

Dependence of Immediate Hypersensitivity in the Adolescent Period on Factors Encountered in Infancy

ILPO SUONIEMI, FRED BJÖRKSTÉN and TARI HAAHTELA*

Hospital for Allergic Diseases, Helsinki University Central Hospital, and *Dept. of Pulmonary Diseases, Tiuru Hospital, Tiurunemi, Finland

708 unselected adolescents 15–17 years old were studied. They were physically examined, interviewed and skin prick tested with 12 common allergens. Questionnaires were distributed to the adolescents and their parents to investigate past and present symptoms and environmental influences. Emphasis was on the first year of life. Exposure to allergens (pollens and cat epithelium) during the first 6 months of life, eczema during the first year of life, and atopic heredity were found to be major risk factors in the development of positive skin tests and respiratory allergy apparent in the teenage period. Infections and wheezing during the first year of life were also risk factors, but less important.

Key words: allergy; atopic dermatitis; cat epithelium; eczema; epidemiology; immediate hypersensitivity; infancy; infection; pollen; teenager; wheezing.

Accepted for publication 26 January 1981

CLINICAL ASPECTS

This study suggests that factors encountered during the first 6 months of life influence the development of subsequent allergies. Exposure to allergens during this period increases the risk of the occurrence of the corresponding allergies in the teenage period. It was also noted that allergic teenagers had been affected in their infancy by eczema, infections and wheezing more often than non-allergic adolescents. Here cause and effect remain uncertain. Further studies may suggest new preventive measures.

The development of type I allergy or immediate hypersensitivity is dependent on hereditary and environmental factors (12). Events in infancy may be of special importance. Thus we found that pollen contacts during the first 6 months of life increase the risk of developing pollen sensitivity for a period of 20 years or more (2, 3).

We have previously studied the occurrence of clinical allergy and positive skin prick tests in unselected adolescents (8, 9). Using this group we now try to relate immediate hypersensitivity in the adolescent period to anamnestic information on allergen contacts and illness in infancy. Because of the retrospective nature of the study, interpretations should be cautious.

MATERIAL AND METHOD

We studied 708 unselected ninth-grade students (43% boys) in Imatra schools in southeast Finland. Of these 99% were 15–17 years. The parents of 105 adolescents did not complete the second questionnaire (see below). The adolescents, materials and methods have been described in greater detail previously (8, 9).

The teenagers received a questionnaire in which inquiries were made about symptoms, etc. indicating past or present type I allergy in the subject, his parents or his siblings. Questions about pets in the home at the time or in the near past were included. The subjects were

asked to answer the questions with the help of their parents. Allergic asthma, allergic rhinitis or atopic dermatitis in a parent or sibling was taken as evidence of the presence of atopic heredity (9, 10).

Skin prick testing with 16 extracts of 12 common allergens was carried out on each subject. The allergens included timothy, cocksfoot, birch, alder, mugwort and white oxeye pollens; cat, dog and horse epithelia; mite, house dust and fish. A weal with a diameter of 3 mm or more was taken as a positive response (8). On the same occasion subjects were physically examined and interviewed.

A second questionnaire was administered to the parents with inquiries concerning events during the subject's first year of life. Among the questions were the following: "Did the child suffer from wheezing or difficulty in breathing during an infection or otherwise?" "Did the child suffer from eczema?" "Did the child suffer from an infectious disease, which required treatment by a physician?" "List all pets kept at home when the child was under 6 months and – separately – when the child was 6–12 months!"

We tested the significance of associations in contingency tables using χ^2 -tests. An association discovered was analysed further using partition of the appropriate χ^2 -value (5).

RESULTS

The effects of keeping pets in the home were examined in those 49% of our subjects who had at least one positive skin test reaction, and who therefore were regarded as showing some evidence of atopy. Those who had had a cat in the home for at least 3 months during the first 6 months of life and those who had it at the time of the study tended to have more positive skin test reactions to cat epithelium than others. However, statistical significance was attained only when the cat had been present in the early period ($P = 0.013$). Dog-keeping could not be shown to have any such effect (Table 1).

Children born in the spring meet pollens earlier than those born in the autumn. We found that boys born in December-May had more clinical pollen allergy than boys born in June-November ($P = 0.021$). The phenomenon was not observed in girls (Table 2).

The adolescents' parents were questioned concerning the occurrence of three symptoms (eczema, wheezing or difficulty to breathe, and infection requiring treatment by a physician) in the children during the first year of life. Prevalences are given in Fig. 1. There were no significant differences between boys and girls.

