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Rhinitis in 10-year-old children and early life risk factors for its development

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Aim: To study the prevalence, characteristics of and risk factors for childhood rhinitis. *Methods:* In a whole population birth cohort study ($n = 1456$) the prevalence and characteristics of rhinitis among 10-y-old children were examined. At this age 1373 children (94%) completed standardized questionnaires, 1043 (72%) skin-prick testing, 953 (65%) serum inhalant immunoglobulin E antibody screening and 784 (54%) methacholine bronchial challenges. *Results:* At the age of 10 y the prevalence of hayfever ever was 18.6% and current nasal symptoms (rhinitis) 22.6%. Rhinitis at 10 y was largely seasonal and associated with low morbidity, although 62.7% of cases required pharmacological treatment. Atopy (positive skin test) and other allergic states were associated with rhinitis ($p < 0.001$). Wheeze or diagnosed asthma was higher with coexistent rhinitis. Among wheezing children physician-diagnosed asthma ($p < 0.024$) and inhaled corticosteroid use ($p < 0.001$) were greater with the presence of rhinitis. Significant bronchial hyperresponsiveness (methacholine concentration giving a 20% fall in forced expiratory volume in 1 s <4.0 mg ml^{-1}) was greater if rhinitis was present even when the child did not wheeze ($p < 0.001$). Risk factor analysis for rhinitis identified the independent significance for atopy ($p < 0.001$) and eczema ($p = 0.009$) at the age of 4 y plus paternal rhinitis ($p < 0.001$), maternal rhinitis ($p = 0.033$) and maternal food allergy ($p = 0.016$).

Conclusion: Rhinitis is common at the age of 10 y, with strong associations with atopy, wheezing, asthma and bronchial hyperresponsiveness. An inherited predisposition towards atopy appears to predominate over environment in the aetiology of this state.

Key words: *Asthma, atopy, childhood rhinitis, prevalence, risk factors*

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In recent years a substantial prevalence of childhood allergic rhinitis has been noted in many populations with highest frequencies among affluent westernized societies (1–6). Rhinoconjunctivitis symptoms have been described for 20% of 12–14-y-olds in the UK, Australia and the USA. The reasons for these trends remain unclear but probably reflect interactions of the environment with genetic predisposition to allergy (7). Thus, allergic family history, asthma expression and maternal smoking in the first year of life have been implicated (2, 4) in causing childhood rhinitis. Knowledge of potential risk factors could lower the burden of this disease. Notions of "one airway, one disease" have also heightened awareness of the associations between rhinitis and asthma. Asymptomatic bronchial hyperresponsiveness (BHR) occurs in rhinitis and may predispose to asthma (8, 9). Understanding the interplay of rhinitis and asthma could improve management of both diseases.

A consistent problem with prevalence data for allergic diseases has been the lack of relevant standard definitions. This made comparison between studies difficult, but now the International Study of Asthma and Allergies in Childhood (ISAAC) (1) has provided a standardized research tool. Another shortcoming of many studies has been a lack of objective testing to assess BHR or atopy. This study describes the prevalence, characteristics of and risk factors for rhinitis in 10-y-old children from prospective follow-up of a whole population birth cohort using standardized questionnaires and objective measurements.

Patients and methods

A whole population birth cohort was recruited on the Isle of Wight, UK, in 1989 to study the development of childhood allergies. Approval was given by the Local Research Ethics Committee and informed consent obtained for 1456 (of 1536) children born between 1

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January 1989 and 28 February 1990. Children were enrolled at birth and seen at the ages of 1 ($n = 1167$), 2 ($n = 1174$) and 4 y ($n = 1218$) (10–12). In addition to questionnaires, maternal and cord immunoglobulin E (IgE) were measured in most cases at birth and skin-prick testing (SPT) to common allergens was performed in the majority of children seen at the age of 4 y. Social class at birth was defined by the Registrar General's classification.

