

Letter to the Editor

Milk allergy is associated with decreased growth in US children

To the Editor:

Food allergy has the potential to affect nutrition and growth, yet population-wide studies investigating these issues are limited.¹ Food allergy is often the first manifestation of allergic disease, arising early in life at a time when adequate nutrition is most important for overall growth, brain development, and bone mineralization. Allergen avoidance is the mainstay of treatment for food allergy; however, many of the most common food allergens are integral parts of the typical Western diet and contain macronutrients and micronutrients that are essential for normal growth and development. Even with close supervision, growth in children with food allergy can lag.² Although several studies have assessed the relationship of food allergy, nutrition, and growth in smaller groups of children,²⁻⁸ investigation on a population-wide scale is lacking.

Our objective was to compare anthropometric measurements and dietary intake of calcium, vitamin D, total calories, protein, and fat between children with and without reported food allergy by using National Health and Nutrition Examination Survey (NHANES). NHANES is a continuously obtained, nationally representative cross-sectional survey of the civilian noninstitutionalized population designed with the purpose of assessing the health and nutritional status of the American population. In the 2007-2008 and 2009-2010 NHANES respondents were questioned regarding the presence of food allergy. A full description of these methods is provided in the [Methods section](#) in this article's [Online Repository](#) at www.jacionline.org.

Age-adjusted percentiles for height, weight, and body mass index (BMI) were calculated by using the US Centers for Disease Control and Prevention (CDC)'s Epi Info software package (Epi Info version 3.5.4, 7/23/2008) with comparison with CDC reference growth curves (2000).⁹ Differences in nutrient intake and anthropometric measurements between subjects with and without food allergy were calculated by using linear and logistic regression as appropriate for continuous and dichotomous variables, respectively, in models adjusted for age, sex, race/ethnicity, and income. Survey weights and strata provided with the data were used to account for the complex sampling design and oversampling of NHANES. All of the statistical analyses were conducted with STATA 12.1 software (StataCorp, College Station, Tex).

Six thousand one hundred eighty-nine children aged 2 to 17 years were included in this sample, representing a diverse selection of the US population (see [Table E1](#) in this article's [Online Repository](#) at www.jacionline.org). Overall, 6.3% (95% CI, 5.5% to 7.3%) of children reported a food allergy, with the most common trigger identified as milk (1.8%; 95% CI, 1.3% to 2.3%), followed by peanut (1.2%; 95% CI, 0.9% to 1.6%) and egg (0.6%; 95% CI, 0.4% to 0.8%). After excluding those who reported milk intake in the past 30 days, 1.1% (95% CI, 0.8% to 1.6%) children (n = 58) were classified as having "cow's milk allergy." Characteristics of all children with reported food allergy are shown in [Table E1](#).

Mean weight, height, and BMI percentiles were significantly lower in those with milk allergy in multivariate analyses ([Fig 1](#)) but not in other groups of children with food allergy (see

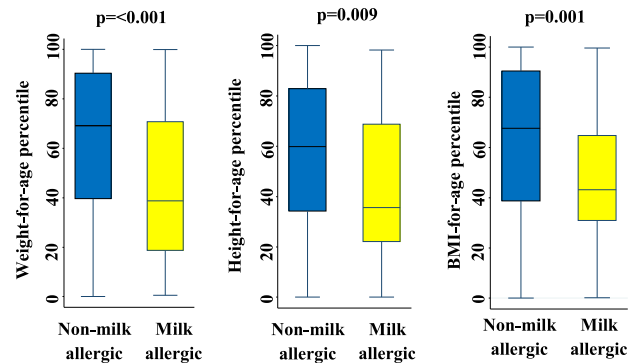


FIG 1. Weighted box plots of anthropometric features for children aged 2 to 17 years comparing children with milk allergy versus those without milk allergy. *P* values are from multivariate linear regression, adjusting for age, sex, race/ethnicity, and income.

