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Risk Factors for Acute Wheezing in Infants and Children: Viruses, Passive Smoke, and IgE Antibodies to Inhalant Allergens

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ABSTRACT. *Objective.* To examine the prevalence of viral infection, passive smoke exposure, and IgE antibody to inhaled allergens in infants and children treated for acute wheezing.

Design. Case-control study of actively wheezing children who were compared with children without respiratory tract symptoms.

Setting. University of Virginia Pediatric Emergency Room.

Patients. Convenience sample of 99 wheezing patients (2 months to 16 years of age) and 57 control patients (6 months to 16 years of age).

Measurements and results. Serum IgE antibody to inhalant allergens, measured by radioallergosorbent test (RAST), was uncommon in wheezing and control patients under age 2. After 2 years of age, the percentage of RAST-positive patients increased markedly and was significantly higher in wheezing patients than controls after age 4 (72%, $n = 54$, and 30%, $n = 40$, respectively, $P < .001$). Total IgE levels and nasal eosinophilia were strongly correlated with a positive RAST after age 2. Viral pathogens, predominantly respiratory syncytial virus, were identified in nasal washes from 70% ($n = 20$) of wheezing patients younger than 2 years of age compared with 20% of controls ($n = 10$), $P < .05$. After age 2, viruses, particularly rhinovirus, were isolated in washes from 31% ($n = 70$) of wheezing patients, 64% of whom were also RAST-positive. Levels of cotinine, a nicotine metabolite, were elevated (≥ 10 ng/mL) in saliva from a large percentage of smoke-exposed, wheezing patients under 2 (74%, $n = 19$) compared with those over 2 (14%, $n = 51$), $P < .001$. Odds ratios for wheezing were significant for virus (8.2, confidence interval [CI] = 1.3 to 5.0), and cotinine (4.7, CI = 1.0 to 21.3) in children under 2, and IgE antibody by RAST (4.5, CI = 2.0 to 10.2), virus (3.7, CI = 1.3 to 10.6), and the combination of IgE antibody and virus (10.8, CI = 1.9 to 59.0) were significant risk factors after age 2.

Conclusion. Wheezing children younger than 2 years of age had a high rate of viral infection and a low rate of IgE antibody to inhalant allergens. When these children were exposed to passive smoke, salivary cotinine levels were elevated suggesting heavy exposure. After 2 years of age, sensitization to inhaled allergens became increasingly important and viruses remained a significant risk factor for wheezing. These data support recommendations to reduce tobacco smoke exposure at home, espe-

cially for young patients, and to consider sensitization to inhaled allergens and allergen avoidance in wheezing children at an early age, particularly after age 2 years. *Pediatrics* 1993;92:535-540; *asthma, bronchiolitis, inhalant allergy, viral respiratory tract infection, environmental tobacco smoke.*

ABBREVIATIONS. RAST, radioallergosorbent test; RSV, respiratory syncytial virus; GM, geometric mean; CI, confidence interval

During the past decade, mortality due to asthma in children has increased.¹ Hospitalization rates for wheezing before age 17 have risen by 4.5% per year with children younger than age 4 contributing disproportionately to this statistic.² These changes have occurred despite our expanding knowledge about the pathophysiology of asthma and emphasis on the usage of anti-inflammatory medications.³ Although some patients experience persistent wheezing, many children have acute wheezing episodes followed by periods of remission. Contributing to the increasing morbidity associated with asthma, environmental exposures to air pollution,⁴ the overuse of inhaled β -agonists,⁵ inadequate anti-inflammatory medications,⁶ and poor access to health care for medically indigent patients have been cited as causes.⁷ In addition, exposure to inhaled allergens, viral infections, and passive tobacco smoke exposure have been correlated with airway hyperreactivity in several studies.⁸⁻¹⁰

In infants, wheezing is often diagnosed as bronchiolitis, and a strong association between viral respiratory tract infections (particularly respiratory syncytial virus [RSV]) and wheezing episodes has been shown.¹¹ Although the prevalence of sensitization (ie, IgE antibody) to inhalant allergens is not clear among infants who wheeze, prospective studies of infants born to allergic families found that IgE antibody to these allergens was not usually detected before age 2 years.^{12,13} In older children, viral pathogens continue to be a risk factor for wheezing.⁹ In addition, sensitization to inhaled allergens, particularly to dust mite allergen, has been demonstrated in up to 60 to 80% of school-aged children with asthma.^{14,15} Passive tobacco smoke exposure has been shown to increase airway hyperresponsiveness in young infants,¹⁶ is related to persistent wheezing in grade school asthmatic children,¹⁷ and is a more

