

Development of seasonal allergic rhinitis during the first 7 years of life

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Background: Against the background of the controversial discussion about an increase in allergic rhinitis in recent years, intraindividual longitudinal data is lacking for IgE-mediated seasonal allergic rhinitis (SAR). Little is known about the development of SAR in terms of prevalence and incidence rates from birth to school age.

Objective: In a prospective birth cohort, we investigated the development of sensitization and symptoms of SAR. SAR should be defined with high specificity, and associated risk factors should be determined.

Methods: Annual longitudinal data about seasonal allergic symptoms and sensitization was available for 587 children from birth to their seventh birthday. The definition of SAR was based on a combination of exposure-related symptoms and sensitization.

Results: Up to 7 years of age, SAR developed in 15% of the children. Incidence and prevalence of symptoms and sensitization were low during early childhood (<2%) and increased steadily with age. Children in which SAR had already developed in the second year all were born in spring or early summer, resulting in at least two seasons of pollen exposure before manifestation of SAR. Risk factors assessed by multiple logistic regression analysis were male sex (odds ratio [OR] = 2.4), atopic mothers (OR = 2.6) and fathers (OR = 3.6) having allergic rhinitis themselves, first-born child (OR = 2.0), early sensitization to food (OR = 3.3), and atopic dermatitis (OR = 2.5), whereas early wheezing was not associated with SAR.

Conclusion: The development of SAR is characterized by a marked increase in prevalence and incidence after the second year of life. Our longitudinal data further indicate that in combination with the risk of allergic predisposition, at least 2 seasons of pollen allergen exposure are needed before allergic rhinitis becomes clinically manifest. (*J Allergy Clin Immunol* 2000;106:832-9.)

Key words: Seasonal allergic rhinitis, allergic sensitization, atopic family history, children

Abbreviations used

CI: Confidence interval
kU/L: Kilounits per liter
MAS: Multicenter Allergy Study
OR: Odds ratio
SAR: Seasonal allergic rhinitis
sIgE: Specific IgE

Studies such as the International Study of Asthma and Allergies in Childhood (ISAAC) have provided cross-sectional data about the prevalence of allergic symptoms. Results of that and other studies have intensified the ongoing discussion about an increase in the incidence of allergic rhinitis and further atopic disorders in recent years.¹⁻⁵ However, up to now, intraindividual longitudinal data has been lacking for IgE-mediated seasonal allergic rhinitis (SAR), especially in large samples of subjects and in young children. Little is known about the development and natural course of SAR in terms of prevalence and incidence rates from birth to school age. Studies with a follow-up of the same children over several years were rarely performed.⁶⁻⁸ However, these investigations had limitations in study design (eg, the observed period was relatively short). In addition, some studies failed to assess a diagnosis accurately because the specific sensitization was determined only once or not at all.

Further previous large studies reported only cross-sectional data mainly in schoolchildren and adolescents.^{1-5,9-13} Few of those studies provided prevalences in younger children.^{12,13} In addition, these data were cross-sectional, not allowing description of the development of SAR.

As part of a prospective birth cohort study—the Multicenter Allergy Study (MAS)—symptoms and specific sensitization were assessed annually in about 100 children followed up consecutively. On the basis of these measurements, we estimated prevalence and incidence rates and evaluated risk factors of SAR during the first 7 years of life.

METHODS

Study population

Subjects in this study were participants of the MAS. The details of the study design are reported elsewhere.¹⁴ Briefly, for this prospective birth cohort study, 1314 newborns were enrolled in 5