At the age of 10 y, records were updated at a visit to the research centre ($n = 1043$). Where this was not possible ($n = 330$), a telephone questionnaire was completed with a parent or a modified postal questionnaire sent for the parent to complete and return. Interviewer-administered ISAAC written and supplementary questionnaires (from prior follow-ups) were completed with the children's parents. Relevant questions were: "has your child ever had hayfever?" (hayfever ever) and "in the past 12 months, has your child had a problem with sneezing, or a runny or a blocked nose when he/she did not have a cold or the flu?" (current nasal symptoms). A positive response for current nasal symptoms was taken as indicating rhinitis at the age of 10 y.

Children attending the centre underwent SPT to a panel of common allergens (ALK, Denmark) plus positive (histamine dihydrochloride, 10 mg ml^{-1}) and negative (physiological saline) controls. Inhalant allergens tested were house dust mite (*Dermatophagoides pteronyssinus*), cat, dog, *Alternaria alternata, Cladosporium herbarium*, grass pollen and tree pollen mix. Food allergens tested were cow's milk, soya, hen's egg, peanut and cod. Atopy was defined as at least one test response with a mean weal diameter 3 mm greater than the negative control. All children with past or current wheezing and a control group of "non-wheezers" were invited to undergo methacholine bronchial challenge to assess BHR with a Koko dosimeter (Pds Instrumentation, Louisville, USA; compressed air source at 8 l min^{-1} and nebulizer output 0.8 l min^{-1}) using the method of Chai et al. (13). The methacholine concentration giving a 20% fall in forced expiratory volume in 1 second (FEV_1) from the post-saline value was interpolated and expressed as PC_{20}–FEV_1. $PC_{20} < 4$ mg ml^{-1} was termed "definite BHR", thus including mild/moderate and severe BHR following the American Thoracic Society guidelines (14). Total serum IgE and an inhalant screen (qualitative) for IgE antibody to common inhalant allergens (Phadiatop; Pharmacia, Uppsala, Sweden) were also measured at the age of 10 y. The inhalant screen tested for house dust mite (*D. pteronyssinus and D. farinae*), cat dander, dog dander, horse dander, timothy grass, cladosporium, silver birch, olive, mugwort and nettle.

Statistical analysis

Data were double entered onto SPSS (v. 10.0; Chicago, USA). Means for continuous variables were analysed by independent sample *t*-tests (with transformation if necessary). Differences in proportions between groups and univariate risk analysis for current nasal symptoms were tested by χ^2 analysis (with Fisher's exact test if indicated). Backward stepwise (likelihood ratio) logistic regression analysis was used to assess independent effects of risk factors with $p < 0.2$ at univariate testing. Results were expressed as adjusted odds ratios (OR) and their 95% confidence intervals (CI).

Results

At the age of 10 y, information was updated on 1373 (94%) of the 1456 children originally recruited. Of these, 1043 (76.0%) attended the centre to complete a questionnaire ($n = 1043$), SPT ($n = 1036$), total IgE assay ($n = 953$), spirometry ($n = 981$) and methacholine bronchial challenge ($n = 784$). The remaining 330 children only completed questionnaires. A personal or family history of allergy was less likely in children where only questionnaires were done. Demographic and disease characteristics for these two groups of children have been reported (15).

At the age of 10 y current nasal symptoms were present in 308/1362 (22.6%) children, while hayfever ever was reported in 256/1373 (18.6%) children. Retrospective reporting at 10 y gave the median onset for current nasal symptoms at 7.0 y (interquartile range: 4.0–8.0). Of children with current nasal symptoms, 205/308 (66.6%) also reported hayfever ever. Most children with *both* hayfever ever and current nasal symptoms, 123/204 (60.3%), described predominantly seasonal disease, while 62/204 (30.4%) described purely perennial disease and 19/204 (9.3%) experienced a mixture of both. Current nasal symptoms did not vary by gender (male 22.6% vs female 22.7%, $p = 1$). Treatment was needed by 190/303 (62.7%) sufferers. Severity sufficient to interfere with daily activity occurred in 79/306)25.8%) children. Only 12/306 (3.9%) had "a lot of impairment of daily activity because of their condition". Atopy (defined by either positive SPT or inhalant screen) and allergic comorbidity at the age of 10 y were more common with current nasal symptoms (Table 1). Log_{10} total IgE at 10 y was also significantly higher (geometric mean 2.01 vs 1.65, $p < 0.001$) in those with current nasal symptoms.

