

Hospitalization for Asthma: Atopic, Pulmonary Function, and Psychological Correlates Among Participants in the Childhood Asthma Management Program

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ABSTRACT. *Background.* Asthma in childhood has a significant impact on children and families, in part because of the frequent need for hospital-based care for acute exacerbations. Sensitization and exposure to inhalant allergens have been identified as risk factors for asthma hospitalization.

Objective. The Childhood Asthma Management Program (CAMP), comprised of 1041 children aged 5 to 12 with mild-to-moderate asthma, provides the opportunity to identify specific risk factors for prior hospitalization for asthma.

Methods. Data gathered during the screening period from CAMP were evaluated to elucidate differences between patients who had ever been hospitalized for asthma before enrollment in CAMP and those who had never been hospitalized.

Results. Univariate analyses indicated that prior hospitalization for asthma was associated with a younger age of asthma onset, longer duration of asthma, greater number of positive allergy skin tests, higher serum immunoglobulin E level, greater peripheral blood eosinophilia, greater recent inhaled corticosteroid use, greater airflow obstruction, greater airway hyperresponsiveness, and lower patient intelligence quotient (IQ). Gender, race, and family income did not differ between hospitalized and never-hospitalized patients. The combination of both sensitization and exposure to high levels of dog allergen (Can f1) was associated with greater likelihood of prior hospitalization. Forward multivariate logistic regression analysis identified younger age of asthma onset, longer duration of asthma, recent use of asthma controller therapy, greater airflow obstruction, and lower patient IQ as significant risk factors for prior hospitalization when all risk factors identified by univariate analysis were included in the model.

Conclusions. Children with mild-to-moderate asthma who had a past hospitalization for acute asthma had greater asthma severity, younger age of onset, and lower patient IQ at the time of entry into CAMP. They also had more markers of atopy than children without prior hos-

pitalization, although atopy was not associated with prior hospitalization on multivariate analysis. Although we have identified these risk factors in a retrospective manner, one can speculate that the persistence of these features should alert the clinician to closely follow abnormalities on pulmonary function tests and general features of atopy to potentially identify patients at risk for future hospitalization. *Pediatrics* 2003;112:e85–e92. URL: <http://www.pediatrics.org/cgi/content/full/112/2/e85>; childhood asthma, hospitalization, Childhood Asthma Management Program, asthma symptoms, lung function, allergen exposures, bronchial hyperresponsiveness, psychosocial factors.

ABBREVIATIONS. IQ, intelligence quotient; CAMP, Childhood Asthma Management Program; FEV₁, forced expiratory volume in 1 second; FEV₁PC₂₀, concentration of methacholine that causes a 20% fall in FEV₁; CBCL, Child Behavior Checklist; IFS, Impact on Family Scale; IgE, immunoglobulin E; OR, odds ratio; PEF, peak expiratory flow.

Asthma is the most common chronic disorder in childhood, affecting >4 million children in the United States.¹ Acute exacerbations of asthma in children aged 0 to 14 years resulted in over 190 000 hospitalizations in 1999.² Furthermore, despite advances in understanding the pathobiology of asthma and proliferation of guidelines on the diagnosis and management of asthma, the rates of hospitalization and mortality from asthma have begun to gradually decline only recently.² Thus, the impact of asthma on patients, families, and the medical community is substantial.

Atopy is a nearly universal finding in children with asthma.^{3–5} Exposure to environmental factors, particularly inhalant allergens, is commonly reported as a precipitant of acute exacerbations of asthma. Studies have identified an association between allergic sensitization and/or exposure to inhalant allergens and hospitalization for acute asthma.^{6,7} The ability to generalize these findings to other populations of patients with asthma is unclear, as these studies focused on patients with significant asthma-associated morbidities, as reflected by emergency department use and hospitalization, rather than patients with less severe or controlled disease. Furthermore, the comparison groups in these studies consisted of patients without asthma rather than patients with asthma who did not require hospital-

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based care, possibly resulting in an overestimate of the impact of atopy and environmental exposures on emergency department use or hospitalization for asthma.

