Early childhood weight status in relation to asthma development in high-risk children

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Background: Obesity has been proposed to be a risk factor for the development of childhood asthma.

Objective: We sought to examine weight status from birth to age 5 years in relation to the occurrence of asthma at ages 6 and 8 years.

Methods: Two hundred eighty-five full-term high-risk newborns with at least 1 asthmatic/atopic parent enrolled in the Childhood Origin of Asthma project were studied from birth to age 8 years. Overweight was defined by weight-for-length percentiles of greater than the 85th percentile before the age of 2 years and a body mass index percentile of greater than the 85th percentile at ages 2 to 5 years.

Results: No significant concurrent association was found between overweight status and wheezing/asthma occurrence at each year of age. In contrast, longitudinal analyses revealed complex relationships between being overweight and asthma. Being overweight at age 1 year was associated with a decreased risk of asthma at age 6 (odds ratio [OR], 0.32; $P = .02$) and 8 (OR, 0.35; $P = .04$) years, as well as better lung function. However, being overweight beyond infancy was not associated with asthma occurrence. In fact, only children who were overweight at age 5 years but not at age 1 year had an increased risk of asthma at age 6 years (OR, 5.78; $P = .05$).

Conclusion: In children genetically at high risk of asthma, being overweight at age 1 year was associated with a decreased risk of asthma and better lung function at ages 6 and 8 years. However, being overweight beyond infancy did not have any protective effect and even could confer a higher risk for asthma. (J Allergy Clin Immunol 2010;126:1157-62.)

Key words: *Asthma, overweight, children, high-risk birth cohort*

Both asthma and obesity are major public health concerns that often begin in childhood and share some common risk factors. With the increased prevalence of these 2 conditions in the last 20 years, a natural speculation arose that the development of asthma and obesity might be related.[1] Current evidence favors the association that obesity precedes asthma in adults.[2] In children inconsistent findings have been observed[3-6]; that is, some studies reported an increased risk for asthma in overweight children, whereas others did not. This discrepancy might result from different study designs, especially different ages of the study subjects.

Early childhood is a dynamic period for growth, as well as for disease development. For instance, inadequate nutrition during infancy, the period with most rapid growth in life, could lead to consequences that might be lifelong, harming not only current but also future growth and development.[7] Because both asthma and obesity have roots in fetal and early childhood periods,[8,9] it is important to examine the associations between these 2 conditions beginning from birth. A recent longitudinal study conducted in The Netherlands found that asthmatic symptoms at age 8 years were related to late overweight status at age 6 to 7 years but not early overweight status at age 1 to 2 years.[10] However, the study did not distinguish the effect of being overweight in infancy (ie, the first year of life) from being overweight in later years. In addition, the weight and height data were reported by parents instead of measured by clinicians.

During infancy, human lung parenchyma undergoes a substantial structural remodeling because of alveolar formation and septal restructuring.[11,12] Stimuli or insults during this critical time period can have profound effects on subsequent development of respiratory systems and lung disease processes, including asthma.[13,14]

The objective of this study was to examine the age-related associations between weight status from birth to age 5 years and asthma at age 6 and 8 years. The data used for this study are generated from the Childhood Origin of Asthma (COAST)[15] cohort, which comprises a birth cohort genetically at high risk of asthma because of a parental history of asthma or respiratory allergies. The frequently collected medical information provided us a unique opportunity for this study.

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Abbreviations used
BMI: Body mass index
COAST: Childhood Origin of Asthma
FEV0.5: Forced expiratory volume at timed interval of 0.5 second
FEV1: Forced expiratory volume at timed interval of 1 second
FVC: Forced vital capacity

METHODS

Study subjects

The design and implementation of the COAST study has been described in detail elsewhere.[15] Briefly, a total of 289 full-term newborns with birth weights of greater than 2,000 g were enrolled from November 1998 through May 2000. To qualify, at least 1 parent was required to have respiratory allergies (defined as ≥1 positive aeroallergen skin test result), a history of physician-diagnosed asthma, or both. Of these children, 285 were followed for age 1 year. Among them, 259 children at age 6 years and 238 at age 8 years had asthma diagnoses defined. Height/length and weight data were collected from medical records. Other information was collected prospectively at each planned clinical visit and also at sick visits. The COAST study was approved by the Human Subjects Committee of the University of Wisconsin.