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German cities during 1990: 499 eligible newborns with elevated cord blood IgE (≥ 0.9 kU/L) or at least 2 close atopic family members and 815 randomly selected newborns with none of these atopic risk factors present. The children were followed up at ages 3, 6, 12, and 18 months and annually to age 7 years. At each visit, parents filled out standardized questionnaires and gave structured interviews about atopic symptoms and diseases of their children, about atopic family history (mothers and fathers were considered separately and defined as atopic if at least one of the following conditions were present: [1] asthma, atopic eczema, or food allergy without allergic rhinitis, or [2] asthma, atopic eczema, or food allergy including allergic rhinitis), and parental educational level (higher level). Cord blood IgE (detection limit: 0.35 kU/L) was determined by the CAP-RAST-FEIA system (Pharmacia, Germany). Mite (Der p 1 + Der f 1) and cat (Fel d 1) allergen exposure levels were obtained from carpet dust samples at age 6 and/or 18 months. The allergen extraction and analysis was performed as previously described by using a sandwich ELISA by ALK (Copenhagen, Denmark).¹⁵ Urinary cotinine concentrations at age 1 year were measured with a detection limit of 1 ng/mL.¹⁶ The study was approved by the local ethics committee, and informed parental consent was obtained. Of the 939 children participating to their seventh birthday, 878 (94%) children with complete follow-up data about allergic symptoms were included. The rationale was to estimate incidence and prevalence rates for each year of life not biased by variation in participation. To define SAR with a high specificity, data about allergic sensitization had to be available. To determine allergic sensitization, not more than 2 consecutive missing blood samples and not more than 3 missing blood samples in total were allowed during the follow-up of 7 years. Finally, 587 children were included in the analysis (Fig 1). A subsample of 186 of these 587 children had a follow-up without any missing blood examinations at each follow-up visit (for handling of missing data see next paragraph).

Specific serum IgE measurements and definition of allergic sensitization

Antibodies of specific IgE (sIgE) to timothy grasses and birch pollen and to food allergens were determined at ages 1, 2, 3, 5, 6 and 7 years by CAP-RAST-FEIA (Pharmacia). A child was defined as sensitized if sIgE levels were equal to or greater than 0.7 kU/L (CAP class 2). This limit was chosen to exclude possibly ambiguous or transient events of sensitization caused by variations in measurement sensitivity during the study period. Because rates of participation in blood sampling varied during the 7 years of observation, children with missing data on sensitization to pollen allergens for more than 2 consecutive years or for more than 3 time points overall were excluded from the analysis. For included children with missing data on sIgE, the last valid value of the sensitization status was carried forward. Transient specific sensitizations defined as sIgE below the detection limit after allergic sensitization in previous measurement(s) were excluded from the analysis ($n = 28$).

Definition of allergic symptoms and SAR

On the basis of the questionnaire data, symptoms of allergic rhinitis were defined as the presence of the following criteria during the period preceding the follow-up visit:

1. Reported symptoms of sneeze attacks or runny, blocked, or itchy nose in the absence of common cold
2. Reported symptoms during pollen seasons (ie, months March to May [birch] or June to August [timothy grass]).

For the diagnosis of SAR, the reported seasonal symptoms had to be associated with the respective seasonal sensitization to birch or grass pollen. This specific sensitization had to be detectable not later than 1 year after the occurrence of symptoms.

Recurrent wheezing was defined as the presence of at least one of the following criteria throughout the period before the respective follow-up visit¹⁷: (1) at least 2 reported episodes of wheezing or shortness of breath within the last 12 months, or (2) asthma diagnosed by the family practitioner or the study physician (considering that symptoms were present especially in pollen season or were not related to infections).

Statistics

Lifetime prevalence rate is defined as the proportion of children with symptoms/sensitization in the total group up to the time point in question. Incidence rate is defined as the proportion of children with symptoms/sensitization in the group of children at risk (ie, children originally free of symptoms/sensitization in whom it could have developed during the period) within the respective period. The 95% confidence intervals (CIs) around the rates were computed with the standard formula: $\text{rate} \pm 1.96 \sqrt{\text{rate}(1 - \text{rate})/N}$. Additional sensitivity analyses were carried out to evaluate the robustness of results and the effect of a potential selection bias by analyzing cohort subgroups limited by the availability of data and by variation in participation rate. Therefore, comparisons were made between the total MAS cohort and the analyzed subsample ($n = 587$) and the subsample only including children with a complete follow-up of blood examinations ($n = 186$). To estimate rates in the total MAS cohort, all children with at least one valid response at one follow-up visit were included. If data were missing on symptoms or sensitization, the child's symptom or sensitization status was interpreted as negative at that time, regardless of whether they were found to have symptoms or to be sensitized at a subsequent examination.