Although environmental factors undoubtedly contribute to asthma exacerbations leading to acute care visits and hospitalization, additional factors are likely to be involved because most, but not all, patients with asthma have evidence of sensitivity to inhalant allergens.^{5,8} Such factors include viral infections,^{9,10} younger age,¹ and poor adherence to asthma medication regimens.¹¹ The inability of families to recognize the early signs of an asthma exacerbation and initiate appropriate therapy at home likely contributes to the development of more severe asthma episodes and, therefore, increased need for hospital-based services.¹² The level of psychological functioning of children and their families influences the care they are capable of providing for asthma, and those families with greater dysfunction may seek emergency care for asthma episodes more often than families with lesser dysfunction. The critical role of psychological functioning in asthma management is illustrated by the identification of nonadherence to medications, family dysfunction, and low intelligence quotient (IQ) as significant risk factors for life-threatening and fatal asthma.^{13–15} Previous studies have focused on one or a small number of factors which may predispose to the need for hospital-based asthma care, but no study has provided a comprehensive examination of factors reflective of disease severity, atopic background, and psychological characteristics, which likely interact to modify the risk of asthma exacerbation and hospital-based care.

The Childhood Asthma Management Program (CAMP), which includes 1041 children aged 5 to 12 years with mild-to-moderate asthma, provides an opportunity to elucidate the role of many of these factors on the need for acute, hospital-based care for asthma. This report compares markers of atopy, pulmonary function, and psychological characteristics of CAMP participants with prior hospitalization at any point during the patient's lifetime with CAMP participants without prior hospitalization in an attempt to delineate the relative importance of these factors.

METHODS

CAMP is a prospective clinical trial initiated in 1991 to examine the long-term effects of 3 treatment strategies on lung growth and development in children with asthma. Eight clinical centers enrolled 1041 children aged 5 to 12 years with asthma of mild-to-moderate severity between December 1993 and September 1995. The details of the study design and methods have been reported elsewhere.¹⁶ Children were eligible for inclusion in the trial if, during 6 of the 12 months preceding trial entry, they 1) had asthma symptoms at least twice per week; 2) used an inhaled bronchodilator at least 2 times per week; and/or 3) used asthma medication daily. Patients were excluded if they had a forced expiratory volume in 1 second (FEV_1) <65% predicted or a concentration of methacholine that causes a 20% fall in FEV_1 (FEV_1PC_{20}) to methacholine of >12.5 mg/mL. Patients with severe asthma, as defined by 2 or more hospitalizations in the year before screening, 6 or more oral steroid bursts in the year before screening, or intubation at any time in the past because of asthma, were also excluded. All participants completed a 28-day screening pe-

riod during which they completed daily asthma diary cards and demonstrated evidence of mild-to-moderate asthma while receiving only albuterol on an as-needed basis.

Research coordinators collected data from parents/guardians regarding demographics, history of asthma symptoms and severity, prior asthma therapy, and characteristics of the home environment. Spirometry was performed at the randomization visit, whereas methacholine challenge and allergy skin testing were performed before the randomization visit as previously described.⁵ Home allergen determinations were performed as previously described.⁵ Each parent or guardian signed an informed consent statement, and participants signed an assent statement approved by each clinical center's institutional review board.

Patient Population

A total of 1041 children were enrolled into the CAMP trial. Asthma severity, as assessed by physician or nurse coordinator, was mild in 47.8% ($n = 498$) and moderate in 52.2% ($n = 543$). The mean age of onset of asthma (physician diagnosis) was 3.9 ± 2.6 years and mean duration of asthma was 5.0 ± 2.7 years. Males constituted a slight majority of the population (59.7%), which included 68.3% white and 31.7% non-white participants.

Thirty-one percent ($n = 320$) of CAMP participants reported being hospitalized for asthma at least once during their lives, with only 6% ($n = 66$) of participants having been hospitalized once during the year before the trial (information on total number of hospitalizations before CAMP was not collected). Because of the low percentage of patients with a hospitalization during the prior year, we focused our analysis on those patients who had been hospitalized at any time during their life.

Psychological Evaluation

Participants underwent a series of neurocognitive and individual and family functioning assessments during the screening period. Neurocognitive assessment instruments administered by psychometricians included the *Wechsler Preschool and Primary Scale of Intelligence* (age 5) and the *Wechsler Intelligence Scale for Children III* (ages 6–18). Psychometricians also administered the following standardized and widely used instruments to assess individual and family functioning: the Child Behavior Checklist (CBCL), the Family Environment Scale, the Children's Depression Inventory, the Revised Childhood Manifest Anxiety Scale, the Medical Outcome Study Social Support Survey, and the Impact on Family Scale (IFS).