Table 1

Dependence of positive skin tests to cat and dog epithelium on the presence of the animal in the home. Subjects with no positive skin tests ("nonatopics") are not included

Skin test	Pet in home during first 6 months of life			Significance of association*	Pet in home at time of skin testing (adolescence)		Significance of association*
	No answer	Yes	No		Yes	No	
	Prevalence (%)				Prevalence (%)		
Positive to cat	65.7	90.9	65.4	$P = 0.013$	73.6	65.9	$P = 0.173$
Negative to cat	34.3	9.1	34.6		26.4	34.1	
	($n = 35$)	($n = 22$)	($n = 289$)		($n = 53$)	($n = 293$)	
Positive to dog	40.0	31.6	28.1	$P = 0.474$	27.6	30.4	$P = 0.664$
Negative to dog	60.0	68.4	71.9		72.4	69.6	
	($n = 35$)	($n = 19$)	($n = 292$)		($n = 116$)	($n = 230$)	

* The χ^2 -test with Yates' correction was used to test the significance of positive association between pet in home and positive skin test.

Table 2

Dependence of pollen allergy on month of birth. Pollen allergy was diagnosed when skin test was positive and subject reported typical symptoms. All subjects with negative skin tests were regarded as having no pollen allergy. Subjects with positive skin test but no symptoms were not included

Month of birth	Boys		Significance of association*	Girls		Significance of association*
	Pollen allergy	No pollen allergy		Pollen allergy	No pollen allergy	
	Prevalence (%)			Prevalence (%)		
December–May	69.6	51.8	<i>P</i> = 0.021	45.5	46.4	<i>P</i> = 0.531
June–November	30.4	48.2		54.5	53.6	
	(<i>n</i> = 46)	(<i>n</i> = 218)		(<i>n</i> = 33)	(<i>n</i> = 308)	

* χ^2 -test with Yates' correction.

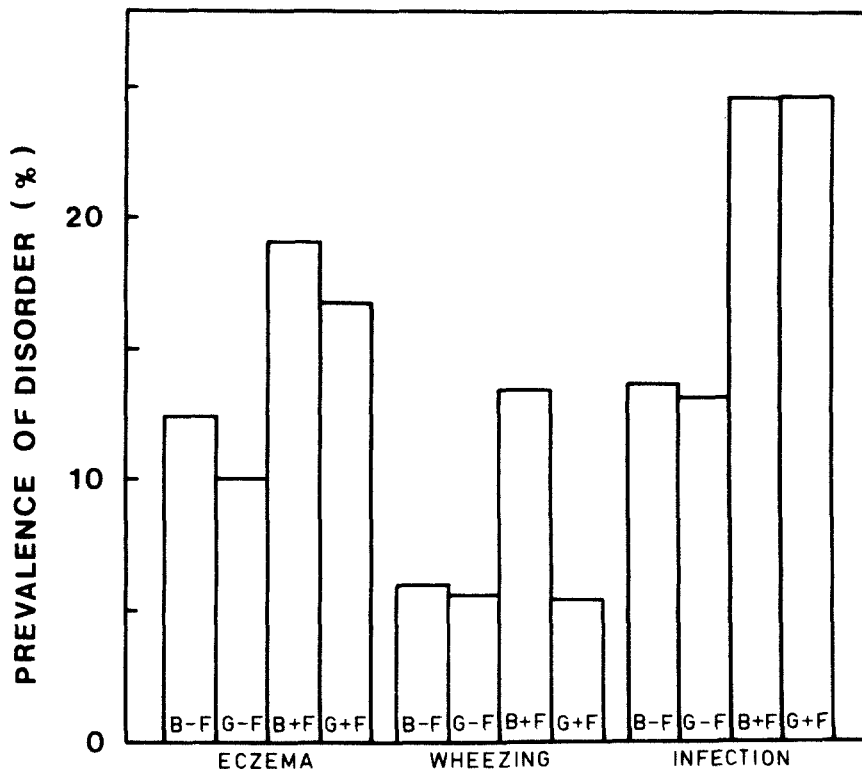


Fig. 1. Prevalence of disorders reported to have occurred during first year of life as a function of sex and heredity.

Symbols: B – F boys with negative family history ($n = 168$)

G – F girls with negative family history ($n = 197$)

B + F boys with positive family history ($n = 89$)

G + F girls with positive family history ($n = 149$)

Reports of symptoms in infancy ($P < 10^{-5}$) and also positive skin test reactions in adolescence ($P = 0.012$) were associated with a history of atopic heredity (Figs. 1 and 2). There was no significant variation in this effect among the three symptom groups, when the χ^2 -statistic was partitioned ($P = 0.409$). The prevalence of

positive skin test reactions was increased in those with at least one symptom in infancy. This was true both of those with positive ($P = 0.019$) and negative ($P = 0.012$) heredity (Fig. 2).

