

Increase in the prevalence of rhinitis among Danish children from 1986 to 2001

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In recent decades, there has been a worldwide increase in the prevalence of atopic diseases. The aim of this study was to investigate whether there has been a change in the prevalence of rhinitis among children in Denmark from 1986 to 2001. We compared data from two random population-based samples of Danish children, aged 7–17 yr, who were examined in 1986 ($n = 527$) and 2001 ($n = 480$) using similar designs. Symptoms of rhinitis, skin test reactivity, and bronchial responsiveness to inhaled histamine were assessed. The prevalence of rhinitis increased from 11.8% in 1986 to 23.3% in 2001 ($p < 0.001$). The increase was most pronounced among subjects who suffered from non-allergic rhinitis ($p < 0.001$), and among subjects with severe symptoms ($p < 0.001$). The prevalence of asymptomatic positive skin prick test (SPT) decreased substantially ($p < 0.001$). A history of asthma and parental atopic disease were strong predictors of non-allergic rhinitis, whereas a history of asthma, parental atopic disease, bronchial hyperresponsiveness, eczema, and age at examination were statistically significant predictors of allergic rhinitis. The prevalence of non-allergic rhinitis among Danish children has increased substantially from 1986 to 2001. Furthermore, in general more severe symptoms of rhinitis were observed in 2001 compared with 1986. These results underline the importance of using objective measurements such as skin test reactivity when estimating time trends in the prevalence of allergic airways disease, as clinical interviews alone can be misleading.

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Rhinitis is a condition defined by sneezing attacks, nasal discharge or blockage for more than an hour on most days for either a limited period of time (seasonal rhinitis, commonly known as hay fever) or throughout the whole year (perennial rhinitis, often caused by allergy to house dust mites or pets) (1). Rhinitis can be classified as mild or moderate-severe according to the ARIA criteria (2). Mild symptoms are defined by the absence of sleep disturbance, impairment of daily activities and/or sports, impairment of school or work, and/or troublesome symptoms, whereas moderate-severe symptoms include any of these impairments. Furthermore, rhinitis can be classified according to its degree of persistence in that intermittent symptoms are defined as the presence of

symptoms less than 4 days a week or less than 4 wk per year, whereas persistent symptoms are symptoms more frequently than this (2). Included in the rhinitis diagnosis are perennial non-allergic rhinitis, vasomotor rhinitis, and nasal polyps (1). These are more uncommon conditions and their dependence on allergic reactions and relation to atopy is less clear. Allergic rhinitis, asthma, and eczema constitute the atopic diseases. Atopic diseases have a complex etiology for which genetics, the prenatal and postnatal environments play a role (3, 4).

Several studies have reported a general increase in the prevalence of atopic diseases, including allergic rhinitis, both among children and adults during the recent decades (5). Linneberg et al. have supported this trend in Denmark

by showing an increase in the prevalence of skin prick test (SPT) positive allergic rhinitis and specific immunoglobulin (Ig) E positive allergic rhinitis during the 1990s in the adult population (6, 7). However, to our knowledge, no study has examined time trends in the prevalence of allergic rhinitis among Danish children.

Some authors have argued that the reported increase in allergic airways disease lack objective evidence and that further work has to be performed to support this conclusion (8, 9). This study deals with these objections by including skin test reactivity in the design.

We studied two population-based samples of Danish schoolchildren and examined whether there had been a change in the prevalence of rhinitis from 1986 to 2001. We diagnosed rhinitis with criteria of increasing stringency and distinguished between allergic and non-allergic rhinitis. Furthermore, we examined the relationship between rhinitis and other atopic conditions, e.g., eczema, asthma, positive SPT, and bronchial hyperresponsiveness (BHR). Finally, we studied several potential risk factors for rhinitis such as parental allergy, birth weight, and body mass index (BMI).

Methods

Two different random samples of children were studied. All subjects lived in the area surrounding the national university hospital (Rigshospitalet) in urban Copenhagen. The first sample was examined in 1986 (10) and the second in 2001 (11). All subjects were drawn at random from the civil registration list before each study, and were born in the first week of each month. The mean age of the subjects was 12 yr; age range 7–17 yr.

In 1986 and 2001, a total of 1000 and 1500 subjects, respectively, were identified. Owing to incorrect information on postal addresses only 983 and 1440 subjects were eligible for participation in 1986 and 2001, and these subjects were invited by letter to participate in a study concerning asthma and allergy. In 1986, a total of 527 (53.6%) participated in the survey, including 262 boys, and in 2001, a total of 480 (33.3%) agreed to participate, including 222 boys.