Data Analysis

All analyses were performed using baseline data from the 1041 CAMP participants. For the purposes of cross-tabulation and logistic regression, dust levels for all allergens other than cockroach were divided into 4 categories: high, moderate, low, and undetectable; cockroach levels were categorized as positive versus undetectable (limit of detection was 0.4 U/g). We categorized the level of dust mite exposure based on levels that have been associated with sensitization and recurrent wheezing (undetectable [<20 ng/g], low [20–1999 ng/g], moderate [2000–9999 ng/g], or high [$\geq 10\,000$ ng/g]).¹⁷ For house dust mites, an undetectable allergen level was used as the reference category for the logistic regressions because there were sufficient samples for analysis that were below the limits of sensitivity of the assays. For cat, dog, and mold allergens, low and undetectable (dog [Can f1] <150 ng/g, cat [Fel d1] <20 ng/g, mold 0 CFU/g) levels of exposure were combined for use as the reference category as there were insufficient samples with levels below the sensitivity of the assays to be labeled undetectable. Pulmonary function measures were analyzed as continuous variables. Immunoglobulin E (IgE) levels and FEV_1PC_{20} were log-transformed. Logistic regressions were done to calculate the adjusted relative odds of a child having been previously hospitalized by asthma history (duration and age of onset), exposure and sensitization to dog allergen, number of positive skin tests, total IgE, medication usage, pulmonary function, psychological characteristics, and demographic variables. Because of the large number of possible explanatory variables, forward logistic regression was used to select the most parsimonious model from the candidate variables. Forward logistic regression enters each variable individually into the model and keeps a variable only if its P value, when added to the variables already in

the model, is $<.05$. Clinic, race, income, and gender were forced to be included in the final model. P values were derived from Wald's test, were nominal, 2-tailed, and were not adjusted for multiple looks or multiple outcomes. Data were analyzed using the SAS System for Windows, version 8.0, with a P value of $<.05$ considered statistically significant.

RESULTS

Demographics

Children with a prior hospitalization for asthma had a significantly earlier age of asthma onset (based on age at physician diagnosis, $P = .0001$) and longer duration of asthma ($P = .0001$) than those patients who had never been hospitalized for asthma (Table 1). The gender and racial distributions did not differ between the children with a prior hospitalization and

the children without prior hospitalization. There was no significant difference in annual family incomes between the 2 groups (28% of patients with prior hospitalization came from families with an annual income $< \$30\,000$ compared with 23% of patients without hospitalization, $P = .07$). Parental reports of cough with or without exercise and nocturnal awakenings due to asthma within the previous 6 months did not differ between these 2 groups.

Atopic Markers and Allergen Exposure

Patients with histories of hospitalization for asthma had a higher frequency of having at least 1 positive allergen skin test ($P = .02$), a greater mean number of positive skin tests per patient ($P = .0004$),

