

Can early household exposure influence the development of rhinitis symptoms in infancy?

Findings from the PARIS birth cohort

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Background: Allergic rhinitis (AR) has become the most prevalent chronic allergic disorder in childhood, and the role of environment has been questioned, particularly in early life.

Objective: To investigate the risk factors for rhinitis symptoms in infants included in the PARIS (Pollution and Asthma Risk: an Infant Study) birth cohort.

Methods: Infants were invited to participate at age 18 months in a health examination conducted by a pediatrician. Allergic rhinitis was defined as the presence of rhinitis symptoms (runny nose, blocked nose, sneezing in the absence of a cold) combined with biological atopy (elevated total immunoglobulin E [IgE], specific IgE, or eosinophilia) and nonallergic rhinitis (NAR) as symptoms without biological atopy. Information about indoor exposures and lifestyle was collected during a telephone interview when the child was 1 month of age. Risk factors for AR and NAR were studied by using a polytomous regression model.

Results: The prevalence of AR and NAR was 70/1,850 (3.8%) and 99/1,850 (5.4%), respectively. Allergic rhinitis and NAR did not share similar risk factors. Male sex (odds ratio [OR] = 1.99 [1.19–3.32]), parental history of AR (OR = 1.89 [1.16–3.08]), low socioeconomic class (OR = 2.23 [1.05–4.72] for low vs high level), and the presence of cockroaches in the home (OR = 3.15 [1.67–5.96]) were risk factors for AR. Conversely, the presence of particle-board furniture less than 12 months old in the child's bedroom was associated with an increased risk of NAR (OR = 1.87 [1.21–2.90]).

Conclusions: This study should raise awareness about the impact of indoor exposures, particularly with regard to cockroaches and particle-board furniture, because they could influence the occurrence of noninfectious rhinitis.

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INTRODUCTION

Allergic rhinitis (AR) is the most prevalent chronic allergic disorder in children.¹ In early life, AR is unrecognized because of confusion between rhinitis symptoms attributable to allergy and those caused by infection.¹ Nevertheless, recent results from the PARIS (Pollution and Asthma Risk: an Infant Study) birth cohort suggest that AR could start as soon as 18 months of life by showing a significant relation between rhinitis symptoms occurring apart from a cold and atopy.²

The recent increase in prevalence of AR suggests an impact of changes in the indoor environment and lifestyle. Apart from sensitization to allergens, early-life risk factors for AR remain poorly explored.¹ However, the identification of risk factors for AR could lead to preventive interventions³ and help reduce the burden of AR and comorbidities such as ear, nose, and throat disorders.⁴ Moreover, it also might prevent the potential subsequent development of asthma.⁵

Apart from AR, a growing interest has been shown in nonallergic rhinitis (NAR), which affects many children.⁶ Numerous hypotheses have been proposed concerning the mechanisms of this other form of noninfectious rhinitis, notably a possible action from inspired pollutants.⁶

This study aimed to investigate the effects of environmental and behavioral factors on the risk of occurrence of AR and NAR in infants aged 18 months. The study is part of the PARIS birth cohort, a population-based study implemented in 2003 dealing with respiratory and allergic disorders in early childhood.

METHODS

Study Design and Ethics

The PARIS birth cohort is a population-based cohort composed of healthy children recruited at birth in 5 Parisian maternity hospitals according to both medical and socio-

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demographic criteria described elsewhere.⁷ The follow-up of children included in the PARIS birth cohort was based on telephone interviews and self-administered questionnaires, as well as health examinations. This paper analyzes the data collected during the health examination at 18 months of age with regard to the questionnaire-based environmental follow-up. The 18-month health examination included a medical examination together with a standardized questionnaire administered by a pediatrician. A blood sample was taken for each child and analyzed for different biological markers of atopy. The 18-month health examination, proposed to the parents of all children followed up in the study, was free of charge and took place in the Paris Health Centre of the National French Health Insurance System. Data on the characteristics of the household environment and lifestyle were collected during a detailed telephone interview when the child was 1 month old. Changes in the environment of the child were recorded by using postal questionnaires at 3, 6, 9, 12, and 18 months of age. Children who moved within Paris area during their first 18 months of life ($n = 298$, 16.1%) were followed-up, and the new household was described with the same detailed environmental questionnaire as that used at 1 month of age. The parents gave their written informed consent, and the research protocol was approved by the National Ethics Committee (permissions nos/. 031153 and 051289).

