

Relationship of Serum Antioxidants to Asthma Prevalence in Youth

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The relationship of serum vitamin E, β -carotene, vitamin C, and selenium to asthma was investigated among 7,505 youth (4–16 years old) in the Third National Health and Nutrition Examination Survey. Logistic regression models adjusted for potentially confounding variables, which generally had no effect on the coefficients for the antioxidants. Serum vitamin E had little or no association with asthma. In separate models, a SD increase in β -carotene (odds ratio [OR], 0.9; 95% confidence interval [CI], 0.7, 1.0), vitamin C (OR, 0.8; 95% CI, 0.7, 0.9), and selenium (OR, 0.9; 95% CI, 0.7, 1.1) was associated with a 10–20% reduction in asthma prevalence. Serum cotinine was used to identify youth with no cigarette smoke exposure and passive exposure (7%): Active smokers were too few to be studied further. The selenium–asthma association was stronger in youth who were smoke exposed ($p = 0.075$). A SD increase in selenium was associated with a 50% reduction in asthma prevalence (OR, 0.5; 95% CI, 0.2, 1.4) in youth with passive smoke exposure compared with a 10% reduction in youth with no smoke exposure. The findings support an association of antioxidants with prevalent asthma, which for some antioxidants is stronger among children exposed to cigarette smoke.

Keywords: antioxidants; asthma; child; second-hand smoke

The prevalence of asthma has increased dramatically in recent years, with the largest increases and the highest prevalence in youth 18 years old and younger (1). Taking account of variable clinical and epidemiologic outcome definitions, there is a consensus that the increasing secular trends represent both a true increase in asthma prevalence worldwide and an important public health issue (2, 3).

Dietary factors have been proposed to play a role, both in the origin of asthma and the progression of established disease (4–7). Studies of the relationship of antioxidants to asthma in adults are inconsistent, perhaps because most studies rely on dietary assessment to estimate the intake of antioxidant nutrients. Among the antioxidants studied in adults, there is less evidence for vitamin E (8–10) and carotenes (8, 10) and somewhat more evidence for vitamin C (8, 9, 11) and selenium (9, 10, 12–14).

Approximately 10 studies, with a variety of methods, investigated antioxidants in relationship to asthma or wheeze in youth, and again, there were mixed findings. Three cross-sectional studies reported an inverse association of dietary intake of antioxidant-rich foods with wheeze (citrus fruit in 18,737 children who were 6 and 7 years old [15]; country-level vegetable intake in

an ecological study [16]; apples and pears in young adults [17]), and two other studies reported no association (vitamin C-rich fruit consumption in 2,650 children [18]; serum vitamin C in 278 children [18]; vegetable and fruit intake in 1,000 youth aged 13 to 17 [19]). A case–control study of asthma in 12-year-old children reported an inverse association of dietary intake of vitamin E with asthma but little or no association of either vitamin C or selenium (20). Finally, a case study found a lower level of serum α -tocopherol and vitamin C in cases compared with noncases (21), although the results were not statistically significant. A few other studies on diet and respiratory outcomes in children suggest a role for antioxidants and other nutrients, but these studies do not bear directly on the hypothesis investigated herein (22–24).

Few epidemiologic studies in children have complete data on serum antioxidants. In this study, we investigated the hypothesis that higher serum levels of the antioxidants vitamin E, β -carotene, vitamin C, and selenium decrease the risk of asthma in childhood. Because antioxidants are hypothesized to mitigate the damage associated with oxidant exposures, we also hypothesized that the relationship of antioxidants to asthma would vary by exposure to cigarette smoke.

METHODS

Study Population

The third National Health and Nutrition Examination Survey (NHANES III), a cross-sectional, multistage, complex sample survey, was conducted from 1988–1994 (25). The Household Youth Questionnaire, answered by a proxy (typically the mother), was used for participants who were less than 17 years old (25). Eligible interviewed persons were invited to a medical examination center for a comprehensive medical examination. The examinee's age at the interview determined which questionnaires and procedures were administered. Details of the complex survey design, examination procedures, and laboratory measurements have been published (25, 26). The use of these NHANES data was reviewed and approved by the Cornell University Committee on Human Subjects.