TABLE 1. Patient Characteristics

	Total (N = 1041)	Prior Hospitalization* (N = 320)	No Prior Hospitalization* (N = 721)	P Value
Demographics and asthma history				
Mean age at randomization (SD), y	8.9 (2.1)	8.9 (2.1)	9.0 (2.1)	.47
Median	8.9	8.7	9.0	
Mean age at asthma diagnosis (SD), y	3.9 (2.6)	2.9 (2.0)	4.3 (2.7)	.0001
Median	3.5	2.5	4.0	
Mean duration of asthma (SD), y	5.0 (2.7)	6.0 (2.5)	4.6 (2.6)	.0001
Median	4.8	5.6	4.3	
Male (%)	59.7	63.8	57.8	.07
Income $< \$30\,000$ (%)	24.2	27.8	22.6	.07
Race				
White (%)	68.3	68.1	68.4	
Black (%)	13.3	15.0	12.5	
Hispanic (%)	9.4	8.4	9.9	.63
Other (%)	9.0	8.4	9.3	
Nocturnal awakening attributable to asthma (≥ 1 /mo last 6 mo; %)	55.3	56.3	54.8	.66
Cough with or after exercise (≥ 1 /mo last 6 mo; %)	75.6	74.4	76.1	.56
Cough independent of exercise (≥ 1 /mo last 6 mo; %)	73.3	71.8	74.0	.45
Atopic features				
At least 1 positive skin test (%)†	83.9	87.8	82.1	.02
Mean number positive skin tests (SD)†	3.4 (2.6)	3.8 (2.6)	3.2 (2.6)	.0004
Median serum IgE (midrange), IU/mL	433 (173, 1221)	517 (208, 1400)	419 (155, 1168)	.02
Mean total eosinophils (SD), cells/mm ³	484.3 (422.2)	541.5 (476.4)	459.1 (393.8)	.004
Asthma medication use in past 6 mo				
Cromolyn or nedocromil (%)	33.2	40.9	29.8	.0004
Inhaled corticosteroid (%)	25.7	29.8	23.9	.046
Oral corticosteroid (%)	35.4	42.5	32.2	.001
Theophylline (%)	2.2	3.8	1.5	.02
Pulmonary function				
Mean Pre-BD FEV ₁ , % predicted‡	93.7 (14.3)	91.6 (14.5)	94.7 (14.1)	.001
Mean Pre-BD FEV ₁ /FVC‡	0.80 (0.08)	0.78 (0.09)	0.80 (0.08)	.0001
Mean % change in FEV ₁ after BD‡	9.0 (7.5)	10.7 (8.3)	8.2 (7.0)	.0001
Mean daily PEF variability (%)§	11.4 (7.4)	12.1 (8.9)	11.1 (6.6)	.05
Mean FEV ₁ PC ₂₀ (mg/mL)¶	1.11 (3.3)	0.96 (3.2)	1.2 (3.2)	.006
Psychological variables				
Mean IFS total impact score (midrange)	32.8 (10.5) (24, 40)	35.1 (11.0) (25, 42)	31.8 (10.1) (23, 39)	.0001
Mean IQ (midrange)**	106 (15) (96, 116)	104 (16) (92, 114)	107 (15) (98, 116)	.001
Mean CBCL total competence (midrange)††	50.2 (8.9) (44, 56)	49.0 (9.0) (43, 56)	50.7 (8.8) (45, 57)	.008

SD indicates standard deviation; BD, bronchodilator.

Data are means (SD), midrange = 25th, 75th percentile.

* Ever during lifetime.

† Ten core allergens were tested (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat, dog, American cockroach, German cockroach, penicillium, aspergillus, Timothy grass, short ragweed).

‡ Mean daily peak flow variability = $|PEF_{AM} - PEF_{PM}| / ((PEF_{AM} + PEF_{PM}) / 2)$.

¶ Geometric mean (SD).

significantly greater median serum IgE level ($P = .02$), and mean peripheral blood eosinophil count ($P = .004$) compared with patients never admitted for asthma (Table 1). There was a significant difference between participants with prior hospitalization and those without hospitalization with respect to the frequency of exposure to high, moderate, and low/undetectable levels of dog allergen (Can f1; 20%, 17%, and 62% for the hospitalized patients vs 16%, 25%, and 59% for the never-hospitalized patients, respectively, $\chi^2 P = .01$). Also, sensitization to dog allergen and current exposure to levels of Can f1 >8000 ng/g was associated with greater likelihood of hospitalization (odds ratio [OR]: 1.8, $P = .01$). There was no difference between participants with prior hospitalization and those without hospitalization with respect to the frequency of exposure to high, moderate, low, or undetectable levels of house dust mite (18%, 21%, 38%, and 23% for the hospitalized patients vs 23%, 20%, 36%, and 21% for the never-hospitalized patients, respectively, $P = .5$). There was no significant difference in the likelihood of a prior asthma admission between patients with a positive skin test to Der p1 and patients with a negative Der p1 skin test after stratifying for the level of Der p1 in the patient's homes (data not shown). Furthermore, sensitization to either *Dermatophagoides pteronyssinus* or *Dermatophagoides farinae* and current exposure to levels of Der p1 + Der f1 >2 mcg/g was not associated with a greater likelihood of prior asthma hospitalization ($P = .6$). No differences were noted for sensitization and current exposure to cat, cockroach, and mold allergens in the home (data not shown).