Wheezing and asthma

Wheezing respiratory tract illness and asthma were defined as previously described.[16] A wheezing illness during the first 5 years was defined as meeting 1 or more of the following criteria: (1) physician-diagnosed wheezing at an office visit; (2) an illness for which the child was prescribed short- or long-acting β-agonists, long-term controller medications, or both; or (3) an illness given the following specific diagnoses: bronchiolitis, wheezing illness, reactive airway disease, asthma, or asthma exacerbation. Current asthma was defined based on the documented presence of 1 or more of the following characteristics in the previous year: (1) physician-diagnosed asthma; (2) use of albuterol for coughing or wheezing episodes (prescribed by physician); (3) use of a daily controller medication: (4) step-up plan, including use of albuterol or short-term use of inhaled corticosteroids during illness; and (5) use of prednisone for asthma exacerbation. Four separate investigators, blinded to any antecedent histories concerning viral illnesses or patterns of aeroallergen sensitization, independently evaluated each subject for the presence or absence of asthma based on the above criteria.

Pulmonary function tests

Pulmonary function tests were conducted yearly beginning at age 5 years. Three primary indicators of lung function were analyzed: forced vital capacity (FVC), forced expiratory volume at timed intervals of 0.5 second (FEV0.5), and 1 second (FEV1) at ages 6 and 8 years. Percent predicted values for FVC and FEV_1 were calculated according to the equations developed by Wang et al.[17]

Weight status

Height/length and weight data were retrieved from physicians' records obtained during routine well-child visits at ages 2, 4, 6, 9, 12, 18, 24, 30, and 36 months and every annual visit after the age of 3 years. Absolute height/length and weight were converted to sex- and age-specific percentiles by using the 2000 Centers for Disease Control and Prevention growth references.[18] Weight-for length percentiles for children at age 2 years or younger and body mass index (BMI) percentiles for children at age 3 years or older were calculated. A value of greater than the 85th percentile was defined as being overweight.[19]

Birth weight was categorized into 3 groups: (1) low, less than the 15th weight-for-age percentile (only 5 participants had birth weight <2,500 g); (2) average, 15th to 85th percentile; and (3) high, greater than the 85th percentile. Rapid weight gain during infancy was defined as an increase in weight-for-age *z* scores of greater than 0.67 SD from birth to 6 months, which is equivalent to crossing one percentile channel on the Centers for Disease Control and Prevention growth chart.

Statistical analyses

All analyses were performed with SAS (version 9.1.3; SAS Institute, Inc, Cary NC) and R (equivalent to S-Plus, downloadable from http://www.r-project.org) software. The Student *t* test or simple regression was used to compare group differences for continuous variables. Fisher exact or χ^2 tests were used in univariate analyses to compute frequency distributions and test differences in proportions for categorical variables. The associations between asthma and being overweight were examined with logistic regression. Other factors that might contribute to the development of wheezing/asthma were also included in logistic regression models; these included breast-feeding, sex, self-reported maternal asthma, and various environmental factors during the first year of life: dog and cat in the household at birth, smoke exposure, day care attendance, having older children (including siblings and other children) in the household, and wheezing with rhinovirus infection. Breast-feeding groups were defined based on the duration of exclusive breast-feeding for less than 2 months, 2 to 4 months, or 4 or more months. More detailed descriptions of these factors have been described previously.[20-22] Statistical significance was set at an α value of .05 for all analyses.

RESULTS

Study population

Among the 285 COAST children followed up to age 1 year, 259 (91%) at age 6 years and 238 (84%) at age 8 years had sufficient data to be evaluated for asthma by using the preset criteria. No significant difference was found between these subsets of children and the overall group of 285 children with respect to the descriptive statistics in Table I.

Prevalence of being overweight and wheezing from birth to age 8 years

The prevalence of overweight status increased from 15% at age 1 year to 22% at age 3 years and then stayed about the same between 3 and 8 years of age (Fig 1). Proportionately more children with birth weights of less than the 15th percentile experienced rapid weight gain during the first 6 month of life (34%) compared with those with average birth weights (20%) and high birth weights (2%, $P = .0005$). As a result, a similar percentage of children were found to be overweight at age 1 year among all birth weight groups (11%, 15%, and 20% in the low, average and high birth weight groups, respectively; $P = .51$).