If we make the simplifying assumption that effects are additive, the following linear model

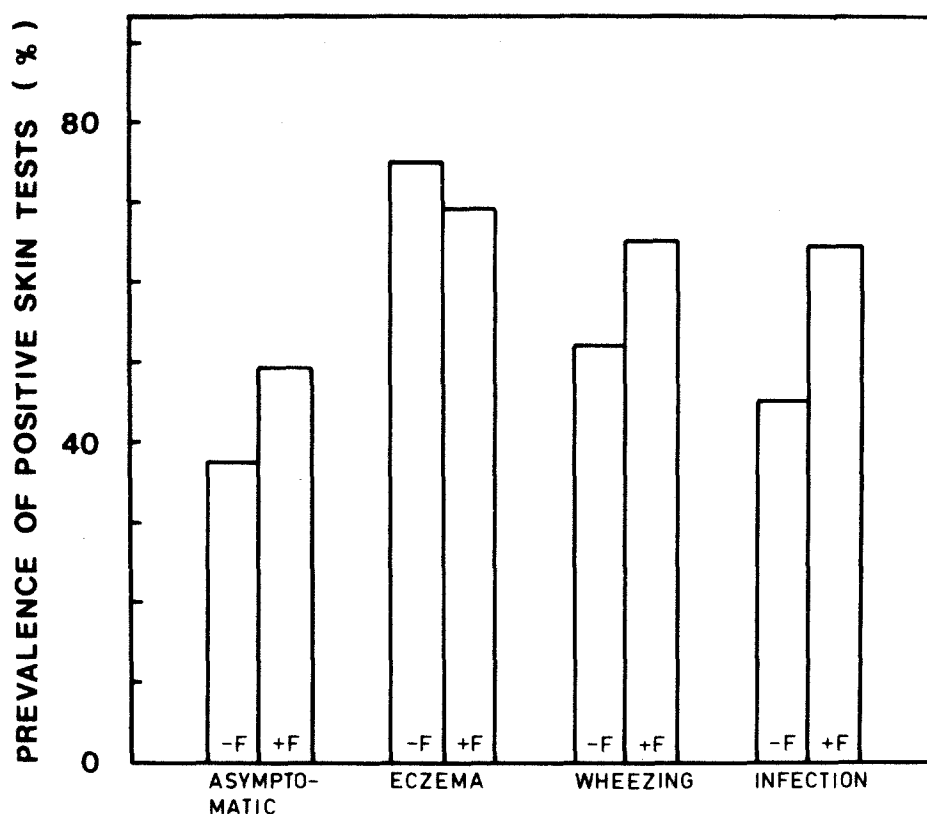


Fig. 2. Influence of family history and disorders reported to have occurred during first year of life on the prevalence of positive skin tests (at least one positive) in adolescence. Note that prevalence of the disorders is not given here but in Fig. 1. -F indicates negative and +F positive family history.

can be fitted to the data to explain the prevalence (P) of positive prick test reactions in various subgroups:

$$P = 0.377 + 0.039S + 0.114H + 0.260E + 0.041W + 0.047I$$

(0.17) (0.029) ($<10^{-5}$) (0.31) (0.19)

In the equation S is sex, H is heredity, E is early eczema, W is early wheezing or difficulty to breathe, and I is early infection. These variables are equal to one when reported positive (sex is one when male), otherwise zero. The magnitude of the coefficients corresponds directly to the relative importance of the factors. The figures in parenthesis give the probabilities of the coefficients being zero as indicated by the t-test, which, however, provides only a rough indication of significance. From the equation it can be seen that eczema is an important factor related to positive skin tests. Atopic heredity is another major factor.

DISCUSSION

We have related immediate hypersensitivity observed by skin prick testing in adolescents to events in infancy. We emphasize that information on events which had occurred early in life, some 15 years ago, was obtained from parents through anamnesis and could be subject to preferential recall by the parents of those children who have had an allergy. Where anamnestic information is involved, our conclusions should not be considered as final, but rather as working hypotheses.

The prevalence of infections, which occurred during the first year of life and which required treatment by a physician, appears low, at least by present Finnish standards (Fig. 1). This may in part reflect poor recall, but the prevalence has also been affected by the relatively poor availability of physicians at the time. We found no

effect of either heredity or skin test positivity on the tendency to leave relevant questions unanswered (cf. Table 1). For those unwilling to answer, we always provided a "don't know/don't remember" option in the questionnaire.

A clear association between positive family history, early eczema, and respiratory allergy is known to exist (12). Respiratory allergy may also be dependent on childhood respiratory illness. Thus first attacks of asthma (12) and other signs of sensitization to allergens (7) may appear soon after a childhood respiratory infection. Children with asthma have more viral respiratory infections than others (11). Asthmatoïd bronchitis in small children can develop into overt respiratory allergy (6). Unspecified childhood respiratory illness has been found to be a risk factor for adult obstructive airway disease including wheezing and asthma (4).