Venipuncture was performed on participants aged 1 year or older, and serum antioxidants and cotinine were measured as follows: cotinine, carotenoids, and vitamin E in youth 4 years old or more, vitamin C in youth 6 years old or more, and selenium in youth 12 years old or more (25). Serum selenium was measured by atomic absorption spectrometry and serum vitamin E (α -tocopherol), carotenoids, and vitamin C by isocratic high-performance liquid chromatography (26). The range for the coefficient of variation suggested excellent assay quality as follows: cotinine, 3.0–5.7%; vitamin E, 2.2–4.3%; β -carotene, 6.3–10%; vitamin C, 5.2–7.8%; and selenium, 3.9–6.4% (26).

Data Analysis

Using logistic regression in SUDAAN (Research Triangle Park, NC), we examined the association of serum antioxidants with prevalent asthma, accounting for the complex survey design. To investigate the antioxidant–asthma association, we used a definition of prevalent asthma similar to the definition used by the National Center for Environmental Health, National Asthma Control Program (<http://www.cdc.gov/nceh/airpollution/asthma/default.htm>) and almost exactly the same as the definition used in the most recent report of asthma prevalence

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in the National Health Interview Survey (27). In the National Health Interview Survey (27), two questions were used to identify children with asthma: The first question asked whether the child was ever told by a doctor that he or she had asthma. The second question asked whether the child had an attack of asthma in the past 12 months. The NHANES III questions are almost identical to the National Health Interview Survey questions and produce very similar prevalence estimates, with the exception that the question on current asthma does not refer specifically to the past 12 months but rather asks whether the child "still has asthma." The verbatim text of the questions in NHANES III is this: "Did a doctor ever say that ___ had asthma?" (586 answered yes); "Does ___ still have asthma?" (415 out of 586 answered yes); "Has ___ ever been treated by a doctor for asthma?" (410 out of 415 answered yes); "Apart from when ___ has a cold, does ___'s chest ever sound wheezy or whistling?" (236 out of 415 answered yes; 262 answered yes only to this and no to all other asthma questions).

After examining unadjusted associations, we fitted a series of models to assess the influence of confounding variables. We modeled the antioxidant nutrients one at a time and simultaneously. At first, a minimal set of covariates, including age, race, and sex, was adjusted. For lipid-soluble vitamins, serum cholesterol and triglycerides were also adjusted. Final models adjusted for body mass index, education level of the head of household, an index of household crowding, urban residence, passive and active cigarette smoke exposure, parental history of asthma and/or hayfever, child history of hayfever, child history of severe allergic reaction to shot and/or skin test, and child avoidance of pets due to allergies. Next, the analyses were extended to consider effect modification by cigarette smoke exposure using standard definitions based on serum cotinine (28) to classify children into groups: no smoke exposure, cotinine less than 2.9 ng/ml; passive smoke exposure, cotinine 2.9–20 ng/ml; or active smoke exposure, cotinine of more than 20 ng/ml. Because of the small numbers of active smokers, we did not consider this subgroup ($n = 100$). The statistical significance of interactions was assessed by the deviance, that is the difference in $-2\log$ likelihood

between models with and without the interaction terms. The deviance is distributed as a chi square, with degrees of freedom reflecting the number of terms describing interaction, and exact p values are reported in the results section. In addition, confidence intervals based on Wald's test are given in the text and tables.

RESULTS

Among the 7,962 participants who were less than 17 years of age, 457 were missing all laboratory data and were excluded from further consideration. A further 180 were excluded because they reported chronic bronchitis but no other prevalent respiratory disease. In the age group under consideration, chronic bronchitis is considered a nonspecific diagnosis (29), and inclusion of these subjects in either the diseased or nondiseased subgroup may lead to bias. Three participants were excluded because they could not be classified as either diseased or nondiseased, and a further 1,169 participants were missing data on all of the antioxidant variables of interest. Thus, the final sample was comprised of 6,153 youth: 5,305 without respiratory disease, 415 with prevalent asthma, and 433 with possible asthma and/or wheeze. The latter group was omitted from most of the analysis to avoid misclassification because their answers to questions did not meet the standard required to classify them as probable subjects with asthma.