Medication Use

Prior hospitalization was associated with an increased likelihood of having received a long-term asthma controller medication at least once per week in the 6 months preceding CAMP entry, including theophylline (3.8% vs 1.5%, $P = .025$), cromolyn or nedocromil (41% vs 30%, $P = .0004$), and inhaled steroids (30% vs 24%, $P = .046$). Patients with prior hospitalization were more likely to have used oral steroids in the past 6 months (42% vs 32%, $P = .001$; Table 1).

Pulmonary Function

Significant differences in lung function existed between the children with prior hospitalization and those children never hospitalized for asthma (Table 1). Prior hospitalization was associated with significantly more prebronchodilator airway obstruction, as evidenced by lower FEV₁ percent predicted ($P = .001$) and lower FEV₁/FVC ($P = .0001$). Prior hospitalization was associated with a larger percent change in FEV₁ following bronchodilator ($P = .0001$), borderline statistically significant greater variability in peak expiratory flow rates in the 28-day screening period before randomization ($P = .05$), and significantly greater bronchial hyperresponsiveness to methacholine (FEV₁PC₂₀, $P = .006$).

Psychological Features

Families with prior hospitalization had higher IFS total impact scores ($P = .0001$; Table 1), implying a greater impact of asthma on the level of function of these families and their quality of life. The group with a history of hospitalization had a lower mean IQ ($P = .001$). Parents of children who had never been hospitalized reported that their children had greater difficulty with psychological adaptation, as reflected by higher scores on the CBCL ($P = .008$). No differences were detected in CBCL externalizing or internalizing T-scores; Family Environment Scale scores for cohesion, expressiveness, and conflict; Children's Depression Inventory scores; Revised Childhood Manifest Anxiety Scale total anxiety score; or Medical Outcome Study Social Support Survey total support score (data not shown).

Multiple Logistic Regression Analyses

Forward multiple logistic regression analysis was performed using factors identified by univariate analysis as being significantly different between the 2 groups (Table 2). Factors remaining in the final model associated with prior hospitalization when all of the candidate variables were taken into account were: younger age at onset of asthma (OR: 2.22; $P < .001$), longer duration of disease (OR: 1.93; $P = .001$), regular use of cromolyn or nedocromil (at least once a week over the past 6 months; $P = .007$) or inhaled

TABLE 2. Multiple Logistic Regression Analyses

Variable	OR for Prior Hospitalization	95% CI	P Value
Age at onset (below median vs at or above median)*	2.22	1.50, 3.28	<.001
Duration of asthma (at or above vs below median)†	1.93	1.29, 2.87	.001
Cromolyn or nedocromil use in past 6 mo	1.66	1.15, 2.39	.007
Inhaled or oral corticosteroid use in past 6 mo	1.62	1.16, 2.26	.005
Pre-BD FEV ₁ /FVC	0.96	0.94, 0.98	<.001
IQ	0.98	0.97, 0.99	.005

CI indicates confidence interval; BD, bronchodilator.

Forward regression was used to select which explanatory variables to include in the final logistic regression model. Candidate variables not selected for inclusion in the final model were: positive skin tests (any vs none), peripheral blood eosinophils, serum IgE, use of theophylline, IFS, CBCL total competence score, PEF variability, Pre-BD FEV₁ (% predicted), reversibility, FEV₁PC₂₀, and exposure and sensitization to dog allergen. The final model was forced to include gender, race, income, and clinic. $N = 798$ because of missing values.

* Median age at diagnosis was 3.5 years.

† Median duration of asthma was 4.8 years.

or oral corticosteroids was associated with an increased risk of prior hospitalization ($P = .005$), greater airflow obstruction, as measured by prebronchodilator FEV₁/FVC ratio ($P < .001$), and lower IQ ($P = .005$).

DISCUSSION

This study has demonstrated that children with mild-to-moderate asthma with a prior hospitalization for asthma had, on enrollment into the CAMP trial, more severe asthma defined by airway obstruction (lower FEV₁/FVC ratio), as well as recent need for controller medication before entry into CAMP. Prior hospitalization was also more common among children with a younger age of asthma onset, longer duration of disease, and lower IQ.

Despite strong associations on univariate analysis, atopic features (skin test reactivity, IgE level, peripheral blood eosinophils) were not identified by multiple regression as independent risk factors for hospitalization. Airway reactivity also was not included in the final regression model. Given the strength of the associations on univariate analysis, it may be that atopy and airway reactivity underlie the factors identified by the forward multiple regression model (eg, airflow obstruction) and hence contribute to the outcome of hospitalization indirectly.

