Allergy 2000: 55: 767–772
Printed in UK. All rights reserved

ALLERGY
ISSN 0105-4538

Short communication

The prevalence of skin-test-positive allergic rhinitis in Danish adults: two cross-sectional surveys 8 years apart. The Copenhagen Allergy Study

Background: It is disputed whether increases in self-reported respiratory allergy represent a true increase or merely increased recognition. We aimed to investigate whether the prevalence of skin-prick-test (SPT)-positive allergic rhinitis had increased in an adult general population in Copenhagen, Denmark.
Methods: Two cross-sectional surveys were carried out in 1990 and 1998. A screening questionnaire on respiratory symptoms in random samples of 15–41-year-olds preceded both surveys. Among the responders, random samples were invited to a health examination including SPT. Totals of 312 (participation rate 74.6%) and 482 (participation rate 53.4%) subjects were examined in 1990 and 1998, respectively. Diagnoses of SPT-positive allergic rhinitis were based on a history of nasal symptoms on exposure to allergens and SPT positivity to allergens.
Results: The prevalence of a diagnosis of SPT-positive allergic rhinitis increased from 12.9% to 22.5% (adjusted odds ratio 1.94, 95% CI 1.30–2.90), whereas the prevalence of a positive SPT (allergen histamine wheal ratio ≥ 0.5) to one or more of 10 allergens increased from 27.7% to 33.9% (adjusted odds ratio 1.47, 95% CI 1.05–2.05).
Conclusions: The prevalence of SPT-positive allergic rhinitis has increased significantly. Our findings indicate that a true increase in respiratory allergy has occurred.

A. Linneberg, T. Jørgensen
Centre of Preventive Medicine, Department of Internal Medicine M, Glostrup Hospital, University of Copenhagen

N. H. Nielsen
Department of Dermatology, Gentofte Hospital, University of Copenhagen

F. Madsen
Department of Internal Medicine B, Frederiksberg Hospital, University of Copenhagen

L. Frølund
Clinical Unit of Preventive Medicine and Health Promotion, Bispebjerg Hospital, University of Copenhagen

A. Dirksen
Department of Respiratory Medicine Y, Gentofte Hospital, University of Copenhagen, Denmark

Key words: adult; air polution; allergic rhinitis; epidemiology; hay fever; prevalence; respiratory hypersensitivity; skin prick test.

Dr Allan Linneberg
Centre of Preventive Medicine
Glostrup Hospital
57 Ndr. Ringvej
Entrance 8, 7th floor
DK-2600 Glostrup
Denmark

Accepted for publication 27 April 2000

There is considerable evidence that the prevalence of self-reported respiratory allergy has increased over recent decades. It has been discussed whether this increase represents a true increase or is due to an increased recognition of allergic disease. The inclusion of objective measures in studies of time trends is therefore important (1). Skin-prick-test (SPT) reactivity to aeroallergens is a generally accepted marker of respiratory allergy for use in epidemiologic studies (2, 3).

Most studies of time trends of respiratory allergy have been performed in children, and little is known about similar trends in adults (4). However, the reported increases in disease prevalence in children should now be apparent in increased disease prevalence in adults. Recently, we have reported an increasing prevalence of self-reported allergic rhinitis symptoms in an adult Danish population (5). This paper reports the prevalence of allergic rhinitis, using a definition based on the presence of both symptoms and SPT positivity, in an adult population in two surveys 8 years apart.

Material and methods

This study is based on two cross-sectional surveys conducted in 1990 and 1998. Both surveys were preceded by a mailed screening questionnaire survey of respiratory symptoms in a random sample of the population living in the western part of Copenhagen County. The 1990 sample was a nonstratified sample of 15–41-year-olds, whereas the 1998 sample was stratified on two age groups: 15–22-year-olds and 23–41-year-olds. Citizenship (Danish) and birthplace (Denmark) further restricted the samples. Random samples of the responders to the screening questionnaire were invited to a health examination including SPT. Pregnant women were excluded. The Ethical Committee for Copenhagen County approved the studies.

The 1990 survey

A total of 3603 subjects responded to the screening questionnaire (response rate 86.1%). From this total, a random sample of 418 subjects were invited to the health examination, and 312 subjects were examined (participation rate 74.6%). The participants were examined between February 1990 and January 1991. The 1990 survey represents the 15–41-year-old subjects participating in a previously described population survey (6).

