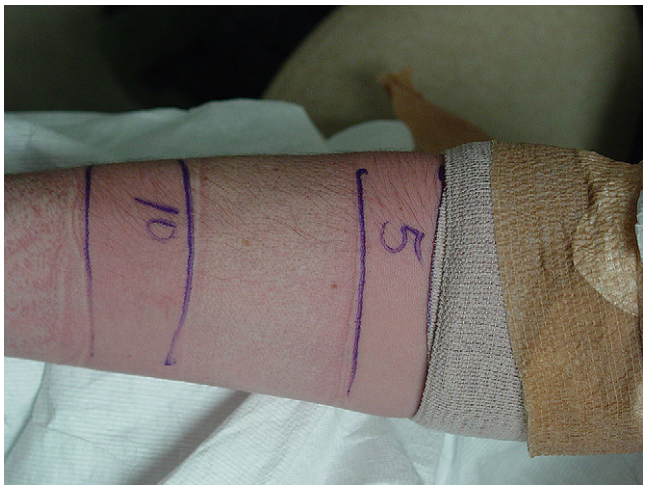

FIG 2. Repeat UV-A phototesting showing erythema starting 15 minutes after testing at both 5 and 10 J/cm^2.

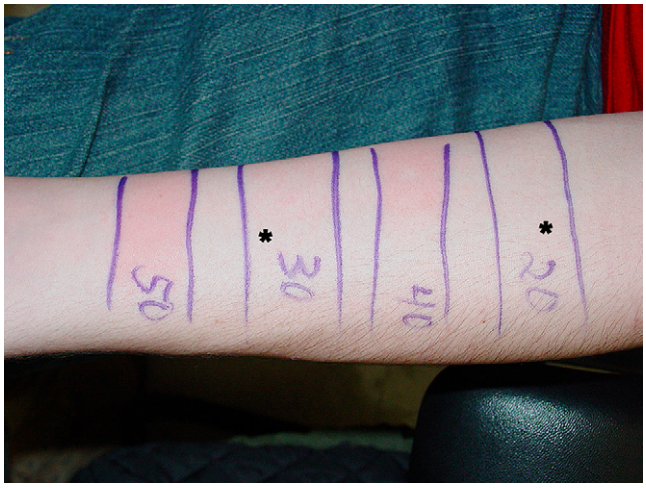

FIG 3. Repeat UV-B phototesting. No erythema at the 20 and 30 mJ/cm^2 sites *(*)* but erythema at 15 minutes at the 40 and 50 mJ/cm^2 sites.

Similar to a case recently described, solar urticaria improved with anti-IgE therapy, although only partially in our case.[3] Interestingly, the UV-B action spectrum improved more than the UV-A spectrum. One explanation could be that the initial classification of solar urticaria into 6 types found that the UV-B action spectrum (280-320 nm) showed passive and reverse passive transfer, suggesting the presence of an abnormal IgE autoantibody that can bind irradiated precursors from either healthy patients or those with solar urticaria (now classified as type II).[6] We also measured the level of free IgE to demonstrate appropriate free IgE suppression as a result of administering omalizumab to a patient with an IgE level greater than 700 IU/mL. Despite a high IgE level, we were able to demonstrate appropriate suppression of free IgE (95% at 8 weeks). We hypothesize that other well described variables regarding omalizumab response including variations in receptor expression, specific/total IgE ratios, and cellular sensitivity may have accounted for his lack of dramatic improvement on repeat phototesting.[7] Two other reports of omalizumab with physical urticaria demonstrated complete resolution after a single dose for cholinergic urticaria,[8] whereas a case of cold urticaria had marked improvement after 2 months with complete resolution at 5 months.[9]