Current wheeze at the age of 10 y (37.0% vs 13.3%, $p < 0.001$) was significantly greater in the presence of current nasal symptoms. Among currently wheezing children at the age of 10 y, diagnosed asthma ever was more common if current nasal symptoms coexisted (75.4% vs 62.1%, $p = 0.024$). Use of inhaled corticosteroids by wheezing children (Table 2) was significantly more common in the presence of current nasal symptoms. However, hospital admissions or specialist referral for wheezing children were no greater with the presence of current nasal symptoms. Baseline FEV_1

Table 1. Prevalence of atopy and other allergic diseases in children with current nasal symptoms at the age of 10 y.

	Current nasal symptoms		
	Yes	No	*p*
Positive skin test	138/269 (51.3)	141/767 (18.4)	<0.001
Positive inhalant screen	142/246 (57.7)	172/706 (24.4)	<0.001
Current asthma[a]	64/293 (21.8)	49/1018 (4.8)	<0.001
Current eczema[b]	64/308 (20.8)	121/1040 (11.6)	<0.001
Current urticaria[c]	38/307 (12.4)	80/1045 (7.7)	0.01

Data are *n* (%).
[a] Asthma: presence of wheeze at 10 y in children ever given a diagnosis of asthma.
[b] Eczema: presence of itchy rash at 10 y in children ever given a diagnosis of eczema.
[c] Urticaria: urticaria within the last 12 mo at 10 y.

also did not differ significantly with the presence of current nasal symptoms. Definite BHR at methacholine challenge, however, was significantly greater in children with current nasal symptoms regardless of wheezing status (Table 2).

Diagnosed allergic conditions at 1 y (eczema, food allergy), 2 y (eczema) and 4 y (asthma, eczema, rhinitis, food allergy), as well as positive SPT at 4 y, were significant univariate risk factors for having current nasal symptoms at the age of 10 y (Table 3). Maternal and paternal rhinitis was also significant, along with paternal asthma, maternal urticaria and food allergy plus sibling eczema (Table 3). Infant feeding method bore no significance in this context. Higher social class at birth was significant for current nasal symptoms. Apparent protective effects of early smoking exposure observed at univariate analysis probably reflect confounding of high social class at birth as a risk factor for current nasal symptoms. Multivariate analysis confirmed independent significant effects on current nasal symptoms at the age of 10 y for maternal and paternal rhinitis, maternal food allergy, atopy at 4 y SPT and diagnosed eczema at 4 y (Table 4).

Discussion

This study suggests that allergic rhinitis is an important childhood respiratory disorder. It shows that this condition does not occur in isolation but frequently coexists with other allergic states in childhood. In particular, associations were identified between rhinitis and wheezing, diagnosed asthma and objectively measured BHR. Furthermore, family and personal history of allergy in early childhood emerged as highly significant risk factors for rhinitis at the age of 10 y, demonstrating independent significance at multivariate analysis. However, this was not so for the environmental factors tested.

The prevalence of ISAAC-defined symptoms of rhinitis in 23% of 10-y-olds confirms that UK children suffer one of the highest prevalences for such symptoms on a global basis. Comparison with data at the age of 12–14 y from ISAAC UK (5) reveals that the (younger) children in the present study had a substantially lower prevalence of current symptoms of rhinitis (23% vs 38%). This would support theories that allergic rhinitis increases in prevalence during the teenage years (4). Further comparison of the current work with ISAAC data (6) on UK 6–7-y-olds reveals a very similar prevalence (21%) of current symptoms of rhinitis to these 10-y-olds, suggesting that substantial increases in rhinitis do not occur until after the age of 10 y.