Owing to the low number of participants, we conducted interviews with an identical questionnaire by telephone among 100 and 116 randomly selected subjects from the group of non-responders in 1986 and 2001, respectively, to ensure the robustness of the sampled population. For every household, the interview was first performed with the child and subsequently a parent was consul-

ted to reach consensus. The subjects interviewed by telephone did not differ significantly from the subjects originally included with respect to sex, age, and disposition to atopy, but on both occasions there were significantly fewer children with symptoms of allergy among the group of non-responders. The additional children interviewed by telephone were not included in the final analysis as SPT results were not obtained from these subjects.

Clinical interview

A physician interviewed the participants both in 1986 and in 2001. All interviews were conducted using identical questionnaires concerning symptoms of rhinitis and the accompanying parent was consulted to obtain consensus. Symptoms among participants were assessed with the following questions adopted from Dirksen (12): (i) How old were you when your eye or nose trouble started? (ii) Do your symptoms come suddenly like attacks? (iii) Do you have days entirely free from eye or nose trouble? (iv) Does the trouble usually last more than an hour? (v) Do your eyes itch? (vi) Do you have sneezing spells (more than three sneezes in a row)? (vii) Do you often have a runny nose? (viii) Do you often have a blocked nose? (ix) Have you lost your sense of smell? (x) Does your eye or nose trouble get worse indoors? outdoors? in the daytime? or at night? (xi) Do you have eye or nose trouble in the winter? (xii) Are your eye or nose troubles worse during a particular season (spring, summer, autumn, or winter)? (xiii) Have you ever come into close contact with anything that you feel caused or worsened your eye or nose trouble (grass, flowers, trees, animals, food, drink, aspirin, dust, smoke, or stress)? and (xiv) Do you take medicine for your eye or nose trouble? (pills, spray-inhaler, drops, injections, or other medicine). Previous validation of these questions showed that they were reliable to identify subjects with rhinitis (12).

We used both a strict and a broad definition to categorize subjects with rhinitis. Rhinitis by the strict definition was present when a positive answer was provided to ≥ 4 of questions 2 and/or 4–13 (13). Rhinitis by the broad definition was present when a positive answer was provided to any symptom except (v) Do your eyes itch? This distinction allowed a more detailed presentation of the data.

Subjects were considered to have asthma if they responded affirmatively to a series of questions adopted from the American Thoracic Society regarding respiratory symptoms (14).

The diagnosis of eczema was based on the question 'Have you ever had eczema in the folds of your elbows or knees (14)?' Birth weight and wheezy bronchitis of the subjects were based on parental report. Parental atopic disease was defined as symptoms of hay fever and/or asthma in at least one parent when exposed to allergens encountered in the standard testing panel described next. Height and weight were measured during the clinical interview and BMI was calculated.

Skin prick test

SPT were performed using standard dilutions of 10 common aeroallergens. The allergens used were birch, grass, mugwort, horse, dog, cat, house dust mite (HDM) (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), and mold (*Alternaria iridis* and *Cladosporium herbarium*) with positive and negative references being histamine, 10 mg/ml, in 50% glycerol and glycerol, 50% respectively. The allergens were identical apart from *D. farinae*, which was not used in 1986. Reactions were read after 15 min. A positive result was defined as a positive reaction to at least one of the allergens, and a reaction was considered positive if the mean wheal diameter was at least 3 mm (15). The participants were requested to discontinue medications that contained antihistamines at least 3 days before skin testing.

Bronchial responsiveness tests

We used the methods by Cockcroft and Yan to measure airway responsiveness to inhaled histamine in 1986 and 2001, respectively (16, 17), the latter having been shown to be faster and easier but a fully viable alternative (18). According to the Cockcroft method, a Wright nebulizer delivered the histamine and the subjects inhaled by normal tidal volume breathing. Nine concentrations of histamine were used, from 0 (saline) to 8 mg/ml and the test was terminated when the maximum concentration was reached or when a drop in forced expiratory volume in 1 s (FEV₁) of more than 20% was observed – the provocative concentration (PC₂₀). The threshold value of BHR was a PC₂₀ of 8 mg/ml.

According to the method by Yan, each aerosol was inhaled starting with saline and followed by increasing doses of histamine until a cumulative dose of 7.8 µmol had been reached. The test was terminated when the maximum concentration had been reached or when a 20% decline in FEV₁ had occurred before the end of the dosing

regimen. For all subjects experiencing at least a 20% decline in FEV₁ the concentration causing a 20% fall in FEV₁ (PD₂₀) was calculated. A positive test result (BHR) was defined as a PD₂₀ below 3.9 µmol.

Statistical analysis

The prevalence of rhinitis in 1986 and 2001 were compared using a Chi-square test.

