

Remission of allergic rhinitis: An 8-year observational study

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Background: Allergic rhinitis (AR) and sensitization are considered chronic conditions. However, few studies have reported remission rates in adults.

Objective: We sought to estimate the incidence of remission of AR during an 8-year period.

Methods: Participants in a population-based study of 15- to 69-year-old patients in 1990 were invited to a follow-up in 1998. Questionnaires on respiratory symptoms and serum for specific IgE (s-IgE) analyses were collected at both visits in 734 subjects (69% of those invited). Pollen AR was defined as rhinitis symptoms on pollen exposure within the last 12 months and s-IgE levels of class 2 or greater against pollen (birch, grass, or mugwort). This was similar for AR to animals (cat or dog) or house dust mites (HDMs). Remission of AR was defined as AR at baseline but no rhinitis symptoms at follow-up and sensitization (s-IgE level class ≥ 2 at baseline and class < 2 at follow-up).

Results: Remission of AR occurred in 12% (pollen AR), 19% (animal AR), and 38% (HDM AR; overall, 17%) and was predicted by low s-IgE levels. Age, sex, asthma, atopic predisposition, age at AR onset, and AR duration had no predictive value. A decrease in s-IgE level was observed in only 22% of remitting subjects yet was seen significantly more often than in nonremitting subjects (7.4%). Remission of sensitization occurred in 6% (HDM) to 11% (pollen–furry animal) and was predicted on the basis of low s-IgE levels (class 2) at baseline.

Conclusion: Remission of AR symptoms was relatively infrequent, and remission of both symptoms and IgE sensitization was rare. The results underline the chronic nature of AR in adulthood. (*J Allergy Clin Immunol* 2004;114:1384-8.)

Key words: Allergic rhinitis, allergy, IgE, longitudinal, remission

Several factors predicting the development of IgE sensitization and allergic symptoms have been identified.¹⁻⁶ Both sensitization and allergic rhinitis (AR) are considered chronic conditions. However, few studies have

Abbreviations used

AR: Allergic rhinitis

HDM: House dust mite

s-IgE: Specific IgE

reported rates of remission in longitudinal studies in adults. Symptom remission has been reported in adults in 2 longitudinal epidemiologic studies with follow-up after 6 years (Japan; physician-diagnosed Japanese cedar pollinosis)⁷ and 3 years (Scandinavia; self-diagnosed hay fever, 11 aeroallergens).⁸ The former identified remission to be associated with male sex, old age, late onset of rhinitis, and low levels of specific IgE (s-IgE).⁷ Remission of sensitization assessed on the basis of skin prick tests in adult and pediatric populations is reported in 1% to 20% of subjects with positive skin test responses.⁹ However, there are few published data on remission of AR and of positive levels of serum s-IgE.

In the present study we aimed to assess the 8-year rate of remission of AR symptoms and s-IgE sensitization to pollen, furry animals, and house dust mite (HDM).

METHODS

Baseline study

The baseline study was conducted according to a 2-stage protocol. In the first stage a screening questionnaire on respiratory symptoms was mailed to a sample (randomly from the Civil Registration System) of 15- to 69-year-old patients ($n = 8000$) living in the western part of Copenhagen, Denmark. A total of 6998 (87.5%) responded to the screening questionnaire. In the second stage the following were invited to a health examination: a random group ($n = 793$; randomly selected among respondents) and a symptom group ($n = 788$; selected among respondents who, in the screening questionnaire, reported itchy-stuffy nose, sneezing, shortness of breath, or trouble breathing on exposure to either pollen or furry animals). The participation rates were 75.5% ($n = 599$) in the random group and 80.6% ($n = 635$) in the symptom group. Because 122 subjects were included in both groups, a total of 1112 subjects (overall participation rate of 77.5%) underwent examinations between February 1990 and January 1991. The invitational procedure and the characteristics of participants and nonparticipants have been described in detail previously.¹⁰

Follow-up study

At the time of follow-up, 28 subjects had died, 8 had emigrated, and 12 could not be located. Therefore a total of 1064 of the participants in the baseline study were eligible for the follow-up study, and these subjects were invited in the same month as they were examined in the baseline study to avoid potential seasonal differences. The participation rate was 69.0% ($n = 734$).¹¹ A total of 63.9%

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TABLE I. Remission of AR from 1990 to 1998 (n = 198)

Disease status 1990	Total, % (n)	Disease status 1998: Symptoms			
		Absent		Present	
		s-IgE ≥ 0.7 kU _A /L		s-IgE ≥ 0.7 kU _A /L	
		Absent, % (n)	Present, % (n)	Absent, % (n)	Present, % (n)
Pollen AR*	100 (170)	2.4 (4)	9.4 (16)	4.1 (7)	84.1 (143)
Furry animal AR*	100 (53)	1.9 (1)	17.0 (9)	9.4 (5)	71.7 (38)
HDM AR*	100 (34)	5.8 (2)	32.4 (11)	0 (0)	61.8 (21)

*Definition: self-reported rhinitis symptoms on allergen exposure within the last 12 months and relevant allergen-specific IgE levels of 0.7 kU_A/L or greater.