[Fig E1](#) in this article's [Online Repository](#) at www.jacionline.org, other data are not shown). Children with milk allergy also had decreased triceps skin folds, a measurement of adiposity (mean difference, 1.8 mm; 95% CI, 0.55-3.05 mm; *P* = .006). Children with milk allergy had lower calcium intake on 24-hour recall and trended toward lower vitamin D and total caloric intake compared with those seen in children without milk allergy ([Table I](#)). However, adjustment for dietary intake of total calories, protein, fat, calcium, and vitamin D did not change our findings of decreased growth measurements in children with milk allergy (see [Table E2](#) in this article's [Online Repository](#) at www.jacionline.org) or adiposity measurements (data not shown). The other groups of children with food allergy had no significant differences in calcium or vitamin D intake, although there were modest differences in fat, protein, and caloric intake with certain other food allergies, including significantly less protein intake in children with peanut allergy (see [Table E3](#) in this article's [Online Repository](#) at www.jacionline.org).

Milk avoidance itself was associated with a trend toward lower mean weight, height, and BMI percentiles for age. However, children with milk allergy had significantly lower weight and BMI percentiles than nonallergic children who were not drinking milk (see [Table E4](#) in this article's [Online Repository](#) at www.jacionline.org). Furthermore, children with milk allergy had significantly smaller triceps skin fold measurements than children without milk allergy who avoided milk (mean difference, 1.85 mm; 95% CI, 0.18-3.52 mm; *P* = .03).

In this nationally representative sample children with milk allergy appeared to be at risk for nutritional compromise in several domains. Our findings are consistent with prior studies involving smaller groups of children suggesting that food allergy in general^{2,6,10} and cow's milk allergy in particular are potential risk factors for decreased weight-for-age percentiles, height-for-age percentiles, or both.^{3,6,7} These studies have also noted decreased growth in the context of low vitamin D and calcium intake.⁶ We found that milk allergy, rather than other reported food allergies, was associated with decreased growth measures.

Although growth differences in children with milk allergy are likely related to the dietary importance of milk, these differences were not entirely explained by milk avoidance or

TABLE I. Mean nutrient intake by milk allergy status

	Milk allergy		Adjusted difference	P value
	Yes	No		
Mean total daily caloric intake (kcal)	1757.6 (1626.5 to 1888.7); SE, 64.4	1887.3 (1851.8 to 1922.8); SE, 17.4	−136.5 (−275.3 to 2.4); SE, 68.1	.054
Mean total daily protein intake (g)	63.1 (55.0 to 71.2); SE, 3.9	67.1 (65.6 to 68.7); SE, 0.8	−4.2 (−12.1 to 3.8); SE, 3.9	.30
Mean total daily fat intake (g)	62.6 (55.0 to 71.2); SE, 4.2	69.2 (67.3 to 71.0); SE, 0.9	−7.0 (−15.5 to 1.6); SE, 4.2	.11
Mean total daily vitamin D intake (D2+D3[IU])	212.2 (107.5 to 316.9); SE, 51.4	308.4 (284.3 to 332.4); SE, 11.8	−84.0 (−169.1 to 1.1); SE, 41.8	.053
Mean total daily calcium intake (mg)	802.2 (702.0 to 902.3); SE, 49.2	1047.0 (1018.5 to 1075.5); SE, 13.9	−251.5 (−359.6 to −143.5); SE, 53.0	<.001

Mean differences determined by using multivariate linear regression, adjusting for age, sex, race/ethnicity, and income, and presented with 95% CIs are shown. Mean values are presented with 95% CIs and SEs. Values in boldface are statistically significant.

energy intake alone. Mechanisms other than inadequate intake could potentially be involved in poor growth, including chronic allergic inflammation, increased metabolic demands, corticosteroid exposure, and comorbid asthma or atopic dermatitis.¹ Although our data suggest that some other mechanism than poor intake might contribute to poor growth in patients with milk allergy, we were not able to distinguish between these possibilities in our analyses. Future research is needed to better understand the factors contributing to poor growth.