Participants excluded from the analysis (Table 1) were slightly younger and thus had lower mean height, FEV₁, and body mass index compared with youth included in the analysis. The younger age of excluded subjects may also account for the higher prevalence of passive smoke exposure (approximately twice the rate), as younger children may spend more time in direct contact with

TABLE 1. GENERAL CHARACTERISTICS OF YOUTH INCLUDED AND EXCLUDED IN ANALYSES OF ANTIOXIDANT NUTRIENTS AND ASTHMA, THE THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 1988–1994

	Included ($n = 6,153$)			Excluded* ($n = 1,809$)		
	Mean	SD	%	Mean	SD	%
Age, mo	115.5	46.0		100.6	45.3	
Height, cm	136.6	22.2		127.9	21.6	
FEV ₁ , ml	2,521	810		2,387	825	
BMI, kg/m ²	18.8	4.5		17.7	4.0	
Years education, household head	10.8	3.9		11.4	3.7	
Cholesterol, mg/dl	165.3	28.9		165.9	27.0	
Triglycerides, mg/dl	96.9	55.8		101.0	59.1	
Vitamin E, μ g/dl	775.9	176.8		759.0	164.1	
β -Carotene, μ g/dl	16.5	10.7		14.0	7.3	
Vitamin C, mg/dl	0.96	0.43		0.95	0.42	
Selenium, ng/dl	117.1	14.3		117.6	15.3	
% Asthma and/or wheeze [†]			13.8			11.5
% Asthma [†]			9.5			7.3
% Current asthma [†]			6.7			4.8
% Female			50.5			51.2
% African American			34.8			36.0
Cigarette smoke exposure [‡]						
% Passive			6.5			10.9
% Active			2.4			3.2
% Crowded [§]			45.7			41.8
% Urban			49.3			54.8

Definition of abbreviation: BMI = body mass index.

* Excluded participants were missing data on main study variables (see text for details).

[†] Asthma or wheeze comprises youth reporting ever diagnosed by an MD with asthma and/or wheeze apart from cold in past 12 months. Asthma comprises youth reporting ever diagnosed by an MD with asthma. Current asthma comprises youth answering yes to "ever diagnosed by an MD with asthma" and yes to "still have asthma."

[‡] Cigarette smoke exposure categories are based on serum cotinine: passive smoke exposure, cotinine 2.9 to 20 ng/ml; active smoke exposure, cotinine of 20 ng/ml or more.

[§] Crowded is defined as the ratio of residents in home to rooms in home of more than 1.

smoking adults. A slightly lower percentage of excluded participants reported physician-diagnosed asthma and/or wheeze, perhaps again the end result of younger age, as they would have had less time at risk. Serum vitamin E, serum β -carotene, and serum vitamin C were slightly lower in excluded participants, and the percentage reporting urban residence was higher.

Comparing the characteristics of diseased and nondiseased participants (Table 2), youth with prevalent asthma had higher mean body mass index and lower mean serum selenium and serum β -carotene. A greater proportion of youth with prevalent asthma was male, African American, passive smokers, and living in an urban residence. A slightly lower prevalence of crowded residence was observed in youth with prevalent asthma. The magnitude of the relationship of established risk factors with prevalent asthma in the NHANES III data has been described elsewhere (30–34). In the analyses presented herein, multivariate models were used to adjust for confounding variables, as described later, although the addition of these variables to the regression model had little or no effect on the antioxidant–asthma association. Most of the confounding variables were both strongly associated with asthma and not confounders of the antioxidant–asthma association, suggesting little or no association of the confounders with the serum nutrients investigated.

Table 3 shows the association of serum antioxidant nutrients with prevalent asthma. There was little or no association of serum vitamin E with prevalent asthma, but each of the other serum antioxidants was inversely associated with prevalent asthma (Table 3). A SD increase in serum β -carotene was associated with about a 10% reduction in prevalent asthma (odds ratio [OR], 0.87; 95% confidence interval [CI], 0.7, 1.0). A SD increase in serum vitamin C was associated with a 20% lower prevalence of asthma (OR, 0.81; 95% CI, 0.7, 0.9). A SD increase in serum selenium was associated with approximately a 10% lower prevalence of asthma (OR, 0.88; 95% CI, 0.7, 1.1). Selenium measurements were made on a subgroup of all youth, resulting in less

power to detect effects of the same magnitude in the subgroup with selenium data.

In these cross-sectional data, we cannot separate the effects on incidence versus duration or progression of disease. However, within the group of youth with asthma, among all the antioxidants studied, selenium alone had a strong, positive, statistically significant association with FEV₁ (regression coefficient 73 ml for a SD increase in selenium; 95% CI, 18, 129). This finding suggests a potential role for selenium in disease progression.