Further study is warranted to determine the role of anti-IgE for solar urticaria for different action spectrums (UV-A, UV-B, visible light). This patient showed a delay in erythema by 15 minutes during phototesting after 10 weeks of omalizumab, although there was only improvement in the minimal urticarial dose for the UV-B spectrum (20-40 mJ/cm^2) . Oral antihistamines still remain the mainstay therapy, improving the intensity of erythema and wheal formation in 63% of patients.[10] However as many as 33% of patients with solar urticaria have elevated IgE levels, and omalizumab may be an option if other therapeutic modalities fail.[9]

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Expression patterns of atopic eczema and respiratory illnesses in a high-risk birth cohort

To the Editor:

Atopic eczema (AE) is the most common chronic inflammatory skin condition in childhood.[1] The natural course is variable and difficult to predict. Some patients completely "outgrow" their disease, while others develop more significant and persistent disease.[2] In addition, AE in early childhood has been linked to an increased risk of allergic rhinoconjunctivitis and asthma. Patterns of expression and identification of factors associated with the persistence of AE may lead to improved primary and secondary prevention strategies to halt the progression of the atopic march, as well as improved prognostication of the clinical course

TABLE I. Risk factors for persistent atopic eczema at year 1

Year 1 risk factor	Group			*P* value		
	None/transient (62%)	Early/recurrent (24%)	Late-onset (14%)	None/transient vs late-onset	None/transient vs early/recurrent	Late-onset vs early/recurrent
MSI	1.9 ± 1.7	2.5 ± 1.7	2.0 ± 1.7	.75	.02*	.16
Wheezing illness	23%	45%	29%	.46	.003*	.15
RSV wheezing illness†	13%	36%	17%	.52	.0003*	.06
Dog at birth†	43%	10%	50%	.38	<.0001*	<.0001*
Any + food FEIA†	18%	48%	11%	.29	<.0001*	.0005*
Any + aero FEIA	9%	23%	10%	.81	.007*	.13
Any + FEIA	21%	53%	16%	.49	<.0001*	.0006*
Food allergy	2%	15%	2%	.98	.001*	.07

aero, Aeroallergen; *FEIA,* fluoroenzyme immunoassay; *MSI,* moderate-to-severe respiratory illness determined by symptoms scores (mean ± SD);[3] *RSV,* respiratory syncytial virus.

*Variables used for latent class analysis and found to be statistically significant (P ≤ .05).

†Included in latent class model. Factors not significant included rhinovirus MSI, rhinovirus wheezing, exclusive breast-feeding, environmental tobacco smoke exposure, older siblings, day care, cat at birth, and total IgE.

of AE. We examined the natural history of AE in children enrolled in the Childhood Origin of ASThma (COAST) study, a high-risk birth cohort composed of children with parental histories of asthma and/or allergies, to define early risk factors for the persistent expression of disease.

The COAST study enrolled 287 high-risk children before birth who participate in annual study visits. Children were followed to age 6 years and were classified as having AE if (1) AE was diagnosed by a physician at a study visit, or (2) the Eczema Area and Severity Index[3] score completed by the study team was ≥1, or (3) a parent reported physician-diagnosed AE. More than 99% of the yearly AE diagnoses were made using criterion 1 or 2. Physician-diagnosed wheezing respiratory illness and asthma were defined as previously published.[4]

Using latent class modeling analysis (see Online Repository Methods for details), children fit into 1 of 3 AE phenotypes (see this article's Fig E1 in the Online Repository at www.jacionline.org). The majority of these children never had AE or had a transient course (n = 167; 62%). Fourteen percent of children (n = 38) had little or no disease in the first 3 years of life, and then developed AE in years 4 to 6 (late-onset AE). Sixty-six children (24%) had early/recurrent AE, with early and persistent skin manifestations throughout the period of observation. There were no significant differences in sex, ethnicity, birth weight, gestational age, or parental atopic history between the groups.