In order to compare prevalence rates of rhinitis, with and without positive SPT (pos-SPT), the population was divided into four groups: (i) asymptomatic subjects with a negative SPT (unaffected), (ii) asymptomatic subjects with a posSPT, (iii) symptomatic subjects with a negative SPT (non-allergic rhinitis), and (iv) symptomatic subjects with a positive SPT (allergic rhinitis). In this analysis, multinomial logistic regression with backward elimination was performed to examine the effects of explanatory variables on the risk of rhinitis. Year of examination, age, sex, birth weight, wheezy bronchitis, parental atopic disease, BMI, asthma, eczema, and BHR were explanatory variables. Subjects with incomplete data on any of the explanatory variables were excluded from the analysis. We examined all two-way interactions between year of examination and age, sex, parental atopic disease, and BMI. The results are reported as odds ratios (OR). A p-value < 0.05 was considered statistically significant. Data was analysed with the statistical package SPSS.

The Scientific Ethics Committee approved the study and informed consent was obtained from all participating subjects and their parents.

Results

We found that the overall prevalence of rhinitis by the strict definition increased from 11.8% in 1986 to 23.3% in 2001, OR = 2.28, 95% confidence interval (CI: 1.63–3.20), p < 0.001. The increase was most pronounced among subjects who suffered from non-allergic rhinitis, p < 0.001, whereas the prevalence of allergic rhinitis remained unchanged between 1986 and 2001, p = 0.71. The overall prevalence of rhinitis by the broad definition increased less dramatically from 24.0% in 1986 to 29.1% in 2001, OR = 1.31, 95% CI (0.99–1.73), p = 0.06. The prevalence of unaffected subjects remained unchanged between 1986 and 2001, whereas the prevalence of asymptomatic posSPT decreased substantially. See Tables 1 and 2 for further details.

Table 1. Prevalence of rhinitis defined by the strict criteria

Year	Unaffected subjects	Asymptomatic posSPT	Non-allergic rhinitis	Allergic rhinitis	Total
1986	382 (73.6%)	76 (14.6%)	12 (2.3%)	49 (9.4%)	519 (100%)
2001	331 (70.4%)	29 (6.2%)	48 (10.2%)	62 (13.2%)	470 (100%)
Total	713	105	60	111	989

posSPT, positive skin prick test.

Table 2. Prevalence of rhinitis defined by the broad criteria

Year	Unaffected subjects	Asymptomatic posSPT	Non-allergic rhinitis	Allergic rhinitis	Total
1986	337 (64.9%)	56 (10.8%)	57 (11.0%)	69 (13.3%)	519 (100%)
2001	309 (65.7%)	24 (5.1%)	70 (14.9%)	67 (14.3%)	470 (100%)
Total	646	80	127	136	989

posSPT, positive skin prick test.

Table 3. Risk factors for rhinitis defined by the strict criteria

Variable	Asymptomatic posSPT		Non-allergic rhinitis		Allergic rhinitis	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Year of examination	0.35 (0.22–0.58)	<0.001	3.61 (1.84–7.08)	<0.001	1.10 (0.68–1.78)	0.71
Parental allergy	2.14 (1.39–3.30)	0.001	2.36 (1.34–4.13)	0.003	2.66 (1.66–4.24)	<0.001
BHR	3.22 (1.60–6.45)	0.001	1.30 (0.55–3.08)	0.55	2.86 (1.48–5.52)	0.002
Eczema	1.21 (0.65–2.23)	0.55	1.47 (0.77–2.79)	0.25	2.20 (1.29–3.74)	0.004
Asthma	1.86 (0.78–4.47)	0.16	3.05 (1.24–7.51)	0.02	5.75 (2.91–11.40)	<0.001
Age	0.92 (0.85–1.00)	0.04	0.92 (0.83–1.01)	0.09	0.84 (0.77–0.92)	<0.001

Reference category is unaffected subjects.

Abbreviations: posSPT, positive skin prick test; OR, odds ratio; CI, confidence interval; BHR, bronchial hyperresponsiveness.

Table 4. Risk factors for rhinitis defined by the broad criteria

Variable	Asymptomatic posSPT		Non-allergic rhinitis		Allergic rhinitis	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Year of examination	0.37 (0.21–0.64)	<0.001	1.10 (0.73–1.65)	0.66	0.71 (0.46–1.10)	0.13
Parental allergy	2.10 (1.28–3.43)	0.003	2.09 (1.40–3.12)	<0.001	2.84 (1.86–4.35)	<0.001
BHR	3.90 (1.82–8.36)	<0.001	1.11 (0.54–2.27)	0.78	2.58 (1.37–4.84)	0.003
Eczema	0.98 (0.47–2.04)	0.95	1.52 (0.92–2.53)	0.10	2.32 (1.41–3.83)	0.001
Asthma	1.39 (0.50–3.83)	0.53	1.68 (0.73–3.89)	0.23	5.00 (2.56–9.74)	<0.001
Age	0.90 (0.83–0.99)	0.03	0.94 (0.87–1.01)	0.08	0.86 (0.80–0.93)	<0.001

Reference category is unaffected subjects.