Overall, there was little variation in the magnitude of the association of antioxidants with asthma when modified definitions of asthma were considered, but associations were weaker when youth reporting only wheeze apart from a cold were included. The antioxidant–asthma associations were somewhat stronger in fully adjusted models, but the addition of covariates led to slightly wider confidence intervals (Table 3).

To consider the overlap among the antioxidants (vitamin E, β -carotene, vitamin C, and selenium), a simultaneous regression model included all four antioxidants. Because some antioxidants were measured in fewer youth (e.g., selenium only measured on those 12 years old or older), this analysis was limited to the subgroup with complete data (approximately a third of the total group, including 123 with prevalent asthma and 1,418 without). The results were consistent with models considering the antioxidants one at a time (Table 3), with the exception that the association of β -carotene was strengthened (OR, 0.6; 95% CI, 0.4, 0.9), and the association with vitamin C was weakened (OR, 0.9; 95% CI, 0.8, 1.2).

Next, the interaction of the serum antioxidants and smoke exposure was investigated (Table 4). Because of the very small number of active smoke exposed youth ($n \sim 100$), this analysis was limited to a comparison of the antioxidant–asthma association in youth with no smoke exposure and in youth with passive smoke exposure. The consideration of interaction started with a comparison of models with and without the interaction terms,

TABLE 2. GENERAL CHARACTERISTICS OF YOUTH PARTICIPANTS WITH AND WITHOUT ASTHMA, THE THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 1988–1994

	Nondiseased (<i>n</i> = 5,305)			Diseased* (<i>n</i> = 415)		
	Mean	SD	%	Mean	SD	%
Age, months	115.8	45.9		117.3	47.2	
Height, cm	136.6	22.1		138.3	22.4	
FEV ₁ , ml	2,528	811		2,453	738	
BMI, kg/m ²	18.7	4.4		19.8	5.7	
Years education, head household	10.7	3.9		11.5	3.4	
Cholesterol, mg/dl	165.4	29.0		166.4	30.0	
Triglycerides, mg/dl	96.9	55.9		98.4	57.7	
Vitamin E, μ g/dl	776.7	176.2		773.0	185.2	
β -Carotene, μ g/dl	16.7	10.8		15.5	10.3	
Vitamin C, mg/dl	0.97	0.43		0.89	0.40	
Selenium, ng/dl	117.3	14.4		115.7	14.5	
% Female			51.6			42.9
% African American			34.0			43.6
Cigarette smoke exposure†						
% Passive			6.3			8.6
% Active			2.3			2.4
% Crowded‡			46.3			36.6
% Urban			48.8			55.4

For definition of abbreviations, see Table 1.

* Diseased comprises prevalent asthma defined as present if youth answered yes to “ever diagnosed by an MD with asthma” and yes to “still have asthma.”

† Cigarette smoke exposure categories are based on serum cotinine: passive smoke exposure, cotinine 2.9 to 20 ng/ml; active smoke exposure, cotinine of 20 ng/ml or more.

‡ Crowded is defined as the ratio of residents in home to rooms in home of more than 1.

TABLE 3. THE ASSOCIATION OF ASTHMA* WITH 1 SD INCREASE IN SERUM ANTIOXIDANT NUTRIENT CONCENTRATIONS, AMONG YOUTH IN THE THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 1988–1994

Serum antioxidant [§]	Adjusted Demographics Only [†]		Fully Adjusted [‡]	
	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Vitamin E	0.96	0.8, 1.1	0.95	0.8, 1.1
β-Carotene	0.86	0.8, 1.0	0.87	0.7, 1.0
Vitamin C	0.82	0.7, 0.9	0.81	0.7, 0.9
Selenium	0.91	0.7, 1.1	0.88	0.7, 1.1

* Asthma defined as present if youth answered yes to “ever diagnosed by an MD with asthma” and yes to “still have asthma.”

[†] All models are adjusted for age, sex, and race, and models with vitamin E or β-carotene are also adjusted for total serum cholesterol and triglycerides.

[‡] All models are adjusted for age, sex, race, body mass index, passive smoke exposure, active smoke exposure, parental history of asthma and/or hay fever, urban environment, household crowding, years of education of the head of household, childhood history of hayfever, and avoidance of pet ownership caused by allergy. Models with vitamin E or β-carotene are also adjusted for total serum cholesterol and triglycerides.