Pearson's χ^2 test was used for comparison of categorical data and the Mann-Whitney U test was used for continuous nonparametric data analysis (allergen concentrations and cotinine levels). Statistical significance was defined by a 2-sided α level of .05. Multiple logistic regression was used to estimate the effect of various (risk) factors on the development of allergic rhinitis. Parsimonious models were derived with stepwise logistic regression adjusting for confounding (parental educational level and study center) as described by Hosmer and Lemeshow.¹⁸ Potential effect modifiers were examined by adding interaction terms in the logistic regression analysis. The statistical significance of a potential risk factor is given as the P value of the likelihood-ratio test statistic relative to the model without the factor in question. Statistical analysis was performed by using spss/pc (SPSS Inc, Chicago, Ill).

RESULTS

The characteristics of the study children and their families are shown in Table I stratified for the analyzed sample ($n = 587$) and the remaining children of the overall MAS cohort. The analyzed group did not differ from the remaining MAS cohort with respect to common atopic risk factors. However, differences in educational level and duration of breast-feeding and smoking during pregnancy were observed possibly indicating an increased health awareness in the analyzed group. Participation in blood examinations was independent of the occurrence of SAR ($P = .76$). The subgroup of children without any missing blood examinations for each follow-up ($n = 186$) matched the analyzed sample well for the general characteristics shown in Table I ($P \geq .16$ for all characteristics).

Through age 7 years, SAR developed in 90 (15%) children, defined as seasonal symptoms associated with pollen-specific sensitization. Of these children, 19 had

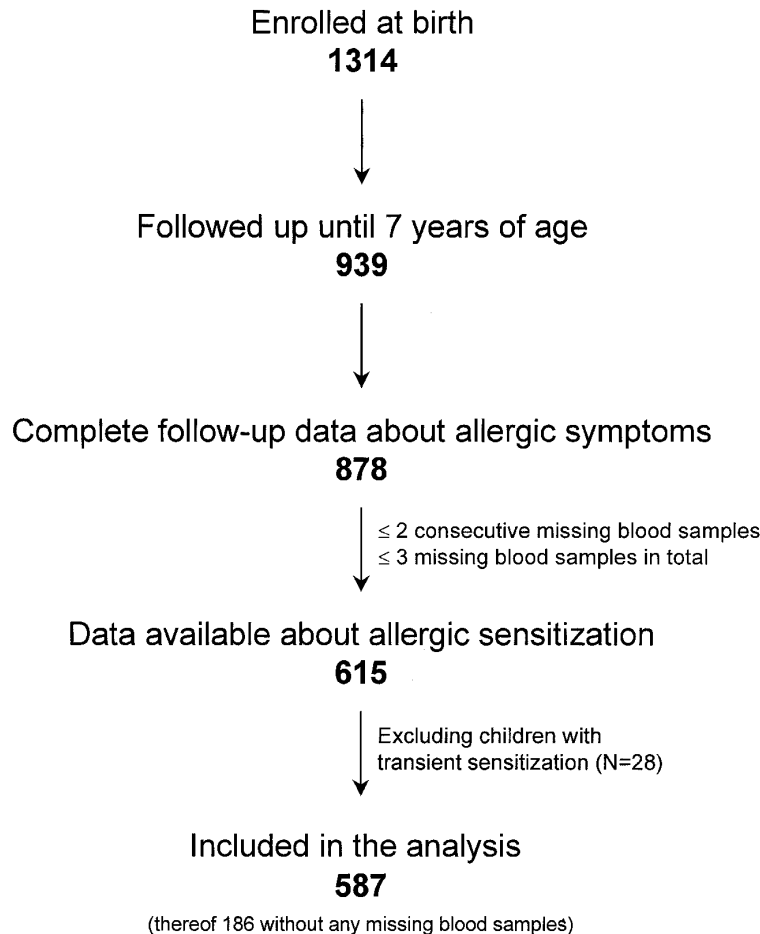


FIG 1. Flow diagram of participants.