Recent studies have suggested an association between allergic sensitization to inhalant allergens and hospitalization for asthma.^{6,7} Features of the control groups used complicate the interpretation of these studies. Sporik et al⁶ studied 82 children admitted to hospital for acute asthma compared with 44 controls who had a positive family history for atopy. They found that 81% of children over 5 years of age admitted to hospital for asthma were sensitive to dust mites or cat and exposed to high levels of allergen compared with 25% of nonasthmatic controls. It is not surprising that children hospitalized for asthma had a higher prevalence of inhalant allergen sensitivity than individuals without asthma, because the prevalence of atopy in children with asthma far exceeds the prevalence of atopy in the general childhood population. Sarpong and Karrison⁷ retrospectively reviewed charts of 138 allergy clinic patients and demonstrated that allergic sensitivity to cat, but not to house dust mite, was significantly associated with hospitalization in the previous year. We have also demonstrated that children with a prior asthma hospitalization are more likely to have allergic sensitization to inhalant allergens than children without a prior hospitalization. However, after adjusting for other asthma-related factors through multiple logistic regression, the effect of atopy was no longer present. In this population, atopy may have been too prevalent for the association to remain when other factors are taken into account. Another potential explanation for the absence of a direct effect of allergic sensitization on prior hospitalization is that allergic sensitization is a dynamic process and it is possible that the pattern of sensitization at the time of a prior hospitalization may have differed from the sensitization pattern demonstrated during screening for CAMP. In contrast to our findings, the National Co-

operative Inner-City Asthma Study demonstrated that children 4 to 9 years of age living in major inner-city areas who were both sensitized and exposed to high levels of cockroach allergen were significantly more likely to have been hospitalized for asthma over a 1-year period.¹⁸

Underlying asthma severity, as evidenced by greater airway obstruction among patients with prior hospitalization for asthma, appears to predispose this group of children to hospitalization. These findings, combined with the greater prevalence of atopic markers, airway reactivity, and reversibility, further strengthen the association between allergic airway inflammation, more severe asthma, and prior hospitalization. Although greater asthma severity is related to prior hospitalization, it should be noted that patients with mild asthma often have severe exacerbations, suggesting that ongoing asthma severity may be dissociated from exacerbation severity.¹⁹

Younger age of asthma onset conferred a greater risk of lifetime asthma hospitalization, perhaps attributable to smaller airway caliber. This finding is consistent with current epidemiologic data for asthma hospitalizations, with the highest rates of hospitalization for asthma over the last 2 decades occurring in the pediatric age group, especially in children 0 to 4 years of age.² The younger age of onset and longer duration of disease also increases the time period during which a child may have been hospitalized for asthma. Previous studies have documented that ethnic minorities and children from lower socioeconomic status groups experience higher rates of hospitalization for asthma.²⁰⁻²² This pattern was not identified in the current study. Potential explanations include a relatively small sample size compared with the large epidemiologic surveys of hospitalization. The large number of patients enrolled from 8 centers across North America makes the CAMP cohort far more representative than most groups of asthmatics studied. The CAMP cohort is not an atypical group of children with mild-to-moderate asthma, but rather a group that is less disadvantaged than those studied in other reports. Selection of children from families with higher levels of motivation and asthma understanding than those in the general population may explain the differences between the current study and the epidemiologic studies that have described racial and socioeconomic disparities in asthma hospitalization.²³ Unlike National Cooperative Inner-City Asthma Study, very few families that participated in CAMP had annual family incomes below \$15 000 (only 6.5% of families), minimizing the number of patients from the lowest socioeconomic status level. Furthermore, the mild-to-moderate disease severity of CAMP participants may influence the pattern of asthma hospitalization. These factors may have also influenced the patterns of health care the children received before CAMP, likely resulting in less reliance on hospital-based acute care for asthma (emergency department, inpatient care) and greater accessibility to health care providers in non-emergency settings, leading to lower rates of hospital admission than have been

shown in other populations. Duration of asthma was identified as a significant risk factor for prior hospitalization, even after adjusting for age of onset of asthma. Although related, both characteristics apparently increase the likelihood of an exacerbation of severity sufficient to warrant hospitalization. It is probable that many of these admissions occurred early in the lives of the participants. This is also reflected by the fact that only 6% of CAMP participants were hospitalized in the year preceding trial entry and that age at randomization was similar in the 2 groups.