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common exposure among children from lower socioeconomic backgrounds.¹⁸

The purpose of the present study was to examine the relationship of sensitization to inhaled allergens, viral infection, and passive smoke exposure in a non-selected population of infants and children treated for wheezing in a pediatric emergency department. An additional objective was to determine at what age IgE antibody to inhalant allergens in these children can be demonstrated as a risk factor for wheezing.

METHODS

Study Population

Study participants included 99 children entering the University of Virginia Pediatric Emergency Room from September 1988 through March 1992 with the diagnosis of bronchiolitis or asthma. Entering wheezing patients were from 2 months to 16 years of age, had wheezing documented by auscultation, required treatment with at least a β -agonist, and had no history suggestive of bronchopulmonary dysplasia. No patient enrolled in the study had taken systemic steroids before his/her emergency department visit. Fifty-seven control patients were enrolled in the same setting and were excluded if they had respiratory symptoms at the time of initial examination or a previous history of wheezing.

Additional information was obtained from family members by questionnaire and included questions regarding immediate family history (in parents and siblings) for allergic disease, birth history, breast feeding, patient's allergic history, and home tobacco smoke exposure. This study was approved by the human investigation committee at the University of Virginia and informed written consent was obtained from parents and/or subjects.

The University of Virginia is a regional medical center for Central Virginia with approximately 400 pediatric emergency department visits for wheezing annually. Most wheezing children younger than 2 years of age are brought to this emergency department from November through March, whereas older asthmatic patients come more frequently in the spring and fall. In the present study, most patients (94%) were enrolled during the months of September through June. Seventy-eight percent of wheezing children under 2 were enrolled from November through February, and 74% of the wheezing patients over 2 were enrolled during a similar period (October through February). Seventeen percent of all wheezing patients were admitted to the hospital for further management. Additional demographic characteristics of the study population are presented in Table 1.

Immunoassays

Serum from patients was obtained by venipuncture and stored at -20°C until analyzed for IgE antibody to inhalant allergens and for total IgE. Allergen-specific IgE antibody was measured by quantitative radioallergen sorbent test (RAST) using cyanogen bromide-activated filter paper discs coated with extracts from Miles Inc., Hollister-Stier Division, Spokane, WA, as described previously.⁸ Briefly, the allergen extracts used included dust mite (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* tested separately), cat epithelium, short ragweed pollen, rye grass pollen, and mixed cockroach containing allergens from German, American, and Oriental species. Discs coated with extracts were then incubated with patient's serum (diluted 1/4 and 1/16) and IgE antibody bound to allergen was detected using radiolabeled goat anti-human IgE. Using *D farinae*-coated discs, a reference control curve was established for each assay with serial twofold dilutions of pooled serum containing 2500 RAST units/mL of IgE antibody to *D farinae*. Three negative and three positive control sera were run with each assay. Sera containing ≥ 40 RAST units/mL to an allergen (equivalent to ~ 4 ng/mL of allergen-specific IgE antibody) were considered positive.⁸ Total serum IgE was measured using a monoclonal antibody-based radioimmunoassay described previously.⁸

Virology

For young children (eg, less than age 5 years) approximately 1 mL of normal saline was instilled into each nostril and secretions aspirated using a Tym-Tap disposable aspirator (Xomed Products, Inc., Jacksonville, FL). Approximately 2 mL of saline were instilled

in the nares of older patients as they held their breath, after which they blew their retained secretions into a sterile plastic cup. The secretions were transferred to vials containing 1 mL of a veal infusion broth (pH 7.4) containing vancomycin (20 $\mu\text{g/mL}$), gentamicin (50 $\mu\text{g/mL}$), and amphotericin B (1 $\mu\text{g/mL}$). For the detection of RSV, cell pellets were processed within 4 hours, and a commercially prepared direct fluorescent antibody assay was used to stain for RSV antigen (Ortho Diagnostic Systems, Inc., Raritan, NJ). Duplicate monolayers of primary rhesus monkey kidney, human embryonic lung fibroblast (WI-38 strain), A-549, and Ohio HeLa cell lines were inoculated with 0.2 mL volumes of sample from each patient to isolate parainfluenza (types 1, 2, 3, and 4) virus, RSV, rhinovirus, adenovirus, influenza A and B viruses, and enterovirus using standard techniques.