[§] Number studied varied by antioxidant (diseased/nondiseased) in fully adjusted models are as follows: vitamin E, 368/4,702; β-carotene, 368/4,702; vitamin C, 289/3,565; and selenium, 124/1,472.

using the deviance test. The exact p values for the deviance test were 0.315, 0.111, 0.107, and 0.075 for the interaction of smoke exposure with vitamin E, β-carotene, vitamin C, and selenium, respectively. Serum vitamin E had little or no association with asthma prevalence regardless of smoke exposure. A SD increase in serum β-carotene was associated with a 10% reduction in asthma prevalence in nonsmokers and a 40% reduction in youth with passive smoke exposure. The pattern for vitamin C was similar to the β-carotene results. The strongest evidence of interaction was observed for serum selenium, and among youth with passive smoke exposure, the OR for a SD increase in selenium was 0.5 (95% CI, 0.2, 1.4). The association was much weaker in youth without smoke exposure (OR, 0.9; 95% CI, 0.7, 1.2).

We also assessed nonlinearity in the antioxidant–asthma association and effect modification by race, age, education, and sex. We examined whether there was nonlinearity in the antioxidant–asthma association using the deviance test to compare models with and without polynomial terms for the antioxidants. We detected evidence of nonlinearity only for β-carotene, but the extent of the nonlinearity was so minor as to be unimportant. Thus, when β-carotene was considered as a tertile variable, the effect estimates were similar in the upper two tertiles compared with the lower tertile (ORs were 0.65 and 0.68 for the top two tertiles versus the lowest tertile, respectively). Because the magnitude of the nonlinearity was small, we presented the simpler analysis of the continuous variable. We also examined whether the antioxidant–asthma association differed by age, race, education, or sex using product terms and the deviance test. There

was little or no evidence of effect modification by age, race, education, or sex (15 of 16 p values exceeded 0.15, most exceeded 0.40). One interaction (race by β-carotene) was statistically significant, suggesting an attenuation of the β-carotene effect among Black youth in the top tertile of β-carotene.

DISCUSSION

This study investigates the association of serum antioxidants with asthma in a large, cross-sectional sample of U.S. youth. Serum vitamin E had little or no association with the prevalence of asthma. Both serum β-carotene and vitamin C were significantly associated with a lower risk of prevalent asthma, with stronger associations suggested in the subgroup of youth exposed to cigarette smoke. The point estimate for the selenium–asthma association was 0.88, with a 95% CI of 0.7 to 1.1. In analyses considering effect modification by cigarette smoke exposure, there was evidence of a stronger association among youth who were smoke exposed. Although conventional levels of statistical significance were not reached, tests of the statistical significance of effect modification are often relaxed, particularly if the effect modification has high biological plausibility. With only a few more youth who were passively smoke exposed, the result would have reached the p = 0.05 threshold.

The NHANES III results support a stronger association of some antioxidants, particularly selenium, with asthma in youth who were smoke exposed, but prior studies do not consider effect modification by smoke exposure. In analyses limited to

TABLE 4. THE ASSOCIATION OF ASTHMA* WITH ONE SD INCREASE IN SERUM ANTIOXIDANT NUTRIENT CONCENTRATIONS, BY CIGARETTE SMOKE EXPOSURE, AMONG YOUTH IN THE THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 1988–1994

	No Smoke Exposure [†]		Passive Smoke Exposure [‡]	
	Odds ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Vitamin E [‡]	1.0	0.9, 1.2	1.2	0.8, 1.7
β-Carotene [‡]	0.9	0.8, 1.01	0.6	0.4, 1.1
Vitamin C [‡]	0.9	0.7, 1.0	0.6	0.4, 1.1
Selenium [‡]	0.9	0.7, 1.2	0.54	0.2, 1.4

* Asthma is defined as present if youth answered yes to “ever diagnosed by an MD with asthma” and yes to “still have asthma.”

[†] Cigarette smoke exposure is based on serum cotinine: no smoke exposure (n = 4,924), cotinine of less than 2.9 ng/ml; passive smoke exposure (n = 353), cotinine 2.9 to 20 ng/ml; the active smokers (approximately n = 100) were omitted from this analysis.