The prevalence of wheezing illnesses decreased from 29% in the first year of life to 14% at age 5 years (Fig 1). Asthma was diagnosed in 28% of children at age 6 years and 33% of children at age 8 years. There were no significant concurrent associations between being overweight and wheezing/asthma at any given age (all $P > .05$).

Associations between weight status at 0 to 5 years and asthma at ages 6 and 8 years

We conducted a longitudinal analysis to determine whether weight status at any age was associated with the subsequent development of asthma ascertained at age 6 or 8 years (Table II for univariate analyses and Table III for multiple regressions). The analyses in Table III show that neither birth weight nor rapid weight gain between 0 and 6 months was associated with asthma. However, being overweight at age 1 year was associated with a lower rate of asthma at age 6 years ($P = .02$) and asthma at age 8 years ($P = .04$). Being overweight beyond age 1 year (ie, age 2, 3, or 5 years) was not related to higher risk of asthma either at age 6 or 8 years (all $P > .05$).

TABLE I. Descriptive statistics of the study population

	Age 1 y (n = 285)	Age 6 y (n = 259)	Age 8 y (n = 238)
Sex			
Male	56% (161)	57% (147)	57% (135)
Female	44% (124)	43% (112)	43% (103)
Maternal allergy			
Yes	83% (230)	82% (207)	83% (195)
No	17% (48)	18% (44)	17% (39)
Maternal asthma			
Yes	42% (115)	43% (106)	41% (93)
No	58% (160)	57% (143)	59% (135)
Exclusive breast-feeding			
<2 mo	43% (122)	42% (110)	41% (98)
2-4 mo	22% (64)	22% (57)	21% (51)
≥4 mo	35% (99)	36% (92)	37% (89)
Smoking exposure during infancy			
Yes	25% (71)	25% (64)	24% (56)
No	75% (214)	75% (195)	76% (182)
Day care attendance during infancy			
Yes	54% (153)	55% (142)	55% (130)
No	46% (132)	45% (117)	45% (108)
Having older children in the household during infancy			
Yes	58% (166)	59% (154)	60% (143)
No	42% (119)	41% (105)	40% (95)
Dog in household at birth			
Yes	35% (101)	36% (92)	36% (85)
No	65% (184)	64% (167)	64% (153)
Cat in household at birth			
Yes	29% (84)	29% (76)	29% (68)
No	71% (201)	71% (183)	71% (170)
Wheezing with rhinovirus infection during infancy			
Yes	16% (47)	17% (45)	17% (41)
No	84% (238)	83% (214)	83% (197)
Birth weight percentile	53.3 ± 29.1	53.6 ± 29.0	53.5 ± 28.9
Weight-for-length percentile at 1 y	49.0 ± 30.6	48.8 ± 30.5	49.0 ± 30.3
Weight for-length percentile at 2 y	49.7 ± 32.2	50.1 ± 32.3	49.8 ± 32.0
BMI percentile at 3 y	55.8 ± 28.6	56.5 ± 28.5	56.5 ± 28.2
BMI percentile at 5 y	59.3 ± 28.2	59.4 ± 28.1	59.0 ± 27.7

We next tested weight change between ages 1 and 5 years in relation to the subsequent development of asthma. We discovered that children who were overweight at age 5 years but not at age 1 year had an increased risk of asthma at age 6 years compared with children who were overweight at age 1 year only ($P = .05$, Table III). Those children overweight at age 5 years only had the highest asthma rate (38% [age 6 years, Table II]), followed by those with normal weight at both ages 1 and 5 years (30%), followed by children overweight at both ages (21%), and the lowest (11%) rate was found in those who were overweight at age 1 year only.

Associations between weight status at age 1 year and lung function at ages 6 and 8 years

Weight-for-length at age 1 year was positively correlated with pulmonary function test values at ages 6 and 8 years (Table IV). In general, weight-for-length at age 1 year was positively correlated with FVC, $FEV_{0.5}$, and FEV_1 values at ages 6 and 8 years. These correlations remained significant after adjusting for height status (ie, on percent predicted FVC and percent predicted FEV_1 at age 8 years; Table IV).