allergic rhinitis to birch pollen, 37 to timothy grass pollen, and 34 children to both. Neither symptoms nor sensitization developed in 335 (57%) children. For the remaining children, we found ambiguous data allowing no clear diagnosis: Only symptoms but no sensitization were reported for 110 (19%) children, whereas 52 (9%) were sensitized without symptoms. These children were interpreted as non-SAR cases leading to a highly specific definition of SAR in our analysis. Are there any differences between the clear and the ambiguous cases? We found significantly higher levels of specific IgE to birch and timothy grass in the clearly defined SAR cases than we did in the sensitized children without symptoms ($P < .01$). Specific IgE in the SAR cases was detectable in earlier years of life than it was in the ambiguous cases who were interpreted as non-SAR cases ($P < .05$). However, the onset of symptoms was reported later in the SAR cases than it was in the ambiguous cases, maybe indicating unspecific and infection-associated rhinitis in early childhood in the latter cases.

To evaluate the robustness of results and the effect of a potential selection bias, additional sensitivity analyses were computed comparing the 3 subsamples ([1] the total MAS cohort vs [2] the analyzed subsample [$n = 587$] vs

[3] the subsample without any missing blood examinations [$n = 186$]). Rates were highest in the subsample with the complete follow-up data. However, at all time points, incidence and prevalence rates did not significantly differ between subsample (2) and (3), whereas from the sixth birthday on, rates in the total MAS cohort (1) were significantly lower. For example, lifetime prevalences of symptoms at age 7 years were 28.0% (95% CI, 25.4-30.6), 35.3% (95% CI, 31.4-39.3), and 34.4% (95% CI, 27.7-41.8), respectively. Lifetime prevalences of sensitization at age 7 years were 20.4% (95% CI, 18.0-22.9), 25.2% (95% CI, 21.8-29.0), and 30.6% (95% CI, 24.2-37.9), respectively.

The natural course of symptoms, specific sensitization, and SAR is shown in Fig 2. Incidence and prevalence of symptoms and specific sensitization were low during the first 2 years of age increasing to 7 years. The incidence of SAR markedly increased after the third birthday up to 3% to 4% for each year. The incidence of specific sensitization increased to 4% at age 3 years and to 5% to 6% after the third birthday, and the incidence of symptoms from the third birthday on were around 8% each year after rates below 4% during the first 2 years of life. Lifetime prevalence of SAR increased significantly