There were several limitations to our analysis, including the use of only one 24-hour dietary recall. Although it is known that the use of the 24-hour recall might not accurately estimate the usual intake, we used only the first day of dietary intake because we found that there were substantial missing data for the second day in our population. This likely introduced some measurement error into our dietary estimates, leading to loss of precision. Other limitations include the fact that although our overall sample size is quite large, the number of subjects reporting each food allergy is relatively small, and we relied on self-report of food allergy, which typically overestimates true food allergy. Although we did restrict our definition of milk allergy to those avoiding milk, we did not have these data for other foods nor did we include analyses of consumption of milk in less concentrated forms. However, perception of allergy and the avoidance that follows might have substantial nutritional risks itself, and therefore these results are informative, even in the absence of confirmatory data regarding true allergy. Finally, because of the cross-sectional design of this study, we cannot characterize long-term outcomes in growth restriction or catch-up growth and cannot easily determine other contributing or exacerbating factors, such as corticosteroid use. Despite these limitations, our study is noteworthy for the first description of growth and nutrition patterns of children with food allergy in a large population-based study of US children.

These findings support the need for nutritional supervision, calcium and vitamin D supplementation (where appropriate), and close monitoring of growth for children with milk allergy.

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METHODS

Children aged 2 to 17 years from NHANES 2007-2008 and 2009-2010 were included. This age range was chosen to include a wide range of respondents with a minimum age of 2 years to allow for use of similar growth curves and parameters in all children. NHANES uses a complex multistage probability design, with oversampling of certain subpopulations (ie, non-Hispanic black and Hispanic subjects and those with low incomes). Approval of study procedures for NHANES was obtained through the National Center for Health Statistics Ethics Review Board. A full description of NHANES procedures is available elsewhere.^{E1,E2}

Data from the NHANES Diet Behavior and Nutrition Questionnaire were used for determination of reported food allergy, as described in the main text. Food allergy is defined in NHANES as “a reaction causing a skin rash, hives, difficulty breathing, wheezing, or itching of the eyes, mouth, throat, or skin.” Self-reported food allergy was defined as a positive response to the question “Do you have any food allergies?,” as well as to the follow-up question “What foods are you allergic to?” Listed foods included cow’s milk, egg, wheat, soy products, fish, shellfish, peanut, other nuts, corn, and “other foods.” Because we had previously shown that many subjects with self-reported cow’s milk allergy reported intake of milk,^{E3} we refined our definition of cow’s milk allergy to those reporting cow’s milk allergy and not reporting consumption of liquid cow’s milk (whole, 2% fat, 1% fat, or skim milk in the form of beverages and on cereal) in the last 30 days. Thirty-day intake of egg, peanut, or other foods was not assessed in this questionnaire, and therefore these allergies were defined by self-report alone.

Data collection included interviews completed at respondents’ homes and physical examination and laboratory data obtained at mobile examination centers (MECs). Participants were asked to self-identify race and ethnicity, which in this analysis were consolidated into 4 groups: non-Hispanic white, non-Hispanic black, Hispanic (including Mexican American and others), and other race (including multiracial). The poverty income ratio, the ratio of family income to the poverty level (as defined by the US Department of Health and Human Services), was used as a marker of income.

NHANES participants completed 2 detailed 24-hour dietary recall interviews on nonconsecutive days. Derived nutrient intakes were calculated by the CDC. For the purpose of this analysis, only the first interview was analyzed

because it was the single interview completed in person at the MEC and was thus completed by more subjects. Calcium and vitamin D intakes were calculated from all sources (reported dietary, supplement, and antacid intakes), and total daily vitamin D levels were determined as the sum of ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3) from all sources. Measurements of height and weight and triceps and subscapular skin fold thickness were collected at MECs. Subjects with missing data for different interview/examination components were excluded from analysis of those variables only.

Additional analyses to determine whether differences in intake explained differences in growth parameters between subjects with milk allergy and nonallergic subjects included adjustment for intake of macronutrients and micronutrients (including total calories, protein, fat, vitamin D, and calcium) in the regression models comparing children with milk allergy and nonallergic children and analyses comparing milk drinkers and nondrinkers overall.

Because cow’s milk allergy was hypothesized to have the most significant effect on growth, milk allergy is presented separately. In addition, because many children with other food allergies also have milk allergy, we did further analyses for food allergy (any food), peanut allergy, and egg allergy, adjusting for milk allergy to determine whether results were independent of milk allergy.