A novel finding in our study was that children with early/recurrent AE had more moderate-to-severe viral respiratory illnesses in the first year of life compared with the healthy/transient group ($P = .02$; Table I). In addition, wheezing illnesses in year 1 continuing though age 4 years were significantly associated with early/recurrent AE (Fig 1, *A*). When viral pathogenesis was investigated, respiratory syncytial virus–associated wheezing in the first year of life was most closely associated with early/recurrent AE (Table I; Fig 1, *B*). A positive relationship between moderate-severe respiratory illnesses in infancy and AE provides evidence contrary to the original hygiene hypothesis. There are limited data examining the relationship between viral respiratory illnesses in early life and the natural history of AE. One large longitudinal study prospectively asked mothers about respiratory illnesses and AE by telephone and reported a positive correlation.[5] Our study extends these findings by identifying a relationship among proven viral illnesses, severity of illness, and the specific phenotype of early/recurrent AE.

The relationship between respiratory tract illnesses and AE suggests that these disorders are linked by a common underlying susceptibility factor, possibly related to immune regulation, epithelial barrier function, or both. Early sensitization may indicate a greater degree of immune dysregulation (eg, defective regulatory T cells), which could contribute to persistent AE and progression through the atopic march. Alternatively, it has been

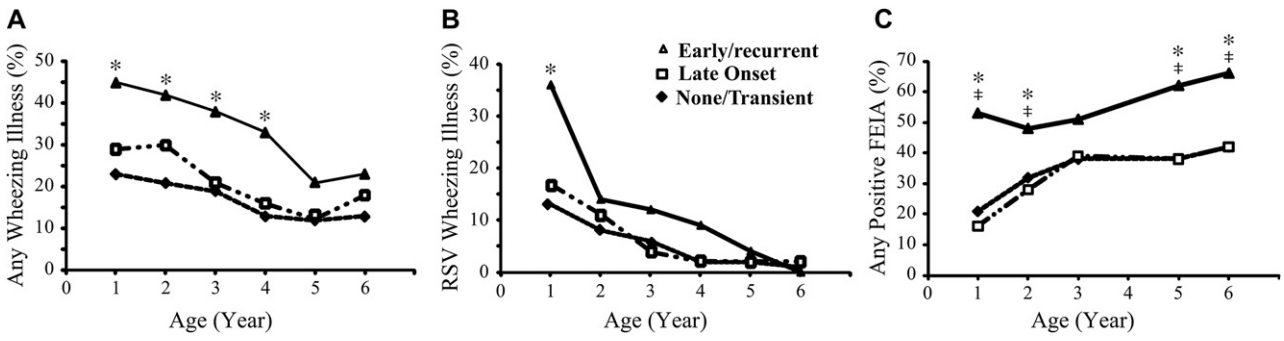

FIG 1. Longitudinal assessment of wheezing and allergic sensitization. For the 3 AE groups, separate graphs depict the prevalence of wheezing illnesses **(A)**, respiratory syncytial virus *(RSV)*–specific wheezing illnesses **(B)**, and age-specific changes in any positive fluoroenzyme immunoassay (*FEIA;* **C,** ≥ 0.35 kU/L for food or aeroallergen) annually from birth to age 6 years. *$P < .05$ healthy/transient versus early recurrent; ‡$P < .05$ early/recurrent versus late-onset.

proposed that the defective skin barrier in AE promotes sensitization after cutaneous contact with allergens.[6]

During the first year of life, children with early/recurrent AE were more likely to develop allergic sensitization (to food and/or aeroallergen) compared with the healthy/transient and late-onset AE phenotypes (Table I). Following the cohort longitudinally, children with early/recurrent AE continued to have significantly higher rates of allergen-specific IgE at age 2, 5, and 6 years (Fig 1, *C* and see this article's Fig E2, *A and B* in the Online Repository at www.jacionline.org), whereas total serum IgE levels did not significantly vary between the defined AE groups until age 6 years. At age 6, children with none/transient AE had a higher total IgE (see this article's Fig E2, *C,* in the Online Repository at www.jacionline.org).