(n = 469) were examined on a date within 2 months (62 days) from the date of examination in the baseline study (median follow-up duration, 94 months; range, 82-104 months). The participants were examined between October 1997 and November 1998. The Ethical Committee of Copenhagen County approved the study.

Measurement of IgE antibodies

In both the baseline and the follow-up study, venous blood was taken on the day of examination and left to coagulate for 2 hours. The serum was then separated by means of centrifugation at 2000g for 10 minutes and frozen immediately. The serum samples used for IgE antibody analyses were kept at -20°C without thawing until the analysis in 1999. Serum samples were available from 98.7% (1098/1112) and 99.5% (730/734) of the subjects examined at baseline and follow-up, respectively, and were analyzed for IgE specific to birch, grass (timothy), mugwort, dog (hair and dander [e5]), cat (hair and dander [e1]), and mite (*Dermatophagoides pteronyssinus*) with the ADVIA Centaur IgE antibody assay system (Bayer Corp, Tarrytown, NY). The stability of IgE antibodies in serum samples stored at -20°C has previously been confirmed.¹² The results of the analysis for IgE antibodies were considered positive if the measurement was in excess of 0.7 kU_A/L (class 2).

Definition of variables

In both studies information on health, lifestyle, and socioeconomic variables was obtained in a detailed questionnaire, which was completed at home. *Age-related parameters* were based on age when entering the baseline study, and *atopic predisposition* was defined as the presence of hay fever, asthma, and/or atopic eczema in first-degree relatives. *Smoking* was categorized into never smokers, exsmokers, and current smokers.¹¹

Allergic rhinitis to pollen was defined as a positive test result for IgE antibodies to at least one of birch, grass, or mugwort and an affirmative answer to the following question: "Have you, within the last 12 months, had an itchy or stuffy nose, and have you been sneezing when near grass, trees, or flowers?" *Allergic rhinitis to animals* was defined as a positive test result for IgE antibodies to at least one of dog or cat and an affirmative answer to the following question: "Have you, within the last 12 months, had an itchy or stuffy nose, or have you been sneezing following exposure to furry animals, e.g. horse, dog, cat, rabbit, guinea pig, or hamster?" *Allergic rhinitis to mite* was defined as a positive test result for IgE antibodies to mite and an affirmative answer to the following question: "Have you, within the last 12 months, had an itchy or stuffy nose or have you been sneezing following exposure to dust when cleaning rooms or making beds or when in bed?" *Remission of AR* in subjects with AR at baseline was defined by the absence of relevant AR symptoms (no to the relevant question) at follow-up.

Asthma was defined in a similar way.¹³ *Sensitization* was defined as positive levels of s-IgE to birch, grass, and/or mugwort

(pollen); dog or cat (furry animal); or *Dermatophagoides pteronyssinus* (HDM). *Remission of sensitization* was defined as the presence of sensitization at baseline and the absence of sensitization at follow-up. The validity of the questionnaire has previously been confirmed.¹²

Statistical analysis

All data were analyzed with SPSS for Microsoft Windows (release 10.0). Independent predictors of remission of AR or sensitization were determined by means of univariate logistic regression analyses. All significant predictors were further tested by using multiple logistic regression analyses.

RESULTS

A comparison of baseline characteristics between participants and nonparticipants to the follow-up has previously been reported.¹¹ Of relevance to the present study is that the prevalence of sensitization and physician-diagnosed hay fever or asthma did not differ between the groups.

In 1990, AR was reported by 198 subjects with a total of 257 cases of AR, and in 1998, 36 subjects experienced 43 cases of remission. Remission of AR varied between 11.8% and 38.2% (overall remission rate, 16.7% [n = 43/257], Table I). The lowest rate of remission was seen for AR to pollen. In 78% of the subjects with remission of AR symptoms, s-IgE levels remained stable (Table I), so remission of both symptoms and sensitization was rare. We chose to investigate the association between remission and demographic and clinical parameters describing the 36 subjects representing 43 cases of remission of either AR caused by pollen, AR caused by animals, or AR caused by mites. Only low levels of s-IgE predicted remission of AR (Table II). The maximal decrease in s-IgE levels was one s-IgE class, which was observed in 22.2% (n = 8/36) of remitting subjects versus 7.4% (n = 12/162) of nonremitting subjects ($P < .01$, χ^2 test). All other subjects remained in the s-IgE class of the baseline study. Subjects receiving allergen-specific immunotherapy (n = 13) were evenly distributed between remission and nonremission (18.8% vs 14.7%; $P > .6$, χ^2 test). Onset of allergic asthma and remission of AR (pollen) was observed in only one subject.