Strong associations were found between rhinitis and obstructive airways disease, with significantly more current wheeze in those with current nasal symptoms than in those without. Among currently wheezing children, physician-diagnosed asthma ever was significantly more frequent if rhinitis coexisted. This is noteworthy since a physician's diagnosis of asthma may serve as a crude measure of asthma morbidity. Regular use of inhaled corticosteroids also indicates a greater degree of asthma severity and this too was higher in children with coexistent rhinitis at the age of 10 y. However, other markers of asthma morbidity such as acute hospital admissions and specialist referral were

Table 2. Association of current nasal symptoms with asthma and bronchial hyperresponsiveness (BHR) at the age of 10 y.

	Current nasal symptoms		
	Yes	No	*p*
Inhaled corticosteroid use	75/113 (66.4)	51/139 (36.7)	<0.001*
Hospital asthma admissions	23/113 (20.4)	32/140 (22.9)	0.631
Asthma specialist referral	21/113 (18.6)	19/140 (13.6)	0.277
Baseline FEV_1 in children:[a]			0.797
with current wheeze	1.99 (1.94–2.05)	1.98 (1.92–2.04)	
without current wheeze	2.05 (2.01–2.09)	2.03 (2.01–2.05)	0.407
Definite BHR[b] in children:	54/99 (54.5)	40/104 (38.5)	0.022*
with current wheeze			
without current wheeze	28/125 (22.4)	47/455 (10.3)	<0.001*

Data are *n* (%) or a mean (95% confidence interval).
[a] Definite BHR: provocative concentration of methacholine giving a 20% fall in forced expiratory volume in 1 s <4 mg ml^{-1}.
[b] Statistically significant ($p < 0.05$).

Table 3. Hereditary and environmental risk factors for current nasal symptoms at the age of 10 y: univariate analysis.

	Current nasal symptoms			
Factor	Yes	No	OR (95% CI)	*p*
Paternal asthma	57/293 (19.5)	126/1013 (12.4)	1.70 (1.21–2.40)	0.002
Sibling eczema	111/293 (37.9)	298/1014 (29.4)	1.47 (1.12–1.92)	0.006
Maternal rhinitis	87/293 (29.7)	227/1014 (22.4)	1.46 (1.10–1.96)	0.010
Paternal rhinitis	85/292 (29.1)	131/1013 (12.9)	2.77 (2.02–3.78)	<0.001
Maternal urticaria	33/293 (11.3)	59/1014 (5.8)	2.05 (1.31–3.21)	0.001
Maternal food allergy	26/293 (8.9)	43/1014 (4.2)	2.20 (1.33–3.65)	0.002
Eczema at 1 y	42/284 (14.8)	82/968 (8.5)	1.88 (1.26–2.79)	0.002
Food allergy at 1 y	25/284 (8.8)	53/968 (5.5)	1.67 (1.02–2.73)	0.041
Eczema at 2 y	39/260 (15.0)	82/875 (9.4)	1.71 (1.13–2.57)	0.010
Asthma at 4 y	66/269 (24.5)	105/884 (11.9)	2.41 (1.71–3.40)	<0.001
Eczema at 4 y	48/270 (17.8)	81/883 (9.2)	2.14 (1.45–3.15)	<0.001
Rhinitis at 4 y	28/271 (10.3)	33/882 (3.7)	2.96 (1.76–5.00)	<0.001
Food allergy at 4 y	13/270 (4.8)	21/883 (2.4)	2.08 (1.03–4.21)	0.038
Atopic SPT at 4 y	85/226 (37.6)	101/712 (14.2)	3.65 (2.59–5.13)	<0.001
Higher social class (I–III) at birth	96/181 (53.0)	278/626 (44.4)	1.41 (1.02–1.97)	0.040
Parental smoking at birth	112/302 (37.1)	471/1033 (45.6)	0.70 (0.54–0.92)	0.009
Parental smoking at 1 y	98/280 (35.0)	407/964 (42.2)	0.74 (0.56–0.97)	0.030

Data are *n*/total *n* (%) or odds ratios and (95% confidence intervals).