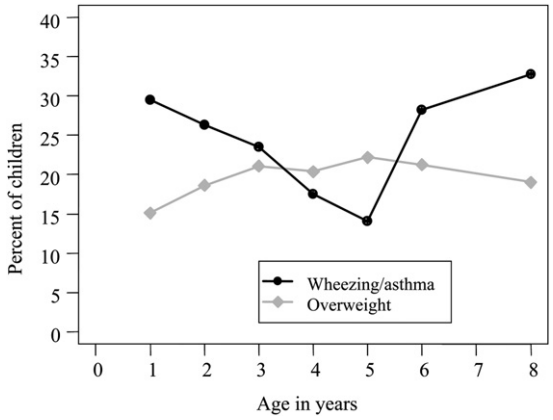

FIG 1. Prevalence of overweight status and wheezing/asthma during the first 8 years of life. Asthma diagnosis was not available for age 5 years or younger, and therefore the prevalence of wheezing was plotted. At age 6 and 8 years, the prevalence of asthma was plotted.

TABLE II. Occurrence of asthma at ages 6 and 8 years by weight status at different ages

	Asthma at 6 y		Asthma at 8 y	
	Percentage	No.	Percentage	No.
Birth weight				
<15th Percentile	30	10 (n = 33)	42%	13 (n = 31)
15th-85th Percentile	27	47 (n = 177)	30	49 (n = 162)
>85th Percentile	33	16 (n = 49)	36	16 (n = 45)
Rapid weight gain at 0-6 mo				
<0.67 z score	27	57 (n = 209)	32	62 (n = 192)
>0.67 z score	30	14 (n = 46)	32	14 (n = 44)
Weight-for-length at 1 y				
<15th Percentile	31	16 (n = 52)	38	18 (n = 48)
15th-85th Percentile	30	51 (n = 169)	33	52 (n = 456)
>85th Percentile	16	6 (n = 38)	24	8 (n = 34)
Weight-for-length at 1 y				
<85th Percentile	31*	67 (n = 214)	36	70 (n = 197)
>85th Percentile	16	6 (n = 38)	24	8 (n = 34)
Weight-for-length at 2 y				
<85th Percentile	28	58 (n = 201)	33	61 (n = 187)
>85th Percentile	27	13 (n = 48)	33	14 (n = 43)
BMI at 3 y				
<85th Percentile	27	53 (n = 195)	33	60 (n = 181)
>85th Percentile	28	15 (n = 54)	27	13 (n = 48)
BMI at 5 y				
<85th Percentile	27	54 (n = 199)	32	60 (n = 186)
>85th Percentile	32	18 (n = 56)	33	16 (n = 49)
Weight change between 1 and 5 y				
Never overweight	30	52 (n = 173)	35	56 (n = 160)
Overweight at 1 y only	11	2 (n = 19)	21	4 (n = 19)
Overweight at 5 y only	38†	14 (n = 37)	35	12 (n = 34)
Overweight at 1 and 5 y	21	4 (n = 19)	27	4 (n = 15)

*$P < .05$, χ^2 test.
†$P < .05$ compared with the group who were overweight at 1 year only.

DISCUSSION

The prospectively followed birth cohort in the COAST project provided us with an excellent opportunity to investigate the associations between weight status in the first 5 years and having asthma at ages 6 and 8 years. The findings demonstrate that in the COAST children, who are genetically at high risk of asthma, being

TABLE III. Adjusted associations between asthma at ages 6 and 8 years and weight status at different ages