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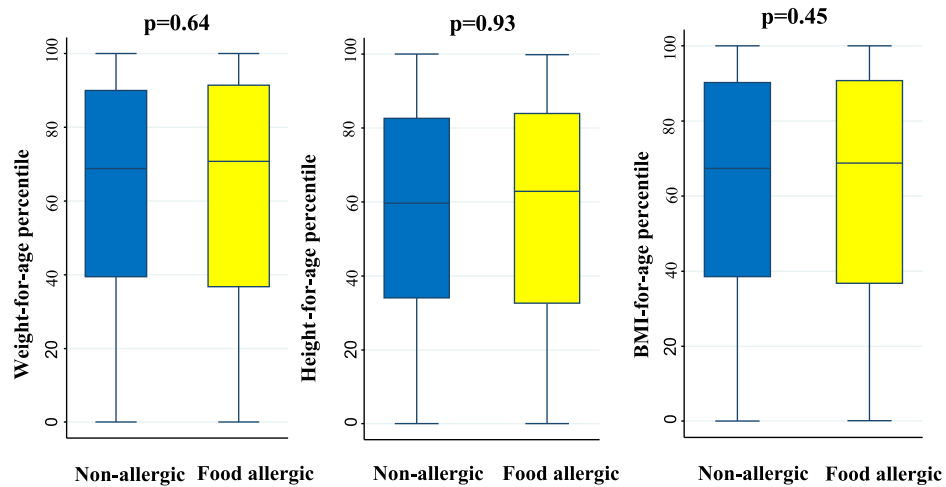


FIG E1. Weighted box plots of anthropometric features for children aged 2 to 17 years comparing children with food allergy (any food) and those without food allergy. *P* values are from multivariate linear regression, adjusting for age, sex, race/ethnicity, and income.

TABLE E1. Study population characteristics

Participant demographics	Entire population	Milk allergy	<i>P</i> value	Food allergy	<i>P</i> value	Egg allergy	<i>P</i> value	Peanut allergy	<i>P</i> value
Male sex (%)	51.1 (49.2-52.9)	36.3 (21.4-54.4)	.10	46.9 (41.1-52.8)	.17	57.1 (34.6-76.9)	.60	56.9 (45.4-67.7)	.32
Mean age (y)	10.0 (9.9-10.2)	10.8 (8.9-12.6)	.40	11.0 (10.3-11.6)	.003	7.9 (5.6-10.1)	.054	9.4 (7.8-11.0)	.39
Ethnicity (%)									
Non-Hispanic white	57.0 (51.4-62.4)	63.6 (48.7-75.8)	.20	54.1 (47.3-60.6)	.057	71.2 (55.9-82.8)	.01	49.9 (37.4-62.3)	.01
Hispanic (Mexican and non-Mexican)	21.0 (16.6-26.2)	10.6 (5.9-18.2)		17.4 (16.8-26.6)		6.9 (2.6-17.5)		11.7 (6.7-19.6)	
Non-Hispanic black	14.2 (11.8-17.0)	15.5 (8.8-25.7)		18.7 (14.6-23.7)		20.5 (10.8-35.4)		21.9 (12.8-34.9)	
Other race (including multiracial)	7.7 (6.1-9.8)	10.7 (4.4-24.0)		9.8 (6.5-14.7)		1.4 (0.2-9.9)		16.5 (8.4-29.9)	
Mean poverty income ratio	2.5 (2.4-2.7)	3.2 (2.7-3.8)	.008	2.5 (2.2-2.8)	1.0	3.3 (2.6-3.9)	.02	2.8 (2.2-3.4)	.051
Reported food allergy									
Any	6.3 (5.5-7.3)								
Milk (reported alone)	1.8 (1.3-2.3)								
Milk (reported and not drinking)	1.1 (0.8-1.6)								
Peanut	1.2 (0.9-1.6)								
Egg	0.6 (0.4-0.8)								

Survey-weighted percentages and means are presented with 95% CIs. *P* values compare the food allergy category with subjects not allergic to that food (or any food for “food allergy”). Values in boldface are statistically significant.