SPT: skin-prick test.

Only factors showing statistical significance ($p < 0.05$) are given. Factors showing trends for significance at univariate analysis ($p < 0.2$) included parental smoking at 4 y, sibling rhinitis, paternal/sibling urticaria, paternal food allergy, asthma and rhinitis at 2 y.

no greater if rhinitis coexisted. It was previously shown (15) that this asthmatic population is largely well controlled on prophylactic medication and clinically stable. Over half of the 10-y-old children with rhinitis had received pharmacological treatment for their disease and few reported marked impairment of activity because of their condition. Thus, the extent to which well-controlled rhinitis might worsen well-controlled asthma and contribute to severe asthma may have been limited in these children. It is known that patients with rhinitis often manifest increased BHR (8, 9). Recently, increased BHR was demonstrated in non-asthmatic patients with food allergy (16). The present study provides further evidence of the relationship between rhinitis and asthma by demonstrating significantly greater BHR to methacholine among children with current wheeze in the presence of current nasal symptoms. Rhinitis may exert independent effects upon BHR since non-wheezing children with current nasal symptoms also showed significantly higher BHR. Thus, this work provides considerable support for an intricate association of rhinitis and asthma, confirming the idea of "one airway, one disease". This probably reflects common underlying inflammatory processes and the importance of aeroallergen sensitization for both states. In the Tucson Children's Respiratory Study (2) the presence of high IgE at 6 y and coexistent asthma were both independent risk factors for rhinitis at that age.

Table 4. Multivariate analysis of early life risk factors for current nasal symptoms at the age of 10 y.

Risk factor	OR	95% CI	*p*
Maternal rhinitis	1.53	1.04–2.26	0.033
Paternal rhinitis	2.85	1.88–4.32	<0.001
Maternal food allergy	2.24	1.16–4.32	0.016
Eczema at 4 y	1.96	1.18–3.27	0.009
Atopic SPT at 4 y	2.55	1.68–3.88	<0.001

Data are adjusted odds ratios (OR) and their 95% confidence intervals (95% CI). Risk factors for current nasal symptoms refer to comparison with children who did not have that condition.

SPT: skin-prick test.

Only factors that showed a significant effect at the final step of each regression model are shown. All factors showing trends for significance at univariate analysis ($p < 0.2$) were included in the regression model except for early life rhinitis diagnoses and social class at birth (excluded because of limited data).

Univariate analysis was used to identify risk factors for rhinitis. However, as this would not account for confounding factors multivariate analysis was done to identify factors with truly independent effects. This showed independent significance for early life atopy. Support for an allergic progression (17, 18) from early life eczema and food allergy to aeroallergen-related disease in later childhood is provided by these data. Univariate analysis found significant associations for infantile eczema and food allergy with later rhinitis; for eczema this effect was retained at multivariate analysis. Family history of allergic conditions, particularly rhinitis, was also significant, with paternal rhinitis emerging as a strong independent predictor. This adds to prior evidence that allergic family history (2, 4, 19, 20) is crucial in rhinitis development.

Much interest has recently surrounded a hygiene hypothesis (21) for allergy development. Children raised in a rural environment (22, 23) with regular animal contact may have less hayfever and atopy. Frequent animal contact may increase the risk of

infections and immune deviation away from atopic phenotypes. The present study found no significant evidence that domestic pet exposure influenced the risk of childhood rhinitis, nor did it confirm significant independent effects for other environmental factors such as parental smoking, contrary to Wright et al. (2).

In conclusion, rhinitis is a common condition in childhood displaying strong associations with asthma. Thus, coexistent rhinitis should be an important consideration in managing childhood asthma. In terms of early life risk factors these findings suggest that the genetic predisposition to atopy and rhinitis is of greater influence than the early life environment in the development of childhood rhinitis.

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