Biological Markers of Atopy

Full blood count was determined, and blood eosinophilia was measured by using flow cytometry (Beckmann Coulter, Miami, Florida). Blood eosinophilia is expressed as the absolute value per cubic millimeter (eosinophils/mm³). Total immunoglobulins E (IgE) were measured by using ImmunoCAP (Phadia, Uppsala, Sweden) and are expressed in units per milliliter (U/mL). Thresholds were used to define elevated levels, blood eosinophilia being defined as a concentration of 470 eosinophils/mm³ or greater and elevated total IgE as a concentration of 45 U/mL or greater.⁸ Sensitization to inhalant allergens (house dust mite, pets, grass pollens, weed pollens, tree pollens, and mold) and food allergens (egg white, cow's milk, peanut, mustard, fish, wheat, soy, hazelnut, sesame, shrimp, beef, and kiwi) was analyzed with ImmunoCAP, Phadiatop, and Trophatop fx26, fx27, and fx28 (Phadia) with a detection limit set at 0.35 U/mL. Atopy was defined as the presence of at least 1 of these biological markers.

Definition of AR and NAR

A child was considered to have rhinitis symptoms if the parents answered "yes" to the following question: "In the past 12 months, did your child have a problem with sneezing, or a runny, or a blocked nose when she/he did not have a cold or the flu?" Allergic rhinitis was defined as the combination of rhinitis symptoms with an atopic status, whereas NAR was defined as the occurrence of rhinitis symptoms in the absence of an atopic status.

Potential Risk Factors

Population characteristics such as parental history of allergy, focusing on having ever experienced AR, asthma, or eczema, duration of exclusive maternal breastfeeding, presence of siblings, and socioeconomic status were considered. Socioeconomic status was determined according to the highest level of occupation among the 2 parents, occupations being divided into 3 categories: low (low-level white-collar workers, blue-collar workers, and unemployed), intermediate (intermediate white-collar workers, craftsmen, and shopkeepers), and high (high-level white-collar workers).

Factors of interest among the characteristics of the household environment included: the use of gas for cooking or heating, presence of molds (visible molds or moldy smell), use of an air dampener, and presence of cockroaches in the home. Potential sources of aldehydes were considered: indoor renovation activities such as change of walls or floor coating in the past 12 months⁹ and presence of particle-board furniture and varnished parquet floors less than 12 months old.¹⁰ Particular attention was given to the bedroom of the child with regard to these potential sources of aldehydes. Factors related to house-dust mite exposure, such as carpet-covered floor, age of bedding, and use of an anti-dust mite cover on the mattress were also examined.

In addition to the characteristics of the household environment, behavioral factors were documented. Prenatal exposure to tobacco smoke included active maternal smoking as well as passive smoking at home or at work during pregnancy. Postnatal exposure to parental smoking at home was considered as presence/absence, as well as the mean number of cigarettes smoked daily at home. Other behavioral factors included the presence of a furred pet, the daily mean time of ventilation in the home, and cleaning habits (frequency of mopping, vacuum cleaning, and use of cleaning sprays). Parents were also asked about do-it-yourself activities using paint, varnish, glue, resin, or other odorous compounds at home.

Statistical Analysis

Analyses were performed using Stata software, version 9.1 (Stata Corp, College Station, Texas). Chi-squared tests were used to assess statistical associations between environmental and behavioral exposure and the occurrence of AR and NAR in univariate analysis. The effect of environmental and behavioral factors was considered separately for AR and NAR by using a polytomous regression model. The analysis was conducted by introducing factors associated with the occurrence of AR or NAR with a $P < .20$, as well as risk factors described in the literature (sex, socioeconomic status, duration of maternal breastfeeding, presence of siblings, and exposure to environmental tobacco smoke) into the polytomous regression model. The model was adjusted for the use of nasal corticosteroids, because these could modify the response to environmental pollutants. The final model was obtained by eliminating variables associated with both AR and NAR with a $P > .05$. Results are presented with crude

and adjusted odds ratios (OR) and their 95% confidence intervals (CI).