Interestingly, dog in the home at the time of birth was less common in the early/recurrent group (10%) compared with the healthy/transient (43%) and late-onset (50%) groups (Table I). Exclusive breast-feeding for the first 6 months of life was associated with late onset disease versus early/recurrent disease ($P = .05$; Table I). Other factors, including daycare attendance, older siblings, and environmental tobacco smoke exposure, were not different. Early/recurrent AE was more closely associated with atopic biomarkers and other atopic diseases throughout early childhood (see this article's Fig E3 in the Online Repository at www.jacionline.org).

The increasing prevalence of AE has led to the search for environmental factors that modify the risk or natural history of AE. In our study, lack of exposure to dogs, but not cats, was associated with early/recurrent AE. This finding is consistent with other reports that exposure to dogs, particularly near the time of birth, has been associated with distinct changes in immune development in early childhood, and lower rates of wheezing by age 3 years.[7] In contrast, breast-feeding was associated with late-onset atopic eczema. It is possible that exclusive breast-feeding delays the onset of AE in children who might otherwise have developed it in infancy. Similarly, our data suggest that breast-feeding may have differential effects depending on the specific phenotype of AE. Published studies have had varied results with respect to effects of breast-feeding on AE, and findings may differ depending on the atopic history of the parents or the failure to consider different phenotypes of AE.[5,8,9]

In conclusion, children in this high-risk cohort can be grouped into 1 of 3 distinct AE phenotypes: healthy/transient, late-onset, and early/recurrent AE. Our data suggest that frequent significant respiratory viral illnesses, early onset of allergic sensitization, and wheezing are associated with early/recurrent AE, whereas exposure to dogs may have beneficial effects. Further studies to define the underlying mechanisms linking AE to respiratory illnesses and other potentially modifiable factors are warranted to identify new therapeutic targets and strategies for prevention.

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Reciprocal interaction of the conjunctiva and cornea in ocular allergy

To the Editor:

Severe ocular allergic diseases such as vernal and atopic keratoconjunctivitis involve not only conjunctival allergic inflammation but also various corneal disorders. Corneal complications such as persistent corneal erosion can threaten vision and are often resistant to therapy, thus remaining a challenge in the treatment of ocular allergy.[1]

The cornea and conjunctiva are physically apposed, separated by only a thin film of tear fluid. However, these tissues have distinct characteristics. The conjunctiva is rich in immune cells and vasculature and possesses only weak barrier properties, with allergic inflammation thus readily evoked. In contrast, primary allergic reactions do not occur in the cornea, given that this tissue

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METHODS

Statistical analysis

Latent class analysis (LCA) is a method of grouping individuals with respect to some underlying, unobservable variable based on observed data from dichotomous or categorical indicators.[E1,E2] In LCA, the observed pattern of AE in a child during the first 6 years of life is assumed to be the manifestation of an unobserved, or latent, phenotype class. The classical LCA model assumes that, conditional on the latent class (AE phenotype), the observed indicators (observed AE indicators at annual visits) are independent of each other and of covariates. Covariates are incorporated in the LCA as predictors of the probability of belonging to a given latent class.

Initially, LCA models with 2 to 6 latent classes were estimated by using the yearly AE observations (years 1-6) without including any covariates. The Schwarz or Bayesian information criterion[E3] was used to select the number of latent classes; a 3-class model was selected. Next, covariates observed during the first year of life were incorporated into a log-linear multinomial regression model as predictors of the probability of belonging to each latent class. The covariates considered were positive food-specific IgE, positive aeroallergen-specific IgE, total IgE, wheezing illness, rhinovirus wheezing illness, respiratory syncytial virus wheezing illness, number of moderate-to-severe respiratory illnesses, number of moderate-to-severe rhinovirus respiratory illnesses, number of moderate-to-severe respiratory syncytial virus respiratory illnesses, exclusive breast-feeding during the first 6 months of life, environmental tobacco smoke exposure, presence of older siblings, daycare attendance, dog ownership, and cat ownership. Stepwise variable selection using the Bayesian information criterion was performed for a model with 3 latent classes. The resulting model included 3 covariates: dog ownership, positive food-specific IgE, and respiratory syncytial virus wheezing illness. Then, LCA models with 2 to 6 latent classes were fit using these covariates; again, the 3-class model was selected by Bayesian information criterion. Classifications from the 3-class LCA model with covariates were used for all subsequent analyses.