Remission of sensitization to pollens and animals occurred in 11%, whereas remission of sensitization to

TABLE II. Association between baseline demographic and clinical parameters and remission of AR symptoms at follow-up in subjects with AR* at baseline

		Subjects experiencing remission of AR* (n = 36/199)		
		% (n cases/n total)	OR (95% CI)	P value†
Sex	Female	16.1 (14/87)	1	.52
	Male	19.6 (22/112)	1.38 (0.61-2.7)	
Age in 1990 (y)	15-34	15.0 (16/107)	1	.28‡
	35-49	21.9 (14/64)	1.6 (0.7-3.5)	
	50-65	21.4 (6/28)	1.6 (0.54-4.4)	
Asthma	Yes	17.2 (22/128)	1	.66
	No	19.7 (14/71)	1.2 (0.56-2.5)	
Smoking	Never	14.0 (14/100)	1	.07‡
	Exsmoker	15.6 (5/32)	1.1 (0.38-3.4)	
	Current	25.4 (17/67)	2.1 (0.95-4.6)	
Age at onset (y)	0-15	20.2 (17/84)	1	.38‡
	16-30	17.4 (15/86)	0.83 (0.39-1.8)	
	>31	12.5 (3/24)	0.56 (0.15-2.1)	
Duration in 1990 (y)	0-5	14.6 (6/41)	1	.38‡
	6-20	17.5 (17/97)	1.2 (0.45-3.4)	
	>21	21.4 (12/56)	1.6 (0.54-4.7)	
Atopic predisposition	Yes	17.3 (18/104)	1	.76
	No	18.9 (18/95)	1.1 (0.54-2.3)	
s-IgE level (class)	2	34.8 (16/46)	1	.009‡
	3	12.3 (8/65)	0.26 (0.10-0.69)	
	4	13.8 (12/87)	0.30 (0.13-0.71)	

OR, Odds ratio.

*AR to pollen, furry animals, and/or HDM.

†Univariate analyses.

‡P value for trend

mite occurred in 5.5% (overall remission, 10.5% [n = 36/342]). A clear decrease in remission rate was observed when the cutoff limit was decreased (Table III). Of 36 cases of remission, detectable levels of s-IgE were observed in the vast majority (87.6% [n = 31], Table III). We investigated the association between remission and demographic and clinical parameters describing the 33 subjects representing 36 cases of remission of sensitization to pollen, animals, or mite: remission was associated with absence of relevant rhinitis symptoms at baseline and with low levels of s-IgE in univariate analyses. Only s-IgE remained significant when both predictors were tested in the same model (Table IV).

All estimates were essentially uninfluenced by adjustment for other covariates, including the season of examination (January-April, May-August, and September-December) at follow-up.

DISCUSSION

In the present study we confirm that AR to aeroallergens is generally a chronic disease.¹⁴ Previously, 2 studies have reported remission rates of AR over time: 16.1% (n = 9/56) of subjects allergic to Japanese cedar,⁷ and 19.8% (n = 64/324) of subjects allergic to one or more of

11 aeroallergens⁸ became asymptomatic during 6 and 3 years, respectively. In our study we found comparable remission rates. We observed a lower remission rate for AR to seasonal allergens (pollen) than for AR to perennial allergens (animal and mite). This difference might be due to the fact that exposure to pollens is more difficult to avoid than exposure to animals and mites.¹⁵ A decrease by no more than one IgE class was observed in only 22% of remitting subjects, and thus remission of both rhinitis symptoms and sensitization was rare. It therefore appears that sensitization persists in the majority of cases with remission of symptoms. Remission of AR might be due to avoidance of allergen exposure, but we have no data on individual allergen exposure to the allergen sources. Regional birch, grass, and mugwort pollen counts in the relevant seasons were not low,¹⁶ supporting the fact that allergic symptoms are affected by factors other than IgE sensitization and exposure.⁶ Remission of AR was not the result of progression to allergic asthma, supporting our earlier findings that allergic asthma coexists with AR.¹³ Remission of symptoms might also be a result of therapy. Remitting subjects were not treated more often with allergen-specific immunotherapy, which might reflect that this treatment is reserved for patients with more severe AR.¹⁷ Nevertheless, subjects with AR treat symptoms to an acceptable level rather than to complete absence,¹⁸

TABLE III. Remission of IgE sensitization (≥ 0.7 kU_A/L) from 1990 to 1998 at different cutoff levels: immeasurable levels (0 kU_A/L), less than class 1 (<0.35 kU_A/L), and less than class 2 (<0.7 kU_A/L)