Nasal Smears for Eosinophils

After obtaining nasal washes, a cotton swab was used to transfer excess mucoid secretions from beneath the inferior turbinate of the nose to a glass slide. When dry, secretions were treated with Hansel's stain (Lide Laboratories, Florissant, MD), and each slide was examined under oil immersion by three individuals who recorded the total number of eosinophils present per 100 cells counted on three or more fields. Using mean values recorded by the three examiners, nasal smears containing >10 eosinophils/100 cells counted were regarded as positive and indicative of at least moderate eosinophilia as judged by a scale proposed by Lim.¹⁹

Tobacco Smoke Exposure Measurements

In addition to obtaining information about the number of smokers in the home, saliva samples were collected from each patient. The samples were centrifuged to remove mucin and the supernatants were stored at -20°C . Cotinine, a principal metabolic derivative of nicotine, was measured using an inhibition radioimmunoassay described previously.²⁰ This assay is sensitive for cotinine levels ≥ 1.0 ng/mL. An excellent correlation between serum and salivary cotinine determinations has been reported using this assay, and others have reported a close relationship between saliva, serum, and urine measurements in distinguishing active from nonactive smokers.^{21,22}

Statistical Analysis

To compare wheezing patients and controls, logistic regression models were derived, and the presence or absence of wheezing was used as the dependent variable.²³ Other variables, such as the presence or absence of virus or IgE antibody by RAST, were used as independent variables. A significant regression coefficient associated with one of the latter variables indicates that the variable is able to discriminate between wheezing patients and controls. Regression coefficients from these models were used to estimate odds ratios and 95% confidence intervals. When samples were small we relied on Fisher's exact test.²³ Two sample *t*-tests were used to compare continuous variables between wheezing patients and controls in the different age groups. All tests of significance were two-sided.

RESULTS

IgE Antibody and Eosinophils

Of the 23 patients less than age 2 years who had wheezing, only two (9%) had specific IgE antibody to one or more of the inhalant allergens tested (ie, were RAST-positive) (Fig 1A). Both of these patients were 22 months old and had IgE antibody to dust mite allergen (one also had IgE to rye grass). In this age group, no control patient had IgE antibody to the allergens tested. Only one nasal smear, from one of the 22-month-old RAST-positive patients, contained >10 eosinophils/100 cells counted (Fig 2). Among 21 wheezing patients between 2 and 4 years of age, sera from 35% were RAST-positive compared with 20% from controls (Fig 1A). In this age group, 32% of the wheezing patients, all but one of whom were RAST-positive, had positive nasal smears for eosinophils (Fig 2).