[‡] All models are adjusted for age, sex, race, body mass index, urban environment, household crowding, and years of education of the head of household. Models with vitamin E or β-carotene were also adjusted for total serum cholesterol and triglycerides.

children with no smoke exposure, β -carotene and vitamin C were associated with a lower risk of prevalent asthma, consistent with three (15–17) of the six studies considering either fruit/vegetable intake or vitamin C intake (15, 16–20). Two prior studies reported lower asthma risk with vitamin E status (20, 21), but serum vitamin E status had little or no association with asthma risk in the NHANES III data. Many of the prior studies in youth reported the relationship of antioxidant nutrients to asthma-related respiratory symptoms, such as wheeze (15, 16, 18, 20). The difference in outcome definitions may partly account for discrepancies with prior studies (35, 36).

Several other methodologic features of this study deserve consideration. First, the NHANES III findings are based on associations of serum antioxidants with outcome. For some nutrients, for example, carotenoids, quantification via dietary assessment is fairly accurate, whereas for others, such as selenium and vitamin E, dietary assessment methods have low accuracy (37), and the use of biomarkers is preferred. Serum antioxidants are advantageous in that they may better reflect antioxidant availability in the body, although exactly how well serum measures reflect lung tissue-specific status is not well understood. In this cross-sectional study, a potential disadvantage is that current serum antioxidant status may or may not reflect antioxidant status at the time of disease development and may be affected by the disease itself, that is, reverse causality. For example, the lack of an association between serum vitamin E and asthma risk may be explained by reverse causality if participants increased their consumption of vitamin E in response to asthma symptoms and/or diagnosis. With the exception of the vitamin E finding, the potential null bias due to reverse causality would lead to an attenuation of the inverse associations observed for β -carotene, vitamin C, and selenium. The optimal method to quantify nutritional exposures requires a deeper understanding of both the underlying nutritional biochemistry and the natural history of asthma.

Second, the outcome definition we used is based on reported physician diagnosis of asthma and reported current asthma, and therefore, this is a study of prevalent, not incident asthma. Thus, postdiagnostic changes in serum antioxidant levels may affect the results. Asthma itself may cause physiologic changes in serum antioxidant status, perhaps because of the increased oxidant burden associated with disease. However, the possibility of physiologic change associated with the natural history of disease does not negate the idea that improving antioxidant status may delay and/or attenuate asthma progression or severity. Indeed, recent results on supplementation of subjects with asthma lend support to this idea (22). As this analysis uses prevalent cases, it is impossible to separate antioxidant effects on incident disease versus effects on disease duration/progression.

An important difference between this study and prior studies is the consideration of smoke exposure. A stronger association of serum vitamin C, β -carotene, and selenium with asthma was observed in youth who were smoke exposed. We speculate that the inverse association of antioxidants to asthma is stronger in youth who were smoke exposed because their higher exogenous oxidant burden increases their potential to benefit from antioxidants. We used serum cotinine to provide a reliable biomarker of smoking status (28). The use of a biomarker is especially important in youth, where passive exposure to cigarette smoke may comprise an important source of exposure. This biomarker is measured at one point in time and may, therefore, be an imperfect indicator of usual passive smoke exposure. Nevertheless, if measurement error is nondifferential (simply adding noise), the true effects among smoke exposed youth may be stronger.

Antioxidant status may affect asthma risk by influencing the development of the asthmatic immune phenotype, the asthmatic

response to antigen provocation, or the inflammatory response during and after an asthma attack. β -Carotene is a lipid soluble antioxidant that helps to prevent membrane lipid oxidation (6). Vitamin C is present in the extracellular fluid of the lung and functions to counter both exogenous and endogenous sources of oxidation (38–40). Selenium functions as a cofactor for the antioxidant enzyme glutathione peroxidase, which is proposed to counter oxidation and to reduce the synthesis and release of leukotriene B₄, an inflammatory mediator (41). Selenium may also, along with vitamin C, attenuate the activation of nuclear factor kappa- β , a transcription factor that upregulates inflammatory cytokines associated with the asthmatic immune response (42, 43).

In a large cross-sectional study of youth in NHANES III, both serum vitamin C and β -carotene were inversely associated with asthma. Selenium was inversely associated with asthma, with evidence of a stronger association among youth exposed to cigarette smoke. In these data, there was little or no association of vitamin E with prevalent asthma. The cross-sectional study design does not permit causal inference, but the novel findings in this age group suggest a potential role of serum antioxidants in either the prevention of asthma onset and/or the progression of asthma. The findings underscore the importance of careful consideration of cigarette smoke exposure in investigating the role of antioxidants in lung disease.

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