The 1998 survey

A total of 592 15–22-year-old subjects and 546 22–41-year-old subjects responded to the screening questionnaire (response rates 72.0% and 78.0%, respectively). The questionnaire employed was identical to the one used in the 1990 survey. Another 102 questionnaires were completed by telephone interview (overall response rate including telephone interviews 81.5%). From among the 15–22-year-old responders to the mailed screening questionnaire, a random sample of 369 subjects were invited to the health examination, and 186 subjects were examined (participation rate 50.4%). From among the 23–41-year-old responders to the mailed screening questionnaire, a random sample of 533 subjects were invited to the health examination, and 296 subjects were examined (participation rate 55.5%). The participants were examined between January and November 1998.

Skin prick tests (SPT)

The Phazet® system (Pharmacia & Upjohn Diagnostics AB, Sweden) was used for the SPTs in the 1990 survey. The Phazet system was not available by the time of the 1998 survey, and the Soluprick SQ® system (ALK Abelló, Denmark) was used in the 1998 survey. Both methods used lancets and standardized allergen extracts (100 000 BU for Phazet and 10 HEP for Soluprick). The panel of allergens comprised birch, grass (timothy), mugwort, horse, cat, dog, two mites (*Dermatophagoides pteronyssinus* and *D. farinae*), and two molds (*Clado-sporium* and *Alternaria*). A negative control and a positive control (10 mg/ml histamine in both studies) were included. The test sites were placed at intervals of 20 mm on the volar side of the forearm in a straight line from approximately 5 cm below the elbow flexure to about 10 cm above the wrist. The skin reactions were read after 15 min by drawing around the perimeter of the wheal with a fine-point, felt-tip pen, and the tracing was then transferred to the data-collection sheet. The largest and the smallest diameters (at the widest point and at the midpoint at 90°) of the wheals were measured with a transparent ruler, and the mean wheal diameter was calculated. The participants were asked to abstain from antihistamines for 72 h (astemizole 8 weeks) before the examination. The same technician performed all SPTs in both surveys. The reproducibility of the SPT in the hands of the technician was established by performing two histamine SPTs on 20 volunteers. The coefficients of variation were 0.14 and 0.10 in 1990 and 1998, respectively. SPT reactivity was expressed as the allergen histamine wheal ratio (AHWR), i.e., the mean wheal diameter at the allergen site divided by the mean wheal diameter at the histamine site, and it was graded from 1+ to 4+, as described by Aas & Belin (7). Thus, grade 2+ corresponds to a AHWR of ≥ 0.5, and each additional plus indicates a doubling of the ratio.

Definitions of allergic rhinitis

Information on respiratory symptoms in participants and nonparticipants was collected in the screening questionnaire, which included four questions on nasal allergy symptoms (symptoms a., b., c., and d. in Table 3). The association between these symptoms and SPT positivity has previously been reported (5). Three specific diagnoses of SPT-positive allergic rhinitis were defined:

1) "Allergic rhinitis due to pollen allergy" was defined by the presence of either symptom a. or b. and SPT positivity to pollen.
2) "Allergic rhinitis due to dander allergy" was defined by the presence of symptom c. and SPT positivity to animal dander.
3) "Allergic rhinitis due to mite allergy" was defined by the presence of symptom d. and SPT positivity to mite.

Subsequently, "Allergic rhinitis due to pollen, dander, or mite allergy" was defined by the presence of at least one of the three specific diagnoses. In the above definitions, SPT positivity was defined as an AHWR of grade 2+ or more. In a detailed questionnaire completed at home before the health examination, the participants were asked whether they had hay fever