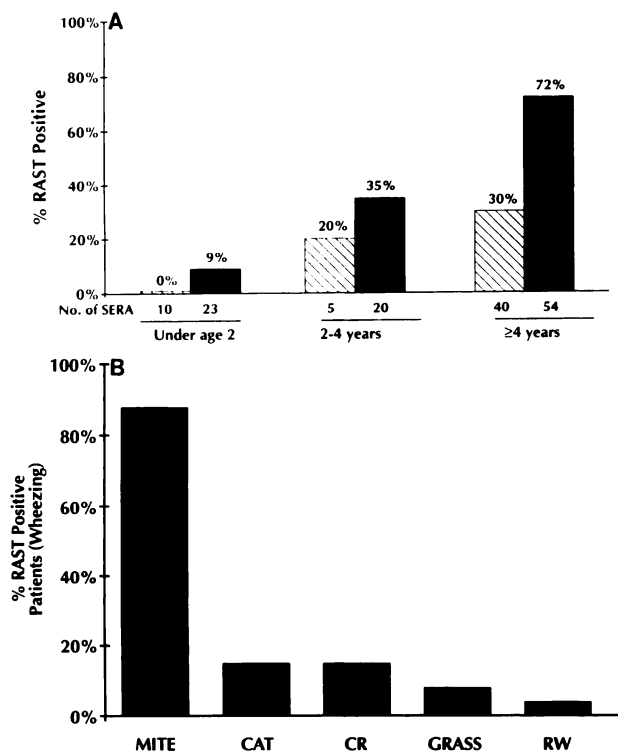


Fig 1. A, IgE antibody to inhalant allergens in sera from wheezing patients (black bars) and controls (hatched bars). In each serum, titers of IgE antibody were measured by radioallergosorbent test (RAST) to dust mite, cat, cockroach, rye grass, and ragweed allergens. Sera containing ≥ 40 RAST units/mL (approximately equivalent to 4 ng of allergen-specific IgE antibody/mL) to one or more of the allergens tested were defined as being RAST-positive. B, Percentage of sera from all RAST-positive wheezing patients (ages 22 months to 16 years), $n = 48$, with IgE antibody specific for allergens in dust mite, cat, cockroach (CR), rye grass, and ragweed (RW) extracts.

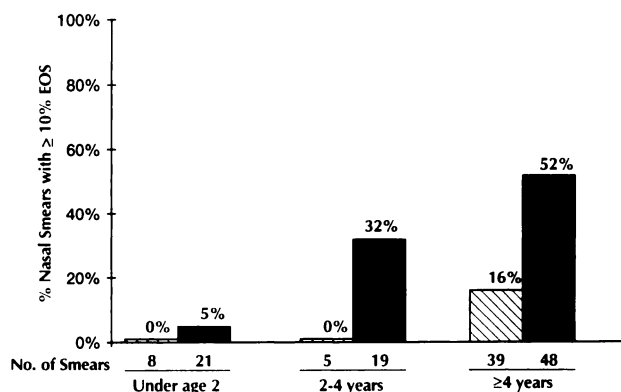


Fig 2. Eosinophils (EOS) in nasal secretions. The percentage of nasal smears containing ≥ 10 eosinophils/100 cells counted is shown for wheezing patients (black bars) and controls (hatched bars). These smears were regarded as positive and indicative of at least moderate eosinophilia as judged by a scale proposed by Lim.¹⁹

After 4 years of age, 72% of the wheezing children were RAST-positive compared with 30% of controls, $P < .001$ (Fig 1A). Most of the RAST-positive patients (86%) had IgE antibody to dust mite allergen (Fig 1B). Nasal smears were positive for eosinophilia in 52% of wheezing patients in this age group, compared with 16% of the controls, $P < .001$ (Fig 2). Among wheezing patients with a positive nasal

smear, 91% were also RAST-positive. Among the RAST-positive wheezing patients, 64% had a positive smear.

Questionnaire analysis for family history showed a higher prevalence of allergy-related symptoms (asthma, rhinitis, and eczema) in immediate family members of wheezing patients, compared with controls older than age 2 years, $P < .001$ (Table 1). This difference was not apparent before age 2. Measurements of total serum IgE revealed low levels for both wheezing and control patients less than age 2 (Table 1). After age 2 years, total IgE levels for wheezing patients differed significantly from controls, $P < .001$. An increase in total serum IgE was evident in wheezing children from 2 to 4 years of age (GM = 86 IU/mL; 95% CI, 37 to 196 IU/mL) and, in addition, RAST-positive wheezing patients after age 2 years had significantly higher total IgE levels than the RAST-negative patients (GM = 365 and 67 IU/mL, respectively, $P < .001$).

Detection of Viruses

Cultures from 70% of nasal washes from wheezing patients under age 2 were positive for virus (Fig 3). Of these, ten (50%) were positive for RSV, three for rhinovirus, one for influenza B, and one was positive for both RSV and enterovirus. In children older than 2 years of age, 31% of the cultures from washes were positive for virus. Sixteen were positive for rhinovirus, only three for RSV, two for enterovirus, and one for influenza A. Among this virus positive group, 64% (14 of 22 patients) were also found to be RAST positive. However, the percentages of virus positive washes from RAST positive and RAST negative wheezing patients were similar ($14/44 = 32\%$ and $8/24 = 33\%$, respectively). In both age groups, significantly fewer washes from control patients were positive for virus (Fig 3).