	Asthma at 6 y			Asthma at 8 y		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Birth weight*			.73			.84
<15th Percentile	0.78	0.24-2.51		1.01	0.32-3.23	
15th-85th Percentile	0.72	0.32-1.63		0.82	0.36-1.90	
>85th Percentile	1.00			1.00		
Rapid weight gain at 0-6 mo			.78			.71
>0.67 *z* score	1.11	0.50-2.51		0.86	0.37-1.96	
<0.67 *z* score	1.00			1.00		
Weight-for-length at 1 y			.07			.10
<15th Percentile	3.42	0.97-12.05		3.78	1.09-13.13	
15th-85th Percentile	3.36	1.19-9.54		2.71	0.97-7.62	
>85th Percentile	1.00			1.00		
Weight-for-length at 1 y			.02			.04
<85th Percentile	3.14	1.17-8.44		2.85	1.07-7.57	
>85th Percentile	1.00			1.00		
Weight-for-length at 2 y			.62			.48
<85th Percentile	1.23	0.55-2.73		1.35	0.59-3.10	
>85th Percentile	1.00			1.00		
BMI at 3 y			.92			.30
<85th Percentile	1.04	0.50-2.15		1.51	0.69-3.30	
>85th Percentile	1.00			1.00		
BMI at 5 y			.81			.49
<85th Percentile	0.91	0.45-1.88		1.31	0.61-2.82	
>85th Percentile	1.00			1.00		
Weight change between 1 and 5 y			.12			.21
Normal	4.20	0.84-20.96		3.40	0.79-14.64	
Overweight at 1 y only	1.00			1.00		
Overweight at 5 y only	5.78	1.03-32.45		2.87	0.57-14.42	
Overweight at 1 and 5 y	1.80	0.25-12.77		1.30	0.20-8.39	

OR, Odds ratio.

*Other variables included in the analysis were sex, maternal asthma, environmental factors during the first year (eg, breast-feeding, dog and cat ownership, smoke exposure, day care attendance and having older children in the household), and wheezing with rhinovirus infection. In addition to these variables, birth weight was included in other models.

TABLE IV. Pulmonary function tests by first-year weight status

		Weight-for-length at age 1 y			
	Correlation*	<15th Percentile	15th-85th Percentile	>85th Percentile	*P* value†
At age 6 y					
FVC (% predicted)	0.13	103.88 (11.19)	106.86 (13.90)	108.44 (13.98)	.46
FEV_1 (% predicted)	0.12	102.50 (12.02)	105.55 (14.44)	105.50 (11.39)	.55
FVC	0.25‡	1.42 (0.20)§‖	1.53 (0.24)	1.60 (0.28)	.02
FEV_1	0.22‡	1.25 (0.18)§‖	1.34 (0.22)	1.37 (0.20)	.06
$FEV_{0.5}$	0.21‡	0.95 (0.17)‖	1.01 (0.18)	1.04 (0.16)	.11
At age 8 y					
FVC (% predicted)	0.25‡	103.74 (12.26)‖	107.20 (12.60)	112.27 (11.74)	.04
FEV_1 (% predicted)	0.24‡	96.42 (14.05)‖	101.21 (13.63)	103.38 (11.19)	.10
FVC	0.30‡	1.84 (0.30)‖	1.92 (0.30)‖	2.08 (0.28)	.01
FEV_1	0.29‡	1.50 (0.28)‖	1.59 (0.26)	1.68 (0.20)	.04
$FEV_{0.5}$	0.25‡	1.12 (0.22)§‖	1.20 (0.22)	1.24 (0.18)	.05

*Correlation coefficients between weight-for-height percentiles at age 1 year and lung function test scores.

†Overall group comparisons from simple regression.

‡$P < .05$, correlation coefficient test.

§$P < .05$ compared with weight-for-length 15th-85th percentile group.

‖$P < .05$ compared with weight-for-length greater than 85th percentile group.

overweight at age 1 year was associated with a decreased risk of asthma and greater lung function at ages 6 and 8 years. Beyond age 1 year, being overweight at 2 to 5 years of age was no longer protective for asthma development at age 6 or 8 years. In fact, in our study population late onset of overweight status (ie, being overweight at age 5 years but not at age 1 year) was associated with a higher risk for asthma at ages 6 and 8 years. These findings provide evidence of the complex relationships between age, overweight status, and wheezing/asthma development.