TABLE E2. Mean weight-, height-, and BMI-for-age percentiles for children with and without milk allergy, adjusting for nutrient intake

	Mean difference	<i>P</i> value	Milk allergy, mean difference adjusted for nutrient intake	<i>P</i> value
Weight-for-age percentile	−19.0 (−28.4 to −9.5); SE, 4.6	<.001	−22.8 (−32.9 to −12.7); SE, 5.0	<.001
Height-for-age percentile	−13.2 (−23.0 to −3.5); SE, 4.8	.009	−18.6 (−30.1 to −7.1); SE, 5.6	.002
BMI-for-age percentile	−14.9 (−23.6 to −6.3); SE, 4.3	.001	−14.0 (−23.2 to −4.7); SE, 4.5	.004

Mean differences determined by using multivariate linear regression, adjusting for age, sex, race/ethnicity, and income. Milk allergy adjusted for nutrient intake is adjusted for daily total calorie, protein, fat, calcium (all sources), and vitamin D (D2 plus D3, all sources) intake. Values are presented with 95% CIs. Values in boldface are statistically significant.

TABLE E3. Mean nutrient intake by food allergy status

	Food allergy (any food)				Adjusting for concurrent milk allergy	
	Yes	No	Adjusted difference	P value	Adjusted difference	P value
Mean total daily caloric intake (kcal)	1861.2 (1741.4 to 1980.9); SE, 58.8	1887.6 (1845.9 to 1929.3); SE, 20.5	−60.2 (−228 to 107.9); SE, 82.5	.47	−44.5 (−231.4 to 142.3); SE, 91.7	.63
Mean total daily protein intake (g)	65.3 (59.5 to 71.0); SE, 2.8	67.2 (65.5 to 69.0); SE, 0.9	−3.8 (−11.4 to 3.9); SE, 3.8	.32	−3.7 (−12.4 to 5.0); SE, 4.3	.40
Mean total daily fat intake (g)	67.3 (63.1 to 71.4); SE, 2.0	69.2 (67.2 to 71.2); SE, 0.99	−3.7 (−9.6 to 2.3); SE, 2.9	.22	−3.0 (−9.6 to 3.6); SE, 3.2	.36
Mean total daily vitamin D intake (D2+D3 [IU])	279.5 (232.8 to 326.2); SE, 22.9	309.3 (284.4 to 334.2); SE, 12.2	−12.6 (−60.7 to 35.5); SE, 23.6	.60	1.8 (−45.2 to 48.8); SE, 23.1	.94
Mean total daily calcium intake (mg)	998.9 (889.7 to 1108.2); SE, 53.6	1047.6 (1015.9 to 1079.2); SE, 15.5	−41.9 (−177.8 to 94.0); SE, 66.7	.54	0.30 (−154.4 to 155.0); SE, 75.9	.99
	Egg allergy				Adjusting for concurrent milk allergy	
	Yes	No	Adjusted difference	P value	Adjusted difference	P value
Mean total daily caloric intake (kcal)	1780.1 (1510.9 to 2049.2); SE, 132.1	1886.7 (1851.2 to 1922.2); SE, 17.4	−67.9 (−298.0 to 162.3); SE, 113.0	.55	−34.4 (−242.4 to 173.6); SE, 102.1	.74
Mean total daily protein intake (g)	64.2 (51.8 to 76.7); SE, 6.1	67.1 (65.6 to 68.6); SE, 0.75	−0.37 (−14.2 to 13.4); SE, 6.8	.96	−0.72 (−13.2 to 14.7); SE, 6.8	.92
Mean total daily fat intake (g)	62.0 (51.6 to 72.3); SE, 5.1	69.1 (67.3 to 70.9); SE, 0.89	−6.4 (−13.9 to 1.2); SE, 3.7	.09	−4.8 (−11.7 to 2.2); SE, 3.4	.17
Mean total daily vitamin D intake (D2+D3 [IU])	417.8 (273.8 to 561.7); SE, 70.7	306.6 (282.7 to 330.6); SE, 11.7	103.1 (−17.9 to 224.2); SE, 59.4	.09	129.9 (12.8 to 246.9); SE, 57.5	.03
Mean total daily calcium intake (mg)	1023.7 (801.8 to 1245.5); SE, 108.9	1044.6 (1016.4 to 1072.8); SE, 13.8	−49.7 (−322.1 to 222.8); SE, 133.8	.71	15.1 (−203.5 to 233.6); SE, 107.3	.90
	Peanut allergy				Adjusting for concurrent milk allergy	
	Yes	No	Adjusted difference	P value	Adjusted difference	P value
Mean total daily caloric intake (kcal)	1748.6 (1586.4 to 1910.8); SE, 79.6	1887.7 (1852.4 to 1923.0); SE, 17.3	−120.1 (−243.3 to 3.2); SE, 60.5	.056	−103.0 (−225.1 to 19.0); SE, 59.9	.10
Mean total daily protein intake (g)	59.3 (52.6 to 66.1); SE, 3.3	67.2 (65.7 to 68.7); SE, 0.7	−6.8 (−12.7 to −1.0); SE, 2.9	.02	−6.4 (−12.7 to −0.16); SE, 3.1	.045
Mean total daily fat intake (g)	62.8 (55.7 to 69.9); SE, 3.5	69.2 (67.4 to 71.0); SE, 0.89	−5.5 (−11.5 to 0.5); SE, 3.0	.07	−4.6 (−10.9 to 1.6); SE, 3.1	.14
Mean total daily vitamin D intake (D2+D3 [IU])	357.3 (277.4 to 437.1); SE, 39.2	306.8 (282.9 to 330.6); SE, 11.7	23.5 (−52.5 to 99.4); SE, 37.3	.53	36.8 (−42.5 to 116.1); SE, 38.9	.95
Mean total daily calcium intake (mg)	1057.7 (867.4 to 1247.9); SE, 93.4	1044.3 (1016.4 to 1072.1); SE, 13.7	4.5 (−173.5 to 182.4); SE, 87.4	.96	42.5 (−122.3 to 207.2); SE, 80.9	.60