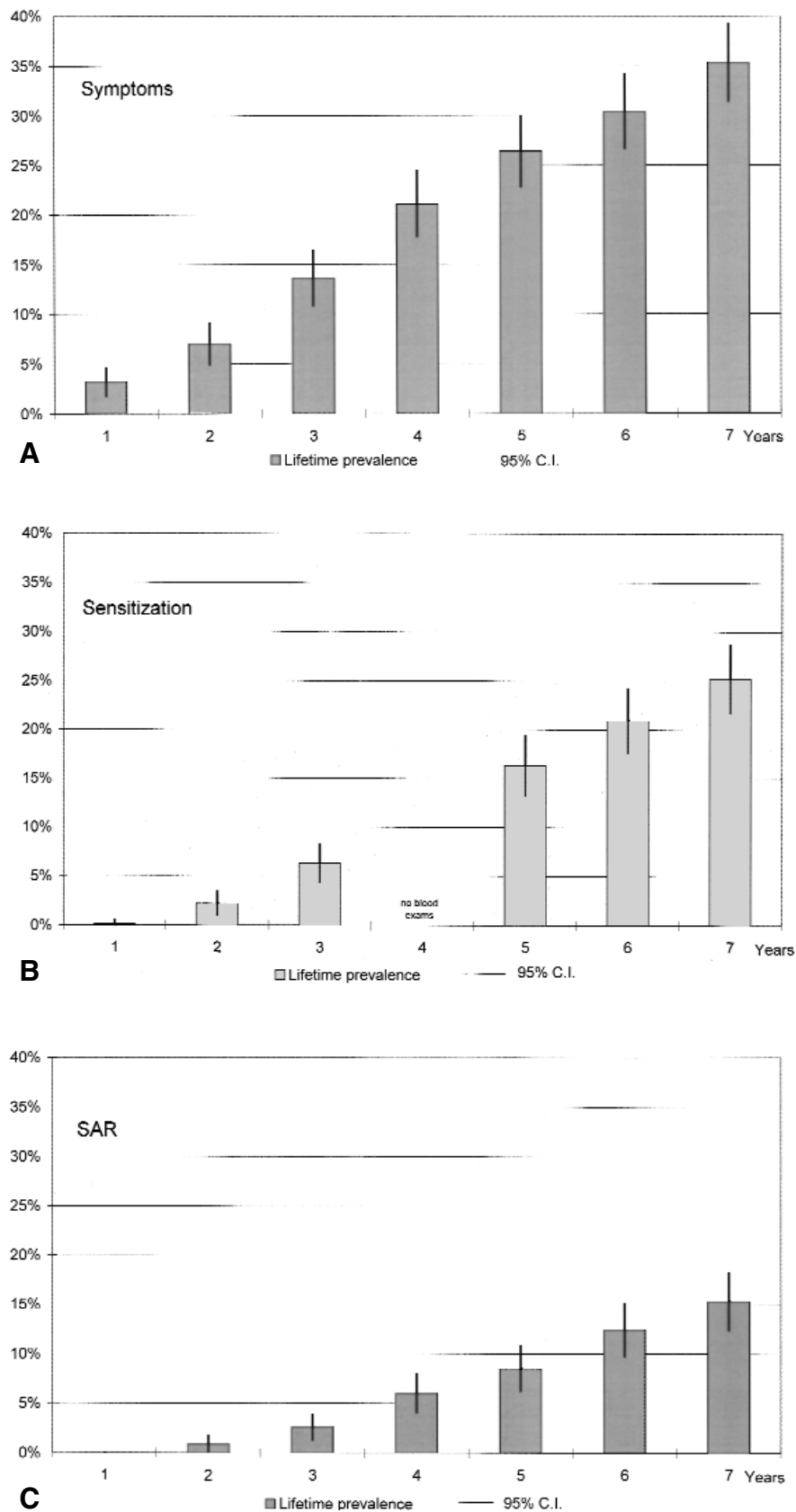


FIG 2. Lifetime prevalence of (A) symptoms, (B) sensitization to birch and timothy grass, and (C) SAR to age 7 years.

TABLE I. Characteristics of the analyzed subcohort (n = 587) and the remaining children of the overall MAS birth cohort (n = 727 at start of follow-up)

Characteristics (N = 1314)	Analyzed subcohort (n = 587)	Remaining subjects of MAS cohort (n = 727*)	P value†
Sex (male)	53	51	.47
Parental educational level			.006
Secondary school	55	53	
High school	11	17	
Higher education	34	30	
Parental atopy			
Atopic mother	33	38	.08
Atopic father	31	30	.70
Detectable cord blood IgE (≥ 0.35 kU/L)	34	37	.19
Season of birth			.59
Spring/Autumn (Mar-May, Sep-Oct)	34	34	
Summer (May-Aug)	38	36	
Winter (Nov-Feb)	28	30	
Duration of breast-feeding			.001
As long as 1 month	25	36	
1-6 months	45	42	
More than 6 months	30	22	
No. of siblings at birth			.21
None	54	60	
1	34	31	
2 or more	12	9	
Parental smoking habit			
Mother smoking during pregnancy	22	28	.015
Mother or father smoking (at 18 months)	43	48	.08
Pets in household (at 18 months)	30	30	.94
Cat allergen exposure by 18 months (median)	63 ng/g	65 ng/g	.88
Mite allergen exposure by 18 months (median)	253 ng/g	203 ng/g	.10

*Because of missing information for some characteristics and loss to follow-up, number of subjects varies between 727 and 579.