Table 1. Prevalence of diagnoses of allergic rhinitis

Diagnoses of skin-prick-test (SPT)-positive allergic rhinitis	Prevalence 1990 (%)	Prevalence 1998 (%)	Odds ratio † (95% CI)
Allergic rhinitis due to pollen allergy (symptom a. or b. and SPT positivity to birch, grass, or mugwort)	10.0 (31/311)	16.8 (81/481)	1.81 (1.15–2.83)*
Allergic rhinitis due to dander allergy (symptom c. and SPT positivity to horse, cat, or dog dander)	2.6 (8/311)	7.7 (37/481)	3.27 (1.49–7.19)*
Allergic rhinitis due to mite allergy (symptom d. and SPT positivity to *D. pteronyssinus* or *D. farinae*)	2.9 (9/311)	7.1 (34/481)	2.24 (1.05–4.79)*
Allergic rhinitis due to pollen, dander, or mite allergy (one or more of three above diagnoses)	12.9 (40/311)	22.5 (108/481)	1.94 (1.30–2.90)*
Self-reported diagnoses			
Self-reported hay fever	16.7 (52/311)	23.7 (114/482)	1.52 (1.05–1.36)*
Self-reported, doctor-diagnosed hay fever	8.0 (25/312)	15.6 (75/482)	2.14 (1.32–3.46)*

† Odds ratios comparing 1998 to 1990 adjusted for sex and age group.
* $P<0.05$.

(''self-reported hay fever'') or had been told by a doctor that they had hay fever (''self-reported doctor-diagnosed hay fever'').

Statistical analysis

Changes in the prevalence of diagnoses and SPT positivity were expressed by odds ratios comparing the 1998 survey to the 1990 survey. The odds ratios were adjusted for differences in sex and age distribution in a logistic regression model. SPT positivity was also adjusted for season of examination (January–April, May–August, and September–December). The test for homogeneity of the odds ratios by sex (or age group) was done by testing for interaction between survey and sex (or age group) in a logistic regression model using a likelihood-ratio test. All data were analyzed with the Statistical Products and Service Solutions package (SPSS) for Windows (Release 8.5), and 95% confidence intervals were used.

Results

Table 1 shows that the prevalence of the three specific diagnoses of SPT-positive allergic rhinitis and the two self-reported diagnoses of hay fever increased significantly. Accordingly, the prevalence of one or more of the three specific diagnoses of SPT-positive allergic rhinitis increased significantly. These increases were independent of sex and age group. In addition, the increases in SPT-positive allergic rhinitis were independent of the grade (1+ to 4+) that was used for defining SPT positivity in the definitions of SPT-positive allergic rhinitis (data not shown).

Table 2 shows that the increased prevalence of SPT positivity to one or more allergens was due to a significantly increased prevalence of SPT positivity to pollen and animal dander, whereas SPT positivity to mite was unchanged. Furthermore, while the prevalence of subjects SPT-positive to two or more allergens increased significantly, the prevalence of subjects SPT-positive to only one allergen was almost unchanged.

The prevalence of nasal allergy symptoms, as reported in the screening questionnaire, increased significantly from 1990 to 1998 (Table 3). This increase was slightly higher among the subjects participating in the health examination than among the subjects invited to the health examination (including both participants and nonparticipants).

Discussion

The results showed a significant increase in the prevalence of SPT-positive allergic rhinitis and a corresponding, but lower, significant increase in the prevalence of SPT positivity.

The prevalence of SPT-positive allergic rhinitis as assessed in the 1990 survey appears remarkably

Table 2. Prevalence of skin-prick-test positivity (allergen histamine wheal ratio ≥ 0.5)

Allergens	Prevalence 1990 (%)	Prevalence 1998 (%)	Odds ratio † (95% CI)
Pollen (birch, grass, or mugwort)	19.3 (60/311)	24.1 (116/481)	1.52 (1.04–2.21)*
Dander (horse, dog, or cat dander)	6.1 (19/311)	13.7 (66/481)	2.72 (1.56–4.76)*
Mite (*Dermatophagoides pteronyssinus* or *D. farinae*)	12.2 (38/311)	14.1 (68/481)	1.03 (0.65–1.62)
One or more of 10 allergens	27.7 (86/311)	33.9 (183/481)	1.47 (1.05–2.05)*
Only one allergen	10.9 (34/311)	11.2 (54/481)	1.13 (0.70–1.82)
Two or more allergens	16.7 (52/311)	22.7 (109/481)	1.55 (1.04–2.29)*

† Odds ratio comparing 1998 to 1990 adjusted for sex, age group, and season of examination.
* $P<0.05$.