Summaries and comparisons for all variables (demographics, early-life risk factors, later-life outcomes) within and between the 3 classes were carried out as follows. Posterior class membership probabilities from the LCA model were used to construct 10 simulated datasets of class memberships. Summary statistics were calculated for each simulated dataset and then averaged across datasets. For comparisons among classes, appropriate models were fit (ANOVA for continuous outcomes, logistic regression for dichotomous outcomes) to each dataset, and estimates were combined by using the Rubin method to produce a composite estimates, SEs, and P values. A 2-sided P value $<.05$ was regarded as statistically significant.

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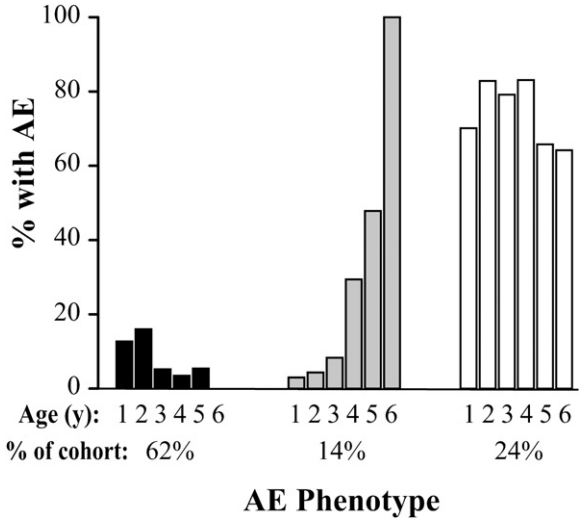

FIG E1. Yearly prevalence of AE in the 3 groups: none/transient, late-onset, and early/recurrent. Latent class analysis models were estimated by using the yearly AE observations (years 1-6; Methods in the Online Repository). Children were grouped into 1 of 3 phenotypes. *Black bars,* None/transient AE; *gray bars,* late-onset AE; *white bars,* early/recurrent AE.