† χ^2 test for differences in the 2 samples.

from 2.6% (95% CI, 1.5%-4.3%) at age 2 years to 8.5% (95% CI, 6.5%-11.2%) at age 5 years and to 15.3% (95% CI, 12.6%-18.6%) at age 7 years. Interestingly, the 5 children in whom SAR already developed in the second year of life all were born in spring or early summer, resulting in at least 2 seasons of pollen exposure before manifestation of SAR. Among the 90 SAR cases, specific sensitization developed before clinical manifestation of seasonal symptoms in 56% (in the median 1 year earlier, range: 1 to 4 years earlier). Contemporary onset of sensitization and symptoms were reported in 20% of the children, and in 24%, sensitization was detected 1 year after reports of symptoms. Fifty-two children (9% of the analyzed cohort) were sensitized without reporting symptoms, with symptoms possibly developing in later years of follow-up. Concerning the question of a possible remission of SAR, we found no conclusive evidence for it; reported symptoms varied from year to year maybe because of varying allergen exposure levels. A clear remission of seasonal symptoms (free of symptoms for at least 2 consecutive pollen seasons after occurrence of SAR) was observed in 10% of the 90 SAR cases. However, all these children continued being sensitized during those symptom-free seasons.

By multiple logistic regression analysis, we calculated the odds ratios (ORs) for the risk of SAR up to age 7

years adjusting for confounding (Table II). Boys had a higher risk of SAR (OR = 2.4, P = .002) as well as children of atopic mothers (OR = 2.6, P = .003) or atopic fathers (OR = 3.6, P = .0001) with allergic rhinitis themselves. If both parents were atopic, the risk increased to an OR of 6.3 (95% CI, 2.7-14.4, P < .0001). However, children with older siblings had only half the risk of SAR developing compared with first-born children (P = .012). If further atopic conditions developed in early childhood such as sensitization to food (P = .0008) or atopic dermatitis (P = .002), the child's risk of SAR increased significantly. The analysis to estimate the probability that a SAR developed in a child showed no significant association between SAR and season of birth (P = .76), detectable cord blood IgE (P = .32), duration of breast-feeding (P = .91), pets in household (P = .92), questionnaire data of parental smoking (P > .49), urinary cotinine concentrations (P > .80), mite and cat allergen exposure levels (P > .21), and early wheezing (P = .31). These factors were not considered in the final model because of their lack of effect on SAR. According to this model, the probability of SAR developing in the first 7 years of life is 75% for a boy without any sibling at birth who has a father with SAR and an early sensitization to food allergens. Such risks for different risk factor constellations can be calculated by the formula given in Table II.

TABLE II. Odds ratios (with 95% CI) of risk factors for SAR in 545 children to age 7 years*

	Seasonal allergic rhinitis			
	Odds ratio (univariate)	P value	Adjusted OR	Likelihood-ratio test
Sex				
Female†	1		1	
Male	2.1 (1.3-3.3)	.003	2.4 (1.3-4.2)	.0024
Atopic family history				
Nonatopic mother†	1		1	
Atopic mother without SAR	1.2 (0.5-2.9)	.76	0.9 (0.3-2.6)	
Atopic mother with SAR	3.1 (1.9-5.1)	.0001	2.6 (1.5-4.7)	.0032
Nonatopic father†	1		1	
Atopic father without SAR	2.7 (1.2-6.2)	.012	2.5 (0.9-6.9)	
Atopic father with SAR	3.6 (2.2-5.8)	.0001	3.6 (2.0-6.5)	.0001
Siblings at birth				
None†	1		1	
1 or more	0.6 (0.4-0.95)	.031	0.5 (0.3-0.9)	.012
Detectable cord blood IgE (≥0.35 kU/L)				
No†	1		1	
Yes	1.7 (1.1-2.8)	.02	1.3 (0.7-2.4)	.32
Sensitization to food allergens to 2 years of age‡				
No† (sIgE < 0.7 kU/L)	1		1	
Yes (sIgE ≥ 0.7 kU/L)	4.6 (2.6-8.1)	.0001	3.3 (1.7-6.5)	.0008
Atopic dermatitis to 2 years of age				
No†	1		1	
Yes	3.1 (1.9-5.1)	.0001	2.5 (1.4-4.6)	.0024
Wheezing to 2 years of age				
No†	1		1	
Yes	1.9 (1.1-3.2)	.021	1.5 (0.8-2.9)	.31