Mean differences determined by using multivariate linear regression, adjusting for age, sex, race/ethnicity, and income, and presented with 95% CIs and SEs are shown. Mean values are presented with 95% CIs and SEs. Values in boldface are statistically significant.

TABLE E4. Mean measurements and differences in weight-, height-, and BMI-for-age percentiles for children avoiding milk compared with children with milk allergy

	No	Milk avoidance						Milk avoiders: with vs without milk allergy	
		Yes/no milk allergy	Mean difference*	P value	Yes/milk allergy	Mean difference*	P value	Mean difference	P value
Weight-for-age percentile	63.4 (62.3 to 64.5); SE, 0.5	60.3 (56.0 to 64.6); SE, 2.1	−3.84 (−8.3 to 0.6); SE, 2.2	.09	44.9 (35.0 to 54.7); SE, 4.8	−19.3 (−28.7 to 9.9); SE, 4.6	<.001	−15.4 (−26.5 to −4.4); SE, 5.4	.008
Height-for-age percentile	57.5 (56.3 to 58.7); SE, 0.6	53.2 (48.2 to 58.3); SE, 2.5	−4.7 (−10.0 to 0.5); SE, 2.6	.08	45.9 (35.5 to 56.3); SE, 5.1	−13.6 (−23.4 to 3.8); SE, 4.8	.008	−8.9 (−19.3 to 1.6); SE, 5.1	.09
BMI-for-age percentile	62.6 (61.5 to 63.6); SE, 0.5	59.8 (55.8 to 63.8); SE, 2.0	−2.6 (−7.0 to 1.8); SE, 2.2	.23	47.1 (38.2 to 55.9); SE, 4.5	−15.1 (−23.8 to −6.5); SE, 4.2	.001	−12.5 (−23.2 to −1.9); SE, 5.2	.02

Mean differences determined by using multivariate linear regression, adjusting for age, sex, race/ethnicity, and income, and presented with 95% CIs and SEs are shown. Mean values are presented with 95% CIs and SEs. Values in boldface are statistically significant.

*Compared with subjects without milk allergy who were not avoiding milk.