RESULTS

Study Population

A total of 2,012 children attended the 18-month health examination, and the analysis was carried out on 1,850 that had information on both rhinitis symptoms and biological markers of atopy. The mean age of the children in our study sample was 19 months $\pm$ 2, and the sex ratio was 1. Although they had a higher socioeconomic status, families participating did not differ from other families included in the original PARIS cohort with regard to parental history of allergy, parental smoking, and siblings (Table 1).

The population was largely urban, more than 92% of families living in apartments with a mean area of 68 ± 23 m². Characteristics of environmental exposures, assessed at 1 month of age, as well as cumulated by 18 months of age, are described in Table 2. Particularly, exposure to tobacco smoke was reported in 384 infants (21.0%) at 1 month of age, with a mean number of cigarettes smoked daily at home amounting to 11 ± 9 . Considering cleaning habits, wet-mopping and vacuum cleaning were done almost every day in 308 (16.9%) and 447 dwellings (24.5%), respectively. In addition, a daily use of cleaning sprays was reported in 96 families (5.3%). The mean time of ventilation at home was 2.7 ± 4.8 hours.

Prevalence of AR and NAR

The prevalence of rhinitis symptoms in the absence of a cold in the last 12 months was 9.1% (169/1,850). The most reported symptom was runny nose, in 117 children (69.2%), followed by sneezing in 54 children (32.0%) and blocked nose in 35 children (20.7%). Rhinitis symptoms were combined with biological atopy in 41.4% of the cases. As a result,

the prevalence of AR and NAR was 70/1,850 (3.8%) and 99/1,850 (5.4%), respectively. No difference was seen in the clinical presentation of AR and NAR as far as the different symptoms, the limitation in daily activities, the use of nasal corticosteroids in the past 12 months, and their mean duration throughout the year were considered (Table 3).

Factors Associated with AR and NAR

Results of the risk analysis for AR and NAR are presented in Table 4. The prevalence of AR was related to different sociodemographic variables (sex, parental history of AR, and socioeconomic status), but the strongest risk factor for AR was the presence of cockroaches in the home, with an adjusted OR (aOR) > 3 (aOR 3.15 [1.67–5.96]). Concerning NAR, the presence of particle-board furniture aged less than 1 year in the child's bedroom led to an 87% increase in the risk of NAR (aOR 1.87 [1.21–2.90]). No effect was found from the duration of exclusive maternal breastfeeding, the presence of siblings, or prenatal or postnatal tobacco smoke exposure; however, these variables were kept in the model as adjustments.

The results of the analysis were unchanged when considering the modifications in the child's environment during his or her first 18 months of life. Indeed, the risk of AR was increased with an aOR of 2.87 (1.52–5.41) when children were exposed to cockroaches, and the risk of NAR was increased with an aOR of 1.67 (1.08–2.58) when children were exposed to particle-board furniture aged less than 1 year in their bedroom by 18 months of age.

DISCUSSION

This study identified different risk factors for AR and NAR among demographic and household characteristics. Risk factors for AR included factors classically implicated in allergic

Table 1. Characteristics of the Analyzed Subcohort Compared with the Original PARIS Cohort

	Analyzed subcohort (n = 1,850)	Children of the original birth cohort not included in the analysis (n = 2,327)	P
Sex			
Male	925 (50.0)	1,207 (51.9)	
Female	925 (50.0)	1,120 (48.1)	.230
Siblings			
No	1,059 (57.2)	1,288 (55.4)	
Yes	791 (42.8)	1,038 (44.6)	.231
Parental history of allergy			
Asthma	345 (18.7)	439 (18.9)	.858
AR	657 (35.5)	772 (33.2)	.114
Eczema	308 (16.7)	418 (18.0)	.265
Socio-economic status			
High	1,231 (66.5)	1,299 (55.8)	
Intermediate	476 (25.7)	706 (30.3)	
Low	143 (7.7)	322 (13.8)	<.001
Maternal age (years, mean $\pm$ SD)	32.5 $\pm$ 4.0	32.1 $\pm$ 4.3	.001
Prenatal exposure to tobacco smoke	551 (29.8)	753 (32.4)	.100
Active parental smoking reported at birth	385 (21.1)	482 (23.1)	.118

Except for maternal age, all values shown are n (%).