Risk (probability) of development of SAR to age 7 years derived from the logistic regression model: $P = \frac{1}{1 + e^{-y}}$ where $y = -2.2277 + (0.8611 \times \text{sex} [\text{female} = 0, \text{male} = 1]) + (-0.6998 \times \text{sibling} [\text{no} = 0, \text{yes} = 1]) + (-0.148 [\text{if mother without SAR}] \text{ or } +0.9698 [\text{if mother with SAR}]) + (0.9305 [\text{if father without SAR}] \text{ or } +1.2905 [\text{if father with SAR}]) + (0.9304 \times \text{atopic dermatitis} [\text{no} = 0, \text{yes} = 1]) + (1.1949 \times \text{food sensitization} [\text{no} = 0, \text{yes} = 1])$.

*Odds ratios were estimated in univariate regressions and in multiple logistic regression analysis, adjusting for parental educational level and study center.

A total of 545 children were analyzed because of missing information for each characteristic from 0 to 42 subjects.

†Reference category.

‡At least once sensitized to at least 1 of 4 tested food allergens (cow's milk, hen's egg, soy bean, and wheat).

With respect to recurrent wheezing, we investigated how strongly this second allergic airway disorder and rhinitis were correlated. In our analyzed cohort (n = 587), early wheezing through the first 2 years of life was neither a significant risk factor (Table II) nor a good predictor for lifetime prevalence of SAR at age 7 years (positive predictive value: 23% [95% CI, 14.7-31.6]). In comparison, the predictive capacity of early symptoms of rhinitis (first 2 years) for later SAR was also poor (positive predictive value: 18% [95% CI, 7.9-33.4]). Of the 90 SAR cases, 30% had concomitant recurrent wheezing at age 7 years; 9% of the 90 cases were persistent wheezers (since early childhood) and 21% were wheezers with later onset (after the second birthday), whereas of the remaining 497 non-SAR cases, wheezing developed in only 4% ($P < .001$). However, for 16% of the 90 SAR cases and for 13% of the 497 non-SAR cases, early transient wheezing episodes were reported (episodes only up to age 2 years, $P = .46$). Among children free of symptoms of rhinitis during the first 2 years, early wheezing was reported in 12%, whereas among

children with early symptoms of rhinitis, 28% also had episodes of early wheezing.

DISCUSSION

To our knowledge, this is the first study with complete longitudinal data about allergic symptoms and sensitizations characteristic for SAR. We were able to describe the development of SAR from birth to age 7 years in a large cohort. In previous studies, results were mostly based on cross-sectional data in school-aged children,^{1-5,9-13} sensitization status was not determined consecutively,^{6,7} or the prospective cohort was not representative because it included high-risk children in an intervention study.¹⁹

For comparisons with other studies, differences in subjects and definition of SAR have to be taken into consideration. Our description of symptoms corresponded well to the ISAAC questionnaire (described as a problem with sneezing, or runny or blocked nose when you (your child) did not have a cold or the flu).¹ An atopic disease is usually defined by the presence of symptoms and by the pres-

ence of positive skin tests or specific IgE. For our definition, both criteria had to be met. However, the lack of consensus of assessment and definition of SAR complicates comparisons between studies.²⁰ Almost all studies investigating prevalence of allergic sensitization used skin prick tests. Findings should be comparable with determination of sensitization by specific serum IgE measurements, but skin prick tests may be more susceptible to variation and errors in measurement techniques.²¹ Previous reports on the prevalence of seasonal allergic nasal symptoms ranged from 4.4% to 42% in school-aged children and adolescents.^{5,7,22} However, the rates for our sample can hardly be compared with other findings because virtually no results are available about the prevalence and incidence of symptoms and specific sensitization over a consecutive follow-up from birth to age 7 years.