Table 3. Prevalence of allergic rhinitis symptoms among subjects invited to health examination (participants and nonparticipants) and among participants in health examination (participants only)

Questions (symptoms)	Participants and nonparticipants			Participants only		
	1990 $n=418$	1998 $n=1004$	Odds ratio† (95% CI)	1990 $n=312$	1998 $n=482$	Odds ratio† (95% CI)
a. Itchy or stuffy nose or sneezing during summer months	24.8%	32.5%	1.46 (1.13–1.90)*	26.5%	35.1%	1.52 (1.10–2.09)*
b. Itchy or stuffy nose or sneezing when near grass, trees, or flowers	16.1%	25.2%	1.78 (1.32–2.41)*	17.4%	27.8%	1.80 (1.26–2.58)*
c. Itchy or stuffy nose or sneezing when near furry animals	10.6%	15.5%	1.50 (1.05–2.16)*	11.3%	17.7%	1.61 (1.05–2.47)*
d. Itchy or stuffy nose or sneezing when cleaning rooms or making beds, or when in bed	17.7%	25.4%	1.55 (1.16–2.08)*	19.0%	29.5%	1.74 (1.23–2.47)*

† Odds ratios comparing 1998 to 1990 adjusted for age and sex.
* $P<0.05$.

similar to that assessed in a Swiss general population of 18–60-year-olds in 1991. Thus, in Switzerland, the prevalences of atopic rhinitis (self-reported allergic rhinitis and at least one positive SPT or Phadiatop test) and hay fever (self-reported hay fever and a positive SPT to pollen) were 13.5% and 10.3%, respectively (8). In Finland the prevalence of SPT-positive hay fever among 5–17-year-olds was 10.9% (9), while in the UK the estimated prevalence of SPT-positive allergic rhinitis among 15–65-year-olds was 16% (10).

A few repeated cross-sectional studies have employed SPTs at two points in time. von Mutius et al. reported an increased prevalence of SPT positivity and self-reported hay fever from 1991–2 to 1995–6 among schoolchildren in the former East Germany during the years following the reunification with the former West Germany (11). In contrast, Peat et al. reported an unchanged prevalence of SPT positivity despite an increase in self-reported hay fever from 1982 to 1992 among Australian schoolchildren (12). In this Australian study, the prevalence of SPT positivity was already high in the initial survey, and we speculate that the prevalence of SPT positivity might have risen prior to the initial survey. One serologic study has reported an increased prevalence of specific IgE positivity to common allergens among 13–14-year-old Japanese schoolgirls between 1978 and 1991 (13).

Some methodological issues should be addressed in the interpretation of our results. First, the participation rates differed in the two surveys. The invitational procedures were kept the same, and it is therefore unlikely that the difference in participation rate was due to methodological differences between the surveys. However, the effect of possible selection bias may be enhanced by the lower participation rate in the second survey. Information on nonparticipants was obtained in the screening questionnaire, a fact which allowed us to analyze the effect of selection bias on the estimated odds ratios. Thus, the overall effect of nonparticipation was examined by comparing the increase in the prevalence of nasal allergy symptoms among the subjects invited to the health examination (including both those participating and those not participating in the health examination) to that among the subjects participating in the health examination (Table 3). This increase was only slightly higher among the subjects participating in the health examination than among the subjects invited to the health examination. Thus, the odds ratios may be slightly overestimated when taking into account the effect of nonparticipation. However, this does not seem to explain all of the observed increase in SPT-positive allergic rhinitis.

Second, the SPT methods applied in the two surveys differed. A comparison in 1992 between the Phazet and the Soluprick methods showed that they were similar, although the Phazet tended to elicit a higher overall number of positive reactions to allergens in patients than the Soluprick method (14). According to this, a possible increase in the prevalence of SPT positivity would tend to be underestimated. Variations of SPT results between fieldworkers may bias epidemiologic studies (15), and it is therefore notable that, in the present study, the same technician performed all SPTs in both surveys.

Data on pollen counts during the pollen seasons in Copenhagen have been available since 1977 (16). There does not seem to be any consistent time trend in the cumulated pollen counts for each season that could account for the increase in sensitization to pollens. Furthermore, a comparison of the 1990 and 1998 pollen seasons showed no major differences (16); therefore, different levels of exposure to pollens during the two surveys were unlikely to have biased our results.