Abbreviations: posSPT, positive skin prick test; OR, odds ratio; CI, confidence interval; BHR, bronchial hyperresponsiveness.

A history of asthma and parental atopic disease were strong predictors of non-allergic rhinitis, whereas parental atopic disease, BHR, eczema, asthma, and age at examination were statistically significant predictors of allergic rhinitis. There were no statistically significant interactions between the variables considered. See Tables 3 and 4.

Discussion

The main finding of this study was that the prevalence of rhinitis had doubled among chil-

dren and adolescents in the period between 1986 and 2001. The increase in prevalence was observed only in subjects who suffered from non-allergic rhinitis, whereas the prevalence of allergic rhinitis remained unchanged. Furthermore, we observed a smaller percentage of asymptomatic subjects with a posSPT in 2001 compared with 1986 and an overall unchanged prevalence of unaffected subjects between the two studies. When we used a less stringent definition of rhinitis which also included subjects with milder symptoms, the prevalence increased only slightly. From this, we conclude that the

overall prevalence of rhinitis symptoms in this population has remained rather stable during the past 15 yr but that the overall morbidity of rhinitis has increased substantially, primarily among subjects with non-allergic disease.

Age was negatively associated both with asymptomatic posSPT and allergic rhinitis. This suggests a cohort effect in that younger generations continuously are being more atopic than the ones before them and/or a decrease in atopy with ageing.

Allergic disease has been shown to run in families and our study supports this. In particular, parental allergy was significantly associated both with asymptomatic posSPT, non-allergic rhinitis, and allergic rhinitis. Whether these relationships are because of genetics, prenatal conditioning, or the environment is still debated (19, 20).

A strong link between asthma and allergic rhinitis has previously been reported and it has been suggested that these are different phenotypic presentations of the same underlying disease (21–24). We found asthma to be significantly related both to allergic and non-allergic rhinitis, indicating that both allergic and non-allergic rhinitis share a common etiology with asthma (23). Also eczema and BHR were positively associated with allergic rhinitis, as has been shown previously (25).

The etiology of allergic airways disease is complex. In particular, both genetic and environmental factors are implicated in the development of the disease (19, 26, 27). However, the increase in atopy worldwide has been so sudden that it cannot be because of genetic factors alone and therefore it must have occurred as a result of changes in environmental exposures, either intra-uterine or postnatal. These environmental changes are not fully understood and several hypotheses have been presented. Among the most discussed are theories about increasing *westernization* (smaller family size, western diet, increasing indoor allergen levels caused by better insulation) and *improved hygiene* (lack of endotoxins in the children's environment) (19, 26–29). Regardless of the explanation for this increase in the prevalence of disease, studies are commencing to report that the prevalence has leveled and that no further increase has taken place during the 1990s (30, 31).

An important limitation of our study is the low participation rates and we therefore dealt with this by interviewing non-participants on the telephone. Both in 1986 and 2001 there was no difference with respect to sex, age or disposition to atopy, whereas there were significantly fewer

subjects with symptoms of allergy among non-participants. It is known that low participation rates can bias surveys on allergic diseases (32). Furthermore, there has been an increasing awareness about atopic disease during the past decades and probably this could have led parents in 2001 to be more aware of these symptoms compared with 1986.

Partition of rhinitis into allergic and non-allergic sub-forms based on skin test reactivity alone poses additional problems that must be kept in mind when interpreting the results. Although a posSPT indicates atopy, its absence does not automatically preclude that allergic mechanisms account – at least partly – for the occurrence of symptoms. It is likely that at least a portion of the subjects who suffered from non-allergic rhinitis previously may have been sensitized, e.g., to pollen. In these subjects, respiratory symptoms and some degree of BHR may have persisted but atopy is no longer detectable. Furthermore, several studies have suggested that local production of IgE in the nasal mucosa may be responsible for symptoms that are independent of systemic atopy (33, 34). Hence, although we crudely decomposed rhinitis into different sub-forms these may still share common features.

We infer from our study that the prevalence, and not least the disease burden, of rhinitis have increased substantially among Danish children and adolescents from 1986 to 2001. The increase was most pronounced among subjects who suffered from non-allergic rhinitis. On the contrary, both the prevalence of unaffected subjects and subjects with allergic rhinitis remained unchanged. From this we conclude that the overall prevalence of symptoms of rhinitis in Danish children and adolescents has remained rather steady between 1986 and 2001, whereas the overall severity of rhinitis has increased. These results underline the use of objective measurements such as skin test reactivity when dealing with atopic disease, as clinical interviews alone can be misleading.

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