Seasonal allergic rhinitis (symptoms and sensitization) developed in 15% of the children, whereas 19% reported only symptoms, and 9% specific sensitization without symptoms, with symptoms possibly developing only in later years. To exclude false-positive observations, these 28% of children were interpreted as non-SAR cases. This definition of SAR is highly specific and not found in other studies. The significant differences between the clear and ambiguous cases in the sIgE measurements supported our strict definition criteria. However, this definition and the exclusion of transient sensitization could result in a possible underestimation of the frequency of SAR despite the atopy-enriched cohort. A further tendency toward an underestimation rather than an overestimation of the rates may be due to our assumption that families participating in the MAS cohort tended to avoid possible risk factors more often than did the general population (ie, increased awareness because of study participation).

Concerning the representativeness of our results, the sensitivity analysis for the 3 subsamples did not indicate a substantial selection bias (our reported CIs are overlapping). The estimated rates in the total MAS cohort were obviously lower than they were in the other 2 subsamples because of the handling of missing data (missing data were assumed to be no symptoms or no sensitization). For the final analysis, we included only children with complete follow-up data about allergic symptoms to be able to calculate true incidence and lifetime prevalence rates. We conclude that the prevalence and incidence rates of SAR are reliable estimates for the description of the development of SAR and for the analysis of associated risk factors in young children, even though a possible selection bias in our study cannot be entirely excluded. According to the multiple logistic regression model, the risks of development of SAR for different risk factor constellations, expressed as probabilities, are relatively high. In our example, it is 0.75 for a boy with no sibling at birth who has a father with SAR and an early sensitization to food allergens. Incidence and prevalence of SAR were low during early childhood (<1%) but increased steadily with age. SAR developed by age 7 years in at least 15%. However, the 7% frequency of reported symptoms at age 2 years was markedly higher than was the rate for SAR. Therefore, the

question is: how specific are reported symptoms of rhinitis in early childhood and of what predictive use are they for the estimation of a subsequent development of an allergic airway disease? According to our data, reported symptoms of "allergic" rhinitis during the first 2 years of life have to be regarded as unspecific and as of no use as a predictive variable for the following reasons: (1) In the clearly defined SAR cases, symptoms were reported later than in the ambiguous cases, (2) specific sensitization mostly preceded the development of symptoms, (3) the prevalence rates between symptoms and SAR differed markedly, and (4) the predictive capacity of symptoms during the first 2 years for predicting subsequent SAR was very poor (positive predictive value: 18%).

According to our results, symptoms such as sneezing and blocked or runny nose seem to be often transient and may not indicate a chronic development of disease. In most cases, those typical symptoms with a plausibility of allergic genesis (ie, detection of specific IgE) can be expected only after 2 periods of seasonal allergen exposure. Therefore, it seems to be plausible that early symptoms of "allergic" rhinitis reported by parents are unspecific and are more likely to be associated with respiratory infections. Such findings have been similarly reported for symptoms of the lower respiratory tract. Wheezing is not a single disorder, and different wheezing-associated respiratory illnesses have been recently described.²³⁻²⁶ Evidence suggests that early wheezing remits in a large number of children in whom these symptoms develop during the first 3 years of life^{24,25} and that having siblings is associated with transient early wheezing.²³ Factors indicating the development of persistent wheezing are family history of allergies, plausible signs of atopy in early life, and higher IgE levels than in transient cases.^{24,25,27} These results correspond very well with our findings such as early symptoms of rhinitis being unspecific, and higher specific IgE levels being detectable in children with clearly diagnosed SAR. A positive family history and having no sibling are risk factors for SAR development as well. These results are further supported by the lack of association of allergic rhinitis with early wheezing in our study.

This study reports reliable estimates of prevalence and incidence rates of SAR during the first 7 years of life. The development of SAR is characterized by a marked increase in prevalence and incidence after the second year of life. Our longitudinal results further indicate that a remission of SAR does not seem to occur, and in combination with the risk of allergic predisposition, at least 2 seasons of pollen allergen exposure are needed before allergic rhinitis becomes clinically manifest.

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