Table 2. Environmental Exposures Assessed at 1 Month of Age and Cumulated by 18 Months of Age

	Exposure assessed at 1 month of age	Cumulated exposure by 18 months of age
Characteristics of household environment		
Gas cooking or heating	1,031 (56.4)	1,100 (60.1)
Indoor renovation activities in the home in the past year	780 (42.7)	1,080 (58.6)
Indoor renovation activities in the child's bedroom in the past year	686 (37.5)	955 (51.6)
Presence of particle-board furniture less than 1 year old in the home	784 (42.9)	885 (48.4)
Presence of particle-board furniture less than 1 year old in the child's bedroom	540 (29.5)	588 (32.2)
Presence of molds in the home	332 (18.2)	345 (18.9)
Use of an air dampener	300 (16.4)	321 (17.6)
Presence of cockroaches in the home	145 (7.9)	154 (8.4)
Carpet in the bedroom of the child	761 (41.6)	816 (44.6)
New mattress in the baby's bedding	968 (52.9)	1,312 (71.2)
Use of an anti-dust mite cover in the baby's bedding	636 (35.0)	808 (43.9)
Behavioral factors		
Maternal breastfeeding at birth	1,534 (83.1)	—
Exclusive maternal breastfeeding		
No	—	313 (17.0)
<3 months	—	1,008 (54.6)
≥3 months	—	526 (28.5)
Prenatal exposure to passive maternal smoking	471 (25.5)	—
Prenatal exposure to active maternal smoking	203 (11.0)	—
Postnatal exposure to environmental tobacco smoke	384 (21.0)	550 (29.9)
Mean number of cigarettes smoked daily in home		
0	1,444 (79.0)	1,292 (70.1)
1–19	302 (16.5)	526 (28.6)
≥20	82 (4.5)	24 (1.3)
Do-it-yourself activities at home	229 (12.5)	402 (21.8)
Presence of furred pets	298 (16.3)	328 (17.8)

All values shown are *n* (%).

Table 3. Characteristics of Rhinitis Symptoms Apart from a Cold

	Rhinitis symptoms apart from a cold (N=169)	AR (N = 70)	NAR (N = 99)	<i>P</i> ^a
Details on the symptoms				
Runny nose	117 (69.2)	49 (70.0)	68 (68.7)	.855
Sneezing	54 (32.0)	18 (25.7)	36 (36.4)	.144
Blocked nose	35 (20.7)	17 (24.3)	18 (18.2)	.335
Disturbance in daily activities	30 (17.8)	11 (15.7)	19 (19.2)	.560
Nasal corticosteroids	103 (56.0)	39 (55.7)	56 (56.6)	.912
Duration of the symptoms throughout the year (months, mean ± SD)	3.9 ± 3.0	4.1 ± 3.1	3.8 ± 2.9	.447

Abbreviations: AR, allergic rhinitis; NAR, nonallergic rhinitis.

Except for the duration of the symptoms, all values shown are *n* (%).

^a *P* for the comparison between AR and NAR.

disorders (male sex and parental history of AR) and allergens (cockroaches). In contrast, these factors did not influence the risk of NAR, which was increased by the presence of furniture capable of emitting air pollutants in the child's bedroom.

The presence of cockroaches in the home was the strongest risk factor for AR found in this work. Exposure to cockroaches, one of the major sources of indoor allergens,¹¹ has been shown to be a risk factor for sensitization, wheezing,

and asthma, particularly in inner-city populations.¹²⁻¹⁴ Our study states that exposure to cockroaches also can be related to nasal symptoms, as previously suggested by Bunyavanich et al,¹⁵ who showed that sensitization to cockroaches was a risk factor for AR in children. Because cockroach allergens are not included in the ImmunoCAP Phadiatop device we used, the sensitization to cockroach allergens was researched in frozen sera of infants with AR and exposed to cockroaches