As judged by the present results, allergy in a parent or sibling increases both the risk of some disorders in early life and the tendency to develop immediate skin test reactivity by the age of 15. The disorders in question were eczema, wheezing or difficulty to breathe, and infections. Early disorders, particularly eczema, showed an additional association with skin reactivity, which was not explained by the common dependence on heredity (Fig. 2 and the equation).

We have previously found evidence for a causal relationship between early pollen contacts and subsequent pollen allergy (2, 3). In agreement with this, we now found that boys born in December-May had a higher prevalence of pollen allergy than those born in June-November. In girls, the phenomenon is more difficult to observe (1), and it could not be seen now (Table 2).

In keeping with the pollen results, we found that cat contacts during the first 6 months of life increased the risk of developing a positive skin test to cat epithelium. Of the 22 "atopic" (at least one skin test positive) adolescents who reported having a cat in the home during infancy 20 had a positive skin test to cat (Table 1). It could be suggested that early cat-keeping may correlate strongly with later cat-keeping and that later cat contacts are in fact the important ones. This can to some extent be refuted, since we found that cat contacts in infancy and at the time of

the study were largely independent. Further, present cat-keeping did not increase the chances of a positive skin test significantly, although a trend in this direction could be seen (Table 1). Early contacts seem to be more important.

We also tried to investigate whether the length of breast feeding had an effect on skin reactivity to allergens in adolescence. No effect could be found. Results were also negative for the size (floor area) of the childhood home and for smoking in the home during the first year of life.

The present results and those of preceding studies (2, 3) suggest that contacts in infancy with airborne allergens can initiate the development of immediate hypersensitivity to these allergens. Overt respiratory allergy may result many years later. Obviously also other factors are involved. Early eczema and infections could enhance the penetration of airborne allergens, or they could stimulate an immunoglobulin-E response through some other mechanism. Later allergen contacts may boost the response.

ACKNOWLEDGEMENTS

This study was made possible through the participation of 700 students, their parents and school personnel in Imatra. The study was supported by grants from Allergiatutkimussäätiö, Yrjö Jahnssonin Säätiö, Kymenlaakson Terveysturva and Ida Montinin Säätiö.

REFERENCES

1. Björkstén, F. & Suoniemi, I.: Dependence of immediate hypersensitivity on the month of birth. *Clin. Allergy* 6, 165-171, 1976.
2. Björkstén, F. & Suoniemi, I.: Time and intensity of first pollen contacts and risk of subsequent allergies. *Acta Med. Scand.* (In press).
3. Björkstén, F., Suoniemi, I. & Koski, V.: Neonatal birch-pollen contact and subsequent allergy to birch pollen. *Clin. Allergy* 10, 585-591, 1980.
4. Burrows, B., Knudson, R. J. & Lebowitz, M. D.: The relationship of childhood respiratory illness to adult obstructive airway disease. *Am. Rev. Respir. Dis.* 115, 751-760, 1977.
5. Fleiss, J. L.: Statistical methods for rates and proportions. J. Wiley, New York, 1973.
6. Foucard, T.: A follow-up study of children with asthmatoïd bronchitis. II. Serum IgE and eosinophil counts in relation to clinical course. *Acta Paediat. Scand.* 63, 129-

- 139, 1974.
7. Frick, O. L., German, D. F. & Mills, J.: Development of allergy in children. I. Association with virus infections. *J. Allergy Clin. Immunol.* **63**, 228–241, 1979.
8. Haahtela, T., Björkstén, F., Heiskala, M. & Suoniemi, I.: Skin prick test reactivity to common allergens in Finnish adolescents. *Allergy* **35**, 425–431, 1980.
9. Haahtela, T., Heiskala, M. & Suoniemi, I.: Allergic disorders and immediate skin reactions in Finnish adolescents. *Allergy* **35**, 433–441, 1980.
10. Haahtela, T. & Jokela, H.: Asthma and allergy in Finnish conscripts. *Allergy* **34**, 413–420, 1979.
11. Minor, T. E., Baker, J. W., Dick, E. C., Demeo, A. N., Oullette, J. J., Cohen, M. & Reed, C. E.: Greater frequency of viral respiratory infections in asthmatic children as compared with their non-asthmatic siblings. *J. Pediatr.* **85**, 442–450, 1974.
12. Smith, J. Montgomery: Epidemiology and natural history of asthma, allergic rhinitis, and atopic dermatitis (eczema). In Middleton, E., Reed, C. E. & Ellis, E. F. (eds.): *Allergy. Principles and practice*, pp. 633–658. C. V. Mosby, Saint Louis, 1978.
- Address:
- Ilpo Suoniemi*
Hospital for Allergic Diseases
Helsinki University Central Hospital
Meilahdentie
SF-00250 Helsinki 25
Finland

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.