Smoke Exposure

Seventy-five percent of all wheezing patients and 58% of control patients had one or more smokers present at home as judged by questionnaire. Analysis of cotinine concentrations in saliva revealed high levels in many of the children younger than 2 years of age. The geometric mean of cotinine determinations was significantly elevated for wheezing patients in this age group compared to controls (9.8 and 4.3 ng/mL, respectively, $P < .05$); however, fewer control patients were exposed to smoke at home (Fig 4). After age 2 years, cotinine concentrations in saliva from wheezing and control patients did not differ significantly (GM = 3.6 and 3.5 ng/mL, respectively). In previous studies of salivary cotinine, levels ≥ 10 ng/mL have been reported to be indicative of heavy passive smoke exposure.²⁴ Among the smoke-exposed patients in this study, cotinine levels ≥ 10 ng/mL were detected in a significantly larger percentage of wheezing children under age 2 (74%, $n = 19$) as compared with wheezing children over age 2 (14%, $n = 51$), $P < .001$ (Fig 4). All wheezing and control patients with cotinine levels ≥ 10 ng/mL ($n =$

TABLE 1. Patient Characteristics

	Children <2 y		Children >2 y	
	Wheezing Patients (n = 23)	Controls (n = 11)	Wheezing Patients (n = 76)	Controls (n = 46)
Mean age, y	0.9	1.2	7.1	9.6
Age range, y	0.2–1.8	0.5–1.8	2.0–15.4	2.3–16.1
Male, %	57	33	73	65
Black, %	74	44	55	31
Payment requirement*				
100%	9	60	19	34
10–75%	14	0	26	10
0%	77	40	55	56
Family history for allergy, %	61	73	81	36
Total IgE (IU/mL)†	15 (9–25)	5 (3–11)	198 (135–206)	28 (18–41)

* Payment requirement categories reflect the proportion of the emergency department bill charged to the patient's family based on annual family income. Shown are the percentage of families required to pay 100%, from 10 to 75%, or 0% of their child's bill.

† Total IgE levels are reported as geometric means followed by 95% confidence intervals in parentheses.

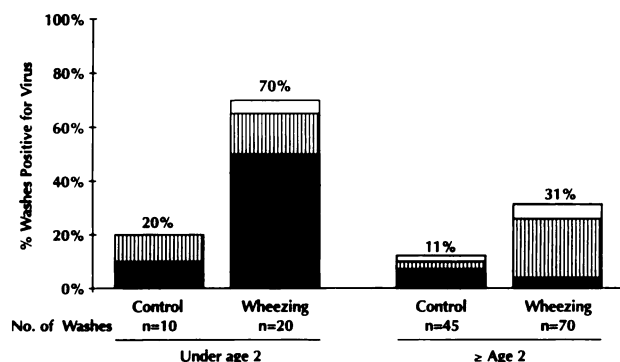


Fig 3. Viral detection in nasal washes. Respiratory syncytial virus (black bars) was detected by a direct fluorescent antibody assay, and all antigen-positive washes were also positive in culture using a WI-38 fibroblast cell line. Hatched bars indicate rhinovirus and open bars indicate other viral isolates. The percentages of cultures positive for virus were significantly greater for wheezing patients compared with controls for children less than age 2 years ($P < .05$) and more than age 2 years ($P < .05$).

27) were noted by questionnaire analysis to be exposed to one or more smokers at home, except one (Fig 4).

Combined Risk Factors

Sixty-six percent of wheezing patients in the study had evidence for two or more of the risk factors compared with 28% of control patients, $P < .001$. Before age 2 years, 67% of wheezing patients had both exposure to tobacco smoke and a positive viral culture. After age 2 years, 64% had at least two of the three risk factors. Odds ratios based on logistic regression models were used to examine the significance of positive RAST results, viral cultures, and heavy passive smoke exposure (cotinine ≥ 10 ng/mL) in wheezing children relative to controls (Table 2). Children less than age 2 years in this study were eight times more likely to be wheezing if they had a positive viral culture than if they did not. They were also more likely to be wheezing if they had cotinine levels ≥ 10 ng/mL. Among children over age 2, RAST positivity was strongly associated with wheezing, and viral infection remained a significant risk factor. In addition, the combination of IgE antibody by RAST together with a positive viral culture was pres-