The effect of overweight status on the subsequent development of asthma during childhood has been previously reported.[3-6,10,23] Many of the studies focused on weight status at birth, during

preschool age, or during school age. Very few of them examined overweight status during infancy.[8] One study conducted in a general population in The Netherlands[8] found that a high BMI between 1 and 2 years of age was not associated with later asthma symptoms if the weight status became normal. Whether being heavier at age 1 year has a protective effect was not analyzed separately in this study.[8] However, the study showed that the late onset of overweight status at age 6 to 7 years, instead of "persistent high BMI" between 1 and 2 years and 6 and 7 years, was associated with a significantly increased risk of asthma symptoms at age 8 years, which might indicate protective effects of early overweight status at age 1 years, 2 years, or both on asthma development.[8] Similar findings were observed in our cohort for asthma at ages 6 and 8 years, although the result at age 8 years did not reach statistical significance. One possible reason for the insignificant test result at age 8 years is that some of the children in the group who were overweight at 1 year only became overweight at 6 to 7 years (data not shown), which might increase their risk of asthma at age 8 years. As noticed in our study, the percentage of asthmatic children at age 8 years in this group who were overweight at 1 year only was almost doubled compared with that at age 6 years (11% at age 6 years vs 21% at age 8 years).

It is interesting to speculate why overweight status at age 1 year was associated with a decreased risk of asthma at ages 6 and 8 years. One possible explanation is that children on the top 15th percentile of growth chart at age 1 year were in general well nourished, and this promoted maximum postnatal lung development and alveolarization. Accordingly, our children with weight-to-height percentiles at greater than 85% had increased lung function at ages 6 and 8 years. Alveolar development begins during gestation and continues through ages 1 and 1.5 years or even longer.[11,12] Most of the alveoli are added through multiplication during this time.[24]

Therefore nutritional influences on alveolarization during infancy could have profound and long-lasting effects on lung function and perhaps the development of lung disease far beyond infancy. The concept of programming, in which growth in early life exerts long-term effects on the structure and function of particular organs and tissues, is well established in epidemiologic and animal studies.[7,25] For example, small body size at birth or in infancy has been associated with an increased risk of asthma[26-30] and low lung function.[31-34] In addition, low weight gain during infancy was found to be associated with modest reductions in adult lung function.[35] On the other hand, abundant nutrition during infancy that would encourage maximum physical growth and development might reduce the risk of subsequent lung disease.

Current evidence shows that children who were overweight during infancy tended to be overweight in later years,[36,37] and a similar trend was observed in our study population (data not shown). Establishing a pattern of overweight status could be problematic given that overweight/obesity is a major risk factor for many metabolic diseases.[36] However, many of the association studies did not evaluate when children became overweight, and this could lead to biased assumptions about weight status in infancy. It is not clear whether health is impaired for children who were overweight in infancy and then subsequently were of normal weight. More studies are needed to thoroughly understand the role of growth during infancy on subsequent health.

The longitudinal design of the COAST study enabled us to examine age-related differences in the relationship between weight and asthma risk, and the excellent retention in this cohort added to the validity of the results. Limitations in the present study include the fact that this is a high-risk population for allergic diseases, and results from this study need to be confirmed in the general population. Second, the sample size was relatively small, and this limited subgroup analyses. Third, overweight status was defined by BMI (weight-for-length percentile if a child was younger than 2 years old) instead of the actual percentage of body fat. However, in children, using BMI to define overweight status has been endorsed by major organizations, and it shows a high degree of correlation with the percentage of body fat.[38,39] Finally, parental weight status was not taken into account. This is not likely to introduce bias in the study because evidence shows that parental obesity is not a significant contributor to early childhood obesity, especially in the first 2 years of life.[40,41]

In conclusion, our findings suggest that association between weight and childhood asthma changes with age. Although obesity might promote asthma in later life, these findings suggest the possibility that nutrition during infancy should be optimized to promote lung growth and development and that this could have effects in reducing asthma risk later in childhood. On the other hand, after the first year of life, attention needs to be focused on balanced nutrition to prevent becoming overweight and obese beyond infancy, which might be a potential risk factor for asthma. Again, further studies are needed to validate these findings in both high-risk and general populations, as well in children who are premature, those with very low birth weight, or both.

Key message

- **High body weight at age 1 year is associated with a decreased risk of asthma and better lung function at ages 6 and 8 years in children with a parental history of asthma or atopy.**

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