IgE sensitization Status 1990	IgE sensitization status 1998		
	Total, n	0 kU _A , % (n)	<0.35 kU _A , % (n)
Pollen	215	0.9 (2)	7.0 (15)
Furry animal	72	2.8 (2)	5.6 (4)
HDM	55	1.8 (1)	3.6 (2)

TABLE IV. The association between baseline demographic and clinical parameters of remission of sensitization*

		Subjects experiencing remission of sensitization* (n = 33/288)		
		% (n cases/n total)	OR (95% CI)	P value†
Sex	Female	13.6 (17/125)	1	.26
	Male	9.8 (16/163)	0.66 (0.32-1.3)	
Age in 1990 (y)	15-34	9.9 (15/151)	1	.29‡
	35-49	12.0 (11/92)	1.2 (0.53-2.8)	
	50-65	15.6 (7/45)	1.7 (0.64-4.5)	
Smoking	Never	10.5 (14/133)	1	.40‡
	Exsmoker	9.8 (5/51)	0.94 (0.32-2.8)	
	Current	13.5 (14/104)	1.7 (0.64-3.2)	
Atopic predisposition	Yes	9.1 (13/143)	1	.16
	No	13.8 (20/145)	1.7 (0.81-3.6)	
Relevant symptoms	Yes	9.2 (21/229)	1§	.09
	No	20.3 (12/59)	2.2 (0.88-5.4)	
s-IgE level (class)	2	30.4 (14/46)	1§	<.0001‡
	3	3.1 (2/65)	0.13 (0.04-0.40)	
	4	4.6 (4/87)	0.13 (0.05-0.39)	

OR, Odds ratio.
*Definition of remission: s-IgE (≥ 0.7 kU_A/L) in serum to pollen, furry animals, and/or HDM in 1990 but not in 1998.
†Univariate analyses (except “Relevant symptoms” and “Specific IgE level”).
‡P value for trend.
§Multiple regression analysis with “Relevant symptoms” and “Specific IgE levels” in the same model because both predictors were significant in univariate analyses.

making drug-induced remission unlikely. Furthermore, subjects were investigated in the same month to avoid seasonal differences of symptoms. The severity of seasonal AR has been found to increase when described postseasonally, and thus false remission caused by poor recollection appears unlikely.¹⁹

The higher remission rate of AR to perennial allergens might be falsely increased in our study because AR to a perennial allergen is difficult to distinguish on the basis of history from other perennial allergens or nonallergic rhinitis.²⁰ To diminish false-positive cases, we chose a relatively high cutoff level for IgE positivity (class 2).

Not much is known about predictors of remission of AR. Okawa et al⁷ identified male sex, old age at baseline, old age at AR onset, and low s-IgE levels to be more prevalent in remitting subjects; only the latter was significant in a logistic regression model. In our study remission was only predicted by low baseline s-IgE levels and not by sex, age, age at AR onset, AR duration, smoking, lower airway symptoms, or atopic predisposition (Table II). The interstudy differences might be due to

a smaller cohort and exclusion of young remitting subjects in the Japanese cedar study, which included only subjects older than 40 years.⁷ Obviously, the present findings require further investigation.

Remission of skin prick test reactivity has been reported: 1% to 20% of positive skin reactions are not reproduced when testing is repeated after more than 12 months.⁹ To our knowledge, no study on s-IgE remission has been published. We observed remission of sensitization (s-IgE class <2 at follow-up) in 11% (n = 36) of sensitized subjects (s-IgE class ≥ 2 at baseline; Table III). Yet it is unknown whether this represents true remission because s-IgE levels became immeasurable in only 5 (1.4%) subjects (Table III). Several factors predicting the development of sensitization have been identified (eg, age, sex, race, genetic predisposition, household size, smoking, and allergen and adjuvant exposure).²⁻⁵ In contrast, few factors predicting remission of sensitization have been identified. We found that low levels of s-IgE predicted remission, whereas sex, age, smoking, atopic predisposition, and absence of symptoms had no predictive value (Table IV). The latter was

significant in the univariate model but not when corrected for s-IgE levels, supporting the hypothesis that asymptomatic sensitization is not a normal transient state of IgE production.²¹ Generally, insight into sentinel immunologic mechanisms underlying spontaneous remission of symptoms, sensitization, or both might provide new targets for therapeutic intervention.

In conclusion, over an 8-year period, remission of AR symptoms occurred in approximately 10% to 40% depending on allergen and involved a reduction of a maximum of one s-IgE class in 22% of cases of remission. Remission of sensitization was observed in 11% of subjects sensitized at baseline. These findings underline the chronic intermittent nature of AR in adulthood.

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