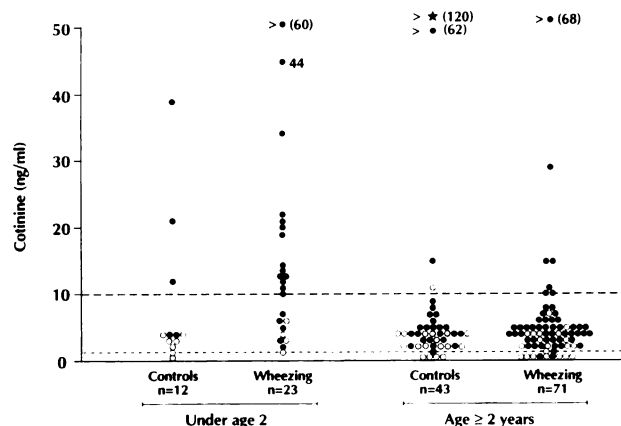


Fig 4. Salivary cotinine levels. Solid circles indicate children who were exposed to one or more smokers at home as disclosed by questionnaire analysis. Open circles represent patients who were not exposed. One 14-year-old control patient actively smoked (indicated by a star). Cotinine levels ≥ 10 ng/mL (long dashed line) have been reported to reflect heavy passive smoke exposure.²⁴ Values < 1 ng/mL (short dotted line) fell below the limits of the assay.

TABLE 2. Odds Ratios for Wheezing Among Children with a Positive Radioallergosorbent Test (RAST), Virus Culture, or Elevated Cotinine Level

Risk Factors	Odd Ratios*	
	< age 2 y	> age 2 y
RAST	—†	4.5 (2.0–10.2)‡
Virus	8.2 (1.3–51.0)§	3.7 (1.3–10.6)§
Cotinine ≥ 10 ng/mL	4.7 (1.0–21.3)§	0.6 (0.2–2.2)
RAST and Virus	—†	10.8 (1.9–59.0)‡

* Reported odds ratios are univariate analyses followed in parentheses by 95% confidence intervals.

† Not determined because of insufficient positive patients.

‡ $P < .001$. The odds ratio of 10.8 was estimated assuming that one control patient was positive for both RAST and virus.

§ $P < .05$.

ent in 14 wheezing children over age 2 years as compared with none of the controls, $P < .001$ (Table 2).

DISCUSSION

This study was designed to investigate the prevalence of IgE antibody to inhaled allergens, viral infections, and tobacco smoke exposure in infants and children treated for wheezing in a pediatric emer-

gency department. To detect allergen sensitization, serum IgE antibody was measured by RAST because skin testing actively wheezing patients is contraindicated. In our laboratory RAST has been established for five inhalant allergens to which clinic patients react frequently on skin tests (ie, 97% of skin test-positive children with asthma react to one or more of these allergens). In addition, the selection of these allergens is in keeping with the inhaled allergens used in other population surveys.^{8,25}

Among wheezing patients under age 2, IgE antibody to inhaled allergens was uncommon. This finding is consistent with prospective studies of infants born to allergic parents in whom sensitization to these allergens, determined by skin tests or RAST, was also infrequent before age 2 years.^{12,13} In one of these studies, a cohort of children was followed periodically until age 11 years.²⁶ Results showed that exposure to increased levels of dust mite allergen in early childhood was a significant factor in the subsequent development of asthma, suggesting that early allergen avoidance may be important for high-risk children. Among high-risk children are also those who have atopic dermatitis during infancy and who have been shown to have an increased risk for developing respiratory allergies and asthma.²⁷ These children may also have bronchiolitis. In our study, none of the young wheezing patients younger than 2 years of age had signs or symptoms of atopic dermatitis.

An increased prevalence of IgE antibody to inhalant allergens was evident in wheezing patients after age 2 years, and a significant association between wheezing and sensitization was observed after age 4 years. In keeping with other studies of asthma in children, most of the RAST-positive patients were sensitized to dust mite allergen.^{14,15} In drier climates, however, mite sensitization may be less common and IgE antibody to other allergens may be more prevalent. After age 2 years, a strong correlation between RAST positivity and total IgE levels was evident in the wheezing children. In addition, the increasing prevalence of IgE antibody to inhalant allergens was paralleled by an increase in nasal eosinophilia observed in wheezing patients after age 2 years. Eosinophils are thought to play an important role in the late-phase events of immediate hypersensitivity reactions.²⁸ Their presence on nasal smears is also consistent with a response to allergen exposure as judged by their appearance in nasal secretions from grass allergic individuals during the grass pollen season as well as after intranasal allergen provocation.^{19,29}