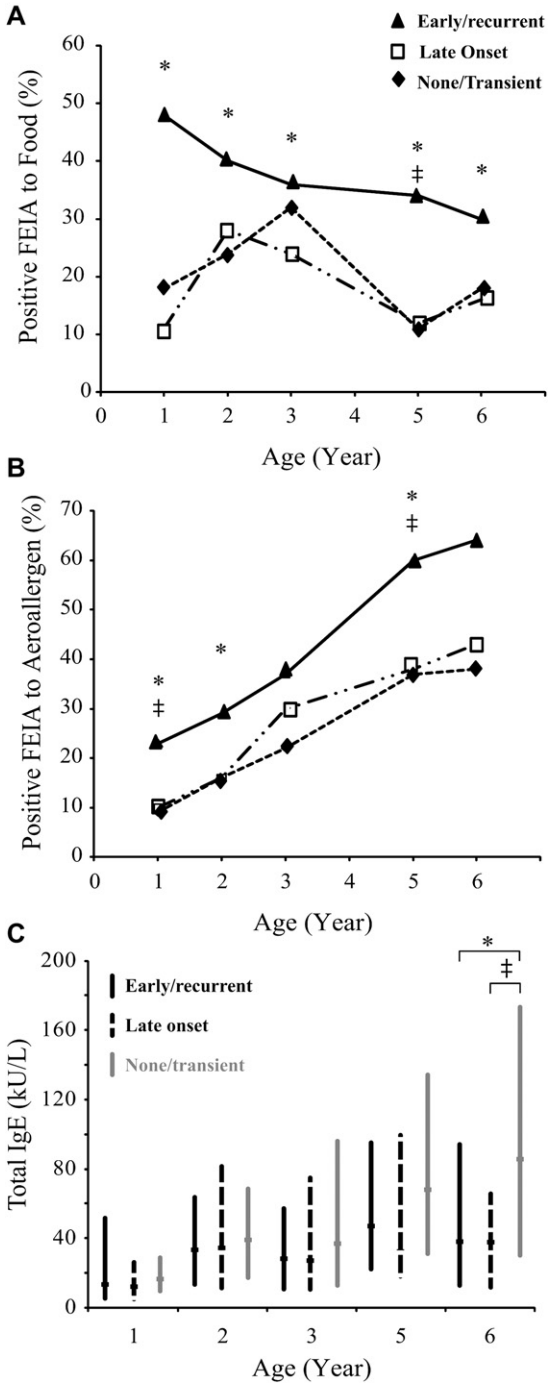

FIG E2. Early allergen sensitization is associated with early/recurrent AE. Age-specific changes in the prevalence of food specific IgE **(A)**, the prevalence of aeroallergen specific IgE **(B)**, and total IgE **(C)** in the 3 AE groups. *Closed diamond,* None/transient AE; *open square,* late-onset AE; *closed triangle,* early/recurrent AE. **P* <.05 healthy/transient versus early recurrent; ‡*P* <.05 early/recurrent versus late-onset. *FEIA,* Fluoroenzyme immunoassay.

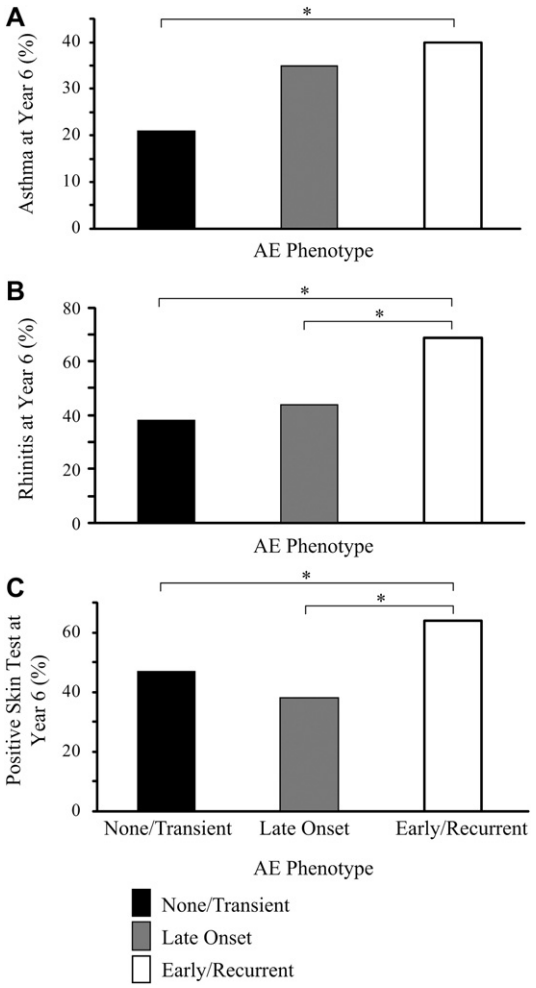

FIG E3. Children with early/recurrent AE are most likely to develop additional atopic diseases. Prevalence of asthma at year 6 **(A)**, allergic rhinitis at year 6 **(B)**, and positive skin tests at year 5 **(C)** in children with each AE phenotype. *Black bar,* Healthy/transient AE; *gray bar,* late-onset AE; *white bar,* early/recurrent AE. *$P < .05$.