Marked urban/rural differences in the prevalence of respiratory allergy have been found in most countries (4, 17), including Denmark (18), suggesting that air pollution is a risk factor for the development of respiratory allergy. It would therefore be of interest to relate the observed increase in prevalence of pollen allergy to trends of air pollution measures in the study area. The Danish Air Quality Monitoring Program has been monitoring different air pollution measures in Copenhagen since 1982 (19). The concentrations of nitrogen oxide, sulfur dioxide, and total suspended particulate matter have been decreasing since the late 1980s, while the concentrations of

nitrogen dioxide and ozone are almost unchanged. This apparent lack of a macroecologic relationship between pollen allergy and air pollution measures does not necessarily exclude air pollution as a potential risk factor for two reasons. Firstly, the critical components may not have been included in the monitoring program. For example, ultrafine particles from diesel combustion are not measured specifically. Secondly, the decrease in air pollution may not yet have had an effect on prevalence figures. Further research on the relationship between respiratory allergy and air pollution is needed to determine this issue. At present, it is not clear which factors are responsible for the recent increases in respiratory allergy. More knowledge about risk factors associated with lifestyle and environment may be provided by large-scale population-based prospective studies, some of which are already underway (20, 21).

There is no generally accepted definition of allergic rhinitis for use in epidemiologic studies (22, 23). The definition used in this study was based on both symptoms and objective measurements, as in the clinical assessment. Most studies of time trends of the prevalence of allergic rhinitis are based on self-reported diagnoses, such as self-reported hay fever. Table 1 makes it possible to compare the prevalence of SPT-positive hay fever ("allergic rhinitis due to pollen allergy") to the prevalence of self-reported hay fever and self-reported doctor-diagnosed hay fever in the subjects studied. It appears that the prevalence of doctor-diagnosed hay fever was reasonably similar to, although slightly lower than, the prevalence of SPT-positive hay fever. This is consistent with previous reports that not all patients suffering from hay fever consult a physician (10). The sensitivity (76.0% and 69.3% in 1990 and 1998, respectively) and the specificity (95.8% and 92.9% in 1990 and 1998, respectively) of SPT-positive hay fever with self-reported, doctor-diagnosed hay fever as the reference indicated good agreement between these two definitions.

It is disputed to what extent the reported worldwide increases in respiratory allergy are real or due to changes in recognition or labeling of disease (1). The present study confirms that the previously reported increases in self-reported symptoms (5) and self-reported diagnoses (18) of respiratory allergy among Danish adults are real. However, the increase in SPT positivity to allergens appeared to be lower than the increase in SPT-positive allergic rhinitis. This may represent either increased morbidity or increased recognition of symptoms among SPT-positive subjects. In this way, our findings are not inconsistent with the hypothesis that the recognition of allergic disease has increased, although this does not fully explain the reported increases in symptoms and diagnoses. A possible increased morbidity, because SPT-positive subjects report more symptoms, might be explained by the increased prevalence of subjects sensitized to more than one allergen (Table 2).

In the present study, the estimated prevalence of SPT-positive allergic rhinitis was high, and it increased over an 8-year period. Although some cases of allergic rhinitis are symptomatically mild, others are associated with considerable morbidity, and some subjects with allergic rhinitis have other atopic diseases, such as asthma. Diseases with substantial increases in prevalence over short periods of time are likely to be caused by environmental or lifestyle factors, and may therefore be prevented. Thus, allergic rhinitis should be considered a major public health problem, and more research into its causes is needed.

Acknowledgments

We thank the staff at the Center of Preventive Medicine for their dedicated assistance. This study was supported by the Danish Medical Research Council, the Danish Health Insurance Fund, the Danish Ministry of Health (the National Health Fund for Research and Development), the Danish Medical Research Council and the Danish Ministry of Health (Research Center for Environmental Health: Environmental Health Research Program 1997), and ALK – Abelló A/S, Denmark.

