0.1	–1.2, 1.1
	$FEF_{25–75}$‡	–1.0	–4.7, 2.8	–2.0	–5.6, 1.8
All fruits	FVC	–0.1	–1.8, 1.7	–1.5	–3.2, 0.3
	FEV_1	–0.0	–1.9, 1.8	–1.1	–3.0, 0.8
	FEV_1/FVC ratio	0.2	–1.0, 1.3	0.4	–0.7, 1.5
	$FEF_{25–75}$	–1.2	–4.7, 2.5	–0.9	–4.4, 2.8
All juices	FVC	–2.6	–5.4, 0.3	–2.2	–5.2, 0.8
	FEV_1	–2.2	–5.1, 0.9	–3.1	–6.2, 0.3
	FEV_1/FVC ratio	0.4	–1.5, 2.4	–1.0	–2.8, 0.9
	$FEF_{25–75}$	–2.2	–7.9, 3.9	–3.2	–9.2, 3.1
Orange juice	FVC	–3.3	–5.4, –1.1	–0.7	–2.7, 1.3
	FEV_1	–2.7	–5.0, –0.4	–1.1	–3.3, 1.1
	FEV_1/FVC ratio	0.6	–0.9, 2.0	–0.5	–1.7, 0.7
	$FEF_{25–75}$	–1.9	–6.4, 2.7	–2.2	–6.2, 1.9
Other juices	FVC	–1.9	–3.7, –0.2	–1.8	–3.7, 0.1
	FEV_1	–2.1	–4.0, –0.2	–1.9	–4.0, 0.2
	FEV_1/FVC ratio	–0.1	–1.2, 1.1	–0.3	–1.5, 0.9
	$FEF_{25–75}$	–3.4	–6.8, 0.3	–2.8	–6.6, 1.2

* The estimates are for the lowest quintile servings/day compared with higher intake (reference group) of vegetables and fruits. For all juices, orange juice, and other juices, the estimates are for no intake compared with some intake (reference group).

† Models are adjusted for community, grade, spirometer, technician, pressure, log (height), age, race, asthma, respiratory illness at pulmonary function test, in utero exposure to maternal smoke, current environmental tobacco smoke exposure, and total energy intake.

‡ CI, confidence interval; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; $FEF_{25–75}$, forced expiratory flow between 25% and 75% of forced vital capacity.

time scale of the cross-sectional studies of lung function level that integrates growth over the life course and serum levels of vitamin C, which is a water-soluble vitamin with a relatively short half-life (3). Short-term biomarkers, such as serum levels, may provide less accurate estimates of the average levels during childhood than those provided by questionnaire methods that characterize usual intake, such as the food frequency questionnaire method.

Several mechanisms for the protective effects of vitamin C on lung function have been investigated. Vitamin C is an important antioxidant in the extracellular respiratory lining fluid that protects proteases, antiproteases, epithelial, and immune cells from oxidant attack, and low levels may leave the lung relatively unprotected from oxidant stress. The importance of vitamin C to antioxidant defenses is illustrated by trials that document the protective effects of vitamin C supplementation on short-term changes in lung function in free-living subjects exposed to high levels of oxidant air pollutants (16, 19, 38). Vitamin C may contribute to lung growth and development and reduce airway hyperreactivity, both of which are determinants of childhood and adult lung function (16, 39). Whether the association of flows with the antioxidant vitamins and juice intake results from enhancement of lung growth, protection against bronchospasm, or reduced airway hyperreactivity in children from the Children's Health Study is presently unknown because this analysis was cross-sectional and we cannot differentiate between acute and chronic deficits in lung function. Future longitudinal follow-up of the cohort may be informative about the acute and chronic effects on lung function growth and maximum attained lung function at maturity.

The present study findings show that deficits in lung function are associated with low vitamin A intake. The findings are supported by results in the single published report concerning the effects of low levels of vitamin A on children's lung function (21). Among 702 rural Ethiopian children aged 6–9 years, FEV_1 was 48.8 ml ($p = 0.006$) lower in children with inadequate vitamin A reserves than in those with adequate reserves. The evidence for a protective effect of vitamin A has been inconsistent in adults (10, 19). The biologic plausibility for the association of lung function with vitamin A is provided by evidence that vitamin A is involved in critical pathways for normal lung function growth in early life, including lung development, normal respiratory epithelial differentiation, pulmonary immune function, resistance to respiratory infections, and antioxidant defenses (40). Our finding that deficits in flow were larger in boys with asthma than in those without asthma warrants further research.

The evidence that vitamin E is associated with lung function is less consistent than for vitamin C (10). Studies in adults suggest that vitamin E intake is positively correlated with lung function; however, the associations appear to be accounted for by correlations with vitamin C or other nutrients (16, 19). No studies of the associations of vitamin E intake with lung function have been reported in children. We found that low vitamin E intake was associated with deficit in FEF_{25-75}, a measure of small airway flow that has not been routinely reported in other epidemiologic studies of nutritional determinants of lung function. It may be that vitamin E plays a role in protecting small airway function, and measures such as FEV_1 may be less sensitive for the effects. Because vitamin E intake and levels may not be measured precisely by food frequency questionnaire methods, our estimates may be biased toward no effect of vitamin E intake.

There are several limitations that arise from our study design and methods. Our data were cross-sectional and were subject to problems with temporality and selection bias. This cross-sectional study cannot distinguish between children who had low lung function as a result of low intake of antioxidant vitamins and children who had respiratory problems that lead to reduced lung function that leads to diet changes. Because deficits were observed in children with and without asthma, it is unlikely that disease-related dietary changes explain our findings. Only a subset of Children's Health Study participants remained enrolled in schools in the 1997–1998 school year. The 10th graders enrolled in the cohort in 1993 had graduated by 1997. The primary reason for not completing the dietary assessment was family relocation to a new residence outside a participating school district. We assessed the reason for moves using a telephone interview and found that moves were almost entirely due to changes in the parents' employment, which were more common in lower income families with lower educational attainment. Because education and income may affect diet and lung function, we adjusted for these factors in sensitivity analyses and found no evidence of bias. We used a validated food frequency questionnaire designed to assess usual dietary intake in children and adolescents; however, measurement error remains an unresolved problem for diet assessment, and the effect estimates for micronutrients are likely to be biased toward no effect. Repeated food frequency questionnaires or repeated serum level measurements in longitudinal studies of lung function have the potential to reduce the bias from measurement errors.

In summary, low intakes of antioxidant vitamins were associated with deficits in pulmonary function levels among boys and girls in the Children's Health Study. The deficits were large enough among boys with asthma to be potentially clinically significant. Low intake during childhood may contribute to risk for obstructive lung diseases during adulthood as well as increased morbidity and mortality associated with low FEV_1. Future longitudinal analyses, as follow-up of the Children's Health Study cohort continues and additional nutrient data are collected, will allow better assessment of the temporal relation between dietary intake and lung function.

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