(extract of *Blattella germanica*, ImmunoCAP, Phadia) in a complementary analysis. The sensitization to cockroach allergens of 2 infants among the 11 for whom sera were available is consistent with the involvement of an IgE mechanism in the increased risk of AR related to cockroach exposure. Seemingly low, this result is actually noteworthy considering the low prevalence of sensitization to inhalant allergens at this age.¹⁶ Besides, another mechanism, involving inflammatory patterns likely to amplify allergen-induced reactions, could account for the effect of cockroach exposure on the risk of AR. Indeed, experimental studies shed light on the ability of cockroach allergens to induce the release of proinflammatory mediators, such as interleukin-8 and tumor necrosis factor- α , in human airway epithelial cells.^{17,18}

Lower socioeconomic level was also related to an increased risk of AR in the current study. The influence of the socioeconomic level on the risk of developing allergic disorders was not clearly established in epidemiological studies.¹ Socioeconomic status was shown to be related to the sensitization to inhalant allergens,^{19,20} but the direction of the association varies depending on the study. In accordance with Lewis et al,¹⁹ we found that infants from a lower socioeconomic class were more sensitized to inhalant allergens compared with infants from a higher level (2.1, 4.3, and 5.0% in the high, intermediate, and low socioeconomic class, respectively; $P = .018$). Moreover, infants from the lower socioeconomic class were breastfed for less time and were more likely to be exposed to environmental factors, such as paren-

tal smoking, furred pets, cockroaches, and daily use of cleaning sprays (data not shown).

Considering NAR, the presence of particle-board furniture less than 1 year old in the child's bedroom almost doubled its risk of occurrence. Particle-board furniture less than 1 year old in the child's bedroom was shown to be a source of aldehydes, and particularly formaldehyde, in previous works from the PARIS birth cohort.¹⁰ Indeed, measurements in indoor air of a random subsample of approximately 200 children included in the cohort showed that the presence of this furniture significantly increased formaldehyde levels. The effects of early exposure to formaldehyde on nasal symptoms have been poorly studied compared with bronchial symptoms, even though experimental studies have suggested that absorption of formaldehyde occurs mainly in the upper respiratory tract.²¹ In the current study, the increase in the risk of nonallergic symptoms suggests a mechanism related to irritation. Indeed, formaldehyde is a well-known irritant to the respiratory tract, which could cause irritating nasal symptoms mimicking AR.²¹ Its irritant effect is related to its electrophilic reactivity, which makes it react easily with nucleophilic sites on cell membranes and in body tissues.²² Other studies actually observed a greater effect of environmental factors in nonatopic subjects.²³ Smedje and Norback²⁴ identified higher concentrations of formaldehyde in classroom air as risk factors for the development of asthma in Swedish schoolchildren without a history of atopy, whereas no effect of this indoor pollutant was seen in children with a

Table 4. Risk Analysis for Rhinitis Symptoms Apart from a Cold

	AR (N = 70)				NAR (N = 99)			
	n (%)	Crude OR (95%CI)	Adjusted OR ^a (95%CI)	P ^b	n (%)	Crude OR (95%CI)	Adjusted OR ^a (95%CI)	P ^b
Sex								
Female	24 (2.6)	1	1		58 (6.3)	1	1	
Male	46 (5.0)	1.93 (1.17–3.19)	1.99 (1.19–3.32)	.008	41 (4.4)	0.71 (0.47–1.07)	0.75 (0.49–1.13)	.170
Parental history of AR								
No	35 (2.9)	1	1		60 (5.0)	1	1	
Yes	35 (5.3)	1.88 (1.17–3.04)	1.89 (1.16–3.08)	.010	39 (5.9)	1.22 (0.81–1.85)	1.21 (0.79–1.85)	.377
Socioeconomic status								
High	38 (3.1)	1	1		71 (5.8)	1	1	
Intermediate	22 (4.6)	1.50 (0.88–2.56)	1.42 (0.82–2.47)	.211	20 (4.2)	0.73 (0.44–1.21)	0.63 (0.37–1.08)	.091
Low	10 (7.0)	2.36 (1.15–4.86)	2.23 (1.05–4.72)	.036	8 (5.6)	1.01 (0.48–2.15)	0.89 (0.41–1.92)	.768
Presence of a particle board furniture less than 1 year old in the child's bedroom								
No	48 (5.8)	1	1		57 (4.4)	1	1	
Yes	22 (5.6)	1.14 (0.68–1.90)	1.09 (0.63–1.87)	.769	40 (7.4)	1.74 (1.14–2.64)	1.87 (1.21–2.90)	.005
Presence of cockroaches in the home								
No	56 (3.3)	1	1		85 (5.1)	1	1	
Yes	14 (9.7)	3.24 (1.75–5.99)	3.15 (1.67–5.96)	<.001	12 (8.3)	1.83 (0.97–3.44)	1.81 (0.95–3.45)	.070