References

1. Magnus P, Jaakkola JJ. Secular trend in the occurrence of asthma among children and young adults: critical appraisal of repeated cross sectional surveys. BMJ 1997;**314**:1795–1799.
2. Position paper. Allergen standardization and skin tests. European Academy of Allergology and Clinical Immunology. Allergy 1993;**48 Suppl 14**:48–82.
3. Droste JH, Kerhof M, de Monchy JG, Schouten JP, Rijcken B. Association of skin test reactivity, specific IgE, total IgE, and eosinophils with nasal symptoms in a community-based population study. The Dutch ECRHS Group. J Allergy Clin Immunol 1996;**97**:922–932.
4. von Mutius E. The rising trends in asthma and allergic disease. Clin Exp Allergy 1998;**28 Suppl 5**:45–49.
5. Linneberg A, Nielsen NH, Madsen F, Frølund L, Dirksen A, Jørgensen T. Increasing prevalence of allergic rhinitis symptoms in an adult Danish population. Allergy 1999;**54**:1194–1198.
6. Nielsen NH, Svendsen UG, Madsen F, Dirksen A. Allergen skin test reactivity in an unselected Danish population. The Glostrup Allergy Study, Denmark. Allergy 1994;**49**:86–91.
7. Aas K, Belin L. Standardization of diagnostic work in allergy. Int Arch Allergy Appl Immunol 1973;**45**:57–60.

8. Wüthrich B, Schindler C, Leuenberger P, Ackermann-Liebrich U. Prevalence of atopy and pollinosis in the adult population of Switzerland (SAPALDIA study). Swiss Study on Air Pollution and Lung Diseases in Adults. Int Arch Allergy Immunol 1995;**106**:149–156.
9. Haahtela T, Heiskala M, Suoniemi I. Allergic disorders and immediate skin test reactivity in Finnish adolescents. Allergy 1980;**35**:433–441.
10. Sibbald B. Epidemiology of allergic rhinitis. Monogr Allergy 1993;**31**:61–79.
11. von Mutius E, Weiland SK, Fritzsch C, Duhme H, Keil U. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. Lancet 1998;**351**:862–866.
12. Peat JK, van den Berg RH, Green WF, Mellis CM, Leeder SR, Woolcock AJ. Changing prevalence of asthma in Australian children. BMJ 1994;**308**:1591–1596.
13. Nakagomi T, Itaya H, Tominaga T, Yamaki M, Hisamatsu S, Nakagomi O. Is atopy increasing? [Letter]. Lancet 1994;**343**:121–122.
14. Nielsen NH, Dirksen A, Mosbech H, Launbjerg J, Biering I, Soborg M. Skin prick testing with standardized extracts from 3 different manufacturers. A comparative randomized study. Allergol Immunopathol (Madr) 1992;**20**:246–248.
15. Braun-Fahrlander C, Wüthrich B, Sennhauser FH, Vuille JC, and the SCARPOL Team. Significant variations of skin prick test results between fieldworkers in different areas. In: Ring J, Behrendt H, Vieluf D, editors. New trends in Allergy IV. New York: Springer Verlag, 1996:13–15.
16. Hodal L, Rasmussen A. Pollen and spores registrations in Denmark. The season 1998 [In Danish]. Copenhagen: Danish Asthma-Allergy Association and Danish Meteorological Institute, 1999.
17. Mygind N, Dahl R. Epidemiology of allergic rhinitis. Pediatr Allergy Immunol 1996;**7**:57–62.
18. Keiding L. Asthma, allergy, and other types of hypersensitivity in Denmark – and the development 1987–1994 [summary in English]. Copenhagen: National Institute of Public Health, 1997.
19. Kemp K, Palmgren F. The Danish Air Quality Monitoring Programme. Annual Report for 1998. Roskilde, Denmark: National Environmental Research Institute, 1999.
20. De Marco R, Zanolin ME, Accordini S, et al. A new questionnaire for the repeat of the first stage of the European Community Respiratory Health Survey: a pilot study. Eur Respir J 1999;**14**:1044–1048.
21. Asher MI, Weiland SK. The International Study of Asthma and Allergies in Childhood (ISAAC). ISAAC Steering Committee. Clin Exp Allergy 1998;**28 Suppl 5**:52–66.
22. Charpin D, Sibbald B, Weeke E, Wüthrich B. Epidemiologic identification of allergic rhinitis. Allergy 1996;**51**:293–298.
23. Braun-Fahrlander C, Wüthrich B, Gassner M, et al. Validation of a rhinitis symptom questionnaire (ISAAC core questions) in a population of Swiss schoolchildren visiting the school health services. SCARPOL team. Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution and Climate. International Study of Asthma and Allergies in Childhood. Pediatr Allergy Immunol 1997;**8**:75–82.