Altogether, viral infections put children both less than and more than the age of 2 at significant risk for wheezing. Although the association between viral respiratory infections and wheezing has been described in other epidemiologic investigations,^{9,11,30} this is the first report to compare specific viruses isolated from younger and older children who were treated for wheezing in an emergency department. Our data from wheezing patients less than 2 years of age support the importance of RSV as a major respiratory pathogen for wheezing in infants.^{11,31} None of

the virus-infected children less than age 2, however, had IgE antibody to inhaled allergens. In previous studies, an IgE-mediated mechanism for wheezing was proposed for some infants with bronchiolitis based on the detection of IgE antibody specific for RSV antigen in nasopharyngeal secretions.³² More recently, increased levels of eosinophil cationic protein were also reported in nasal secretions from RSV-infected infants.³³ In addition, eosinophils have been described in some nasal smears from a study of infants with bronchiolitis; however, a large proportion of these patients had atopic dermatitis.³⁴ By contrast, nasal eosinophilia was not observed in smears from any of the RSV or other virus-infected children less than age 2 years in our study. After the age of 2, virus was isolated from approximately one-third of the washes from children who had wheezing. Rhinovirus was the most prevalent pathogen, and two-thirds of the virus-infected wheezing children were also RAST-positive.

The prevalence of tobacco smoke exposure at home was high for wheezing and control patients. Before the age of 2, however, a larger proportion of wheezing patients than controls were exposed to tobacco smoke. Studies of smoking trends in the United States indicate that rates of cigarette smoking are higher among lower socioeconomic groups.³⁵ Consistent with this, the income status of our patients, judged by the proportion of the emergency department bill charged to parents, was lower for the wheezing children less than age 2 than for controls. Similarly, the income status of all smoke-exposed patients was lower than for nonexposed patients.

The most striking finding regarding passive smoke exposure was the large proportion of children less than age 2 years who had elevated cotinine levels suggestive of heavy smoke exposure. Although cotinine has been detected in breast milk,³⁶ none of the patients under age 2 were being breast-fed at the time of their enrollment. Thus, we speculate that infants and young children, who are likely to be more physically dependent on their parents, may have a higher risk for heavy exposure if their parents smoke. However, a threshold level at which passive smoke exposure becomes clinically significant in causing or aggravating airway hyperresponsiveness has not yet been defined. In addition, when combined with other risk factors, the effects of smoke inhalation may be additive so that lower levels of exposure may have adverse consequences even for older children. Nevertheless, a dose-response relationship has been supported by studies indicating higher rates of asthma and increased usage of asthma medications in children exposed to mothers who smoke at least one-half pack of cigarettes per day.^{10,37} A highly significant correlation between asthma severity and the number of cigarettes smoked by the mother, but not the father, has also been reported.³⁸ Preliminary analysis of our data suggests that children under age 2, who were exposed to mothers smoking one-half pack per day or more, were highly likely to have salivary cotinine levels ≥ 10 ng/mL. This did not appear to be the case after age 2 years. Additional studies of mother's smoking habits together with cotinine de-

terminations in their children may help to further clarify this relationship.

CONCLUSIONS

Results from this study indicate that children who are brought to an emergency department for wheezing before age 2 years can be characterized as having a high rate of viral respiratory tract infection, particularly RSV, and a low rate of sensitization to inhalant allergens. In addition, eosinophils were not apparent on nasal smears from any of these IgE antibody-negative patients. After age 2 years, viral infections, mostly rhinovirus, remained an important risk factor for wheezing. However, IgE antibody to inhalant allergens, especially to dust mite, together with elevated total IgE levels and nasal eosinophilia, became an increasingly significant finding. Passive smoke exposure was common among wheezing children at all ages. However, high salivary cotinine levels suggesting heavy smoke exposure were significantly more common among the children younger than 2 years of age.

Most wheezing patients in this study entered the emergency room with two or more of the risk factors examined. The management of wheezing in the emergency department, however, often focuses exclusively on treatment with medications, after which many patients return home to unaltered environments. In an effort to reduce morbidity, our data would encourage efforts to reduce tobacco smoke exposure at home, especially for young patients, and to consider sensitization to inhaled allergens and allergen avoidance (eg, to dust mite) in wheezing children at an early age, and particularly in those who begin or continue to wheeze after age 2 years.

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