Abbreviations: AR, allergic rhinitis; NAR, nonallergic rhinitis; OR, Odds ratio; CI, confidence interval.

^a Adjusted for duration of maternal exclusive breastfeeding, presence of siblings, prenatal and postnatal exposure to tobacco smoke, and use of nasal corticosteroids.

^b P-value associated with the adjusted odds ratio.

history of atopy. Formaldehyde is the major pollutant released by wood-pressed materials, but they are known to emit a large range of volatile organic compounds²⁵ that could also be involved in the irritation of the nasal mucosa.

No relation was seen between factors related to exposure to house-dust mites and the occurrence of AR in the current study. This result should be considered with regard to the overall low level of exposure of our population. Indeed, levels of house-dust mite allergens measured with the Acarex test in a random subset of dwellings of infants included in the PARIS birth cohort were null or low in almost 99% of the cases. As a consequence, there may not have been enough contrast in the exposure to house-dust mites in our population to show the possible effect of preventive measures. However, the 22 cases of sensitization to house-dust mites (1.2%) observed in our study sample are not conflicting with the low levels of exposure found in this study, because house-dust mite allergens are perennial allergens ubiquitous in the indoor environment that can induce sensitization at very low levels.¹ Besides, the lack of relation between exposure and clinical outcomes is not contradictory to our previous findings showing a relation between the sensitization to house-dust mite allergens and the occurrence of AR-like symptoms.² Indeed, other authors described no relation between exposure to house-dust mite allergens and the occurrence of asthma, even though sensitization to house-dust mites was related to asthma, wheeze, and increased bronchial hyperresponsiveness.²⁶

Contrary to other epidemiological studies in infants,^{20,27,28} our study failed to show a relationship between postnatal exposure to environmental tobacco smoke and rhinitis symptoms. Nevertheless, studies by Wright et al²⁰ and Biagini et al²⁸ showed a significant increase in risk of AR only in infants exposed to 20 or more cigarettes per day. Once more, our population may be too little exposed to show an effect of exposure to tobacco smoke, because only 4.6% of our population was exposed to 20 or more cigarettes per day. Moreover, as reported in another birth cohort,²⁹ several mothers stated that they had tried to minimize exposure of their child, by smoking near an open window, for instance.

From a methodological standpoint, an important topic that should be discussed is the definition employed to describe rhinitis symptoms. Indeed, AR is difficult to diagnose in infancy, and scores developed to diagnose AR in epidemiological surveys³⁰ are not suitable for infants. The strength of our study is that it combined a definition commonly used in epidemiological studies to describe AR-like symptoms in preschool children¹ with an objective assessment of atopy through biological markers. In addition, the participation of four specifically trained pediatricians in the administration of the questionnaire was an opportunity to improve the homogeneity and the quality of the data. The participation rate is a limitation of this study, the analyzed subcohort representing only 44.3% of the original cohort. Nevertheless, the participation was not influenced by parental history of allergy, parental smoking, and siblings. As to the higher participation of upper socioeconomic status parents, it

is commonly described in other birth cohorts, probably because of an increased awareness of the disease.³¹ Considering the assessment of environmental exposure, the strength of this study is that it involved a detailed and regularly updated assessment of early environmental exposure in a large sample of infants. In addition, the telephonic interview at 1 month of age enabled us to reduce classification bias.

In conclusion, the study of AR and NAR showed that, even if they did not differ clinically, they did not share similar risk patterns in infants aged 18 months. The role of genetic factors on the risk of AR was confirmed, and environmental triggers of AR and NAR were identified. This work should raise awareness about the impact of indoor exposure, particularly with regard to cockroaches and particle-board furniture.

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