Patients with a prior hospitalization did not report a difference in asthma symptoms over the 6 months preceding CAMP enrollment. Recent asthma symptoms were also not more prevalent among the subgroup of 66 CAMP patients who were hospitalized during the year before CAMP (data not shown). The lack of association between recent symptoms and prior hospitalization may reflect improved asthma control resulting from greater recent medication use in response to the prior hospitalization. Alternatively, this may reflect a dissociation between ongoing asthma severity and the severity of acute episodes, as severe exacerbations can occur in those patients with mild ongoing asthma severity. Similarly, the more frequent use of corticosteroids, either inhaled or oral, in the 6 months before the start of the trial by patients with prior hospitalization may be an indicator of greater underlying disease severity or may reflect a modification in therapy in response to a prior hospitalization. Although the magnitude of difference between the groups in terms of peak expiratory flow (PEF) variability and bronchodilator responsiveness are small, these differences are statistically significant and are in the expected direction, with previously hospitalized children demonstrating greater PEF variability and bronchodilator reactivity, suggesting greater asthma severity. Although PEF variability and FEV₁ response to bronchodilator might not be useful in making a clinical decision in any given patient, the results focus a clinician on assessing pulmonary function and on the importance of values indicating increased airway reactivity.

The results of the psychological evaluations of patients with prior hospitalization demonstrate that family psychological characteristics may impact risk of hospitalization. The lower IQ in the group with prior hospitalization suggests that this group of patients, as well as their families, may have greater difficulty in mastering the intellectual challenges necessary for optimal asthma management, both on a chronic basis and for acute episodes. Children without hospitalizations had higher CBCL Total Competence scores, indicating that they were perceived to have greater social and academic capability than reported by parents of the hospitalized children. Higher IFS scores in the hospitalized group indicates that these parents perceive the child's asthma as having a more disruptive impact on family life than reported by parents of nonhospitalized children. Collectively, these results suggest that families with less psychological resources, seen in lower IQ and competence scores in the children and more distress over

the child's illness, may have a greater difficulty effectively managing the child's illness well enough to avoid hospitalization.

The results of this study are derived from a group of children who met the enrollment criteria for the CAMP trial. Specifically, the exclusion of children with 2 or more hospitalizations within the year before CAMP was essential to maximize patient safety and exclude patients with more severe and uncontrolled disease. Thus, our findings must be interpreted in the context of children with 0 or 1 hospitalization in the preceding year. It is uncertain how these findings would be altered if patients with more frequent recent hospitalizations were included. Secondly, while patient characteristics were determined at study entry, the data on prior hospitalization is based on parental recall of events, often long in the past. Parent recall does have its limitations. We did not collect data on past hospitalization except for responses to items asking if the child was ever hospitalized and whether there were any hospitalizations for asthma in the year before screening, with 0 and 1 the only counts that were eligible in CAMP. It remains possible that some parents may have incorrectly attributed a prior hospitalization for a different lower respiratory tract illness to asthma.

In this large group of children with mild-to-moderate asthma, prior hospitalization for asthma was associated with several features consistent with greater overall asthma severity, including airflow obstruction, recent use of asthma controller therapy, and psychological functioning. Although strongly associated with prior hospitalization on univariate analysis, atopy was not retained as a risk factor in multivariate analysis, suggesting that the influence of atopy on hospitalization is mediated through other factors. However, sensitization and exposure to high levels of dog allergen at CAMP entry was a risk factor for prior hospitalization in the univariate analyses. Our findings are noteworthy in that most hospitalizations occurred at least 1 year (and likely several years) before CAMP entry; yet such asthma phenotypic differences remained years later. This emphasizes the long-standing impact that follows a hospitalization. It remains probable that the findings described in this report, although determined following a past hospitalization, served as predisposing factors for hospitalization and persist over time. Although we have identified these features in a retrospective manner and that the magnitude of difference between the 2 groups is small, one can speculate that the persistence of these features should alert the clinician to closely follow abnormalities on pulmonary function tests and general features of atopy to identify patients at risk for future hospitalization.

Appendix

CAMP Credit Roster

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