

Asthma and Allergy in Finnish Conscripts

TARI HAAHTELA and HANNU JOKELA

Dept. of Pulmonary Diseases, Tiuru Hospital, Tiuruniemi and Imatra Health Centre, Imatra, Finland

We studied the occurrence of asthma, bronchial wheezing, allergic rhinitis and atopic dermatitis in 295 young men aged 18-19 years. The relationship of these symptoms to the immediate skin test reactivity was also determined. Symptoms indicating past or current allergy and bronchial wheezing were observed in 36%. The cumulative prevalence of asthma was 2.7%, bronchial wheezing 9%, in addition, allergic rhinitis (including allergic conjunctivitis) 20%, and atopic dermatitis (including allergic urticaria) 20%. Positive immediate skin prick test reactions were observed in 50% of the population. Allergic rhinitis was most clearly connected with a positive skin test. This study shows that the respiratory disorders, generally considered to be allergic in origin, and atopic dermatitis are more common in Finland than has been assumed. The results are, however, in accordance with the observations made in other industrialized countries.

Susceptibility to asthmatic reactions and allergic symptoms should be taken into account, more so than at present, when judging the capability of a young man to manage compulsory military service.

Key words: allergen extracts; allergic disorders; asthma; epidemiology of allergy; skin tests

Accepted for publication 26 May 1979

In 1976, 10.8% of the young men examined for compulsory military service in Finland were either rejected or their service postponed for medical reasons. Asthma came third after mental disorders and diabetes, with a rejection per cent of 0.4 (24). The same year 5.5% of those who started military service had to discontinue for health reasons. Asthma in 0.18% was the second highest cause. This figure had doubled in 4 years. Atopic dermatitis was also an important reason for discontinuation and has been on the increase, being 0.08% in 1976.

This study reports the prevalence of asthma, bronchial wheezing, allergic rhinitis and atopic dermatitis in a group of conscripts aged 18-19 years. The relationship between these

symptoms and immediate skin reactivity to common allergens was also determined.

MATERIAL AND METHODS

The investigation was carried out in conjunction with a compulsory health survey for military service in Imatra, a small town in south-eastern Finland with 36,000 inhabitants. The subjects were each supplied with a questionnaire about any disorders indicating allergy during the last year, allergic symptoms which had occurred earlier and/or were noted by the family doctors, the occurrence of asthma, allergic rhinitis and atopic dermatitis in the immediate family, and information about smoking habits. The subjects were asked

to answer the questions with the help of their parents. The skin test was performed on 295 young men. Eighty-eight per cent (290) of the eligible population born in 1959 was included. Four persons refused to participate in the study and two were not tested because of disorders of the central nervous system. The skin test was made by two qualified assistants on the volar aspect of the forearm. The prick method was used with 16 extracts and 12 common allergens from two manufacturers. The allergens were: birch, alder, timothy grass, orchard grass, mugwort, white oxeye, dog and cat dander, house dust, house dust mite (*D. farinae*) (Dome Laboratories, England) as well as dog, horse and cat dander, house dust, house dust mite (*D. farinae*) and fish (Bencard, Brentford, England). The extracts contained glycerol 50% and phenol 0.4–0.5%. Histamine acid phosphate, 10 mg/ml, was used as a positive reference and glycyero-carbol saline from both manufacturers for negative controls.

The allergen activity of 13 extracts was measured by the direct RAST method (direct titration technique) (41). The activity obtained (Au/ml) was converted to biological HEP units using coefficients derived from a previous study (8). We were not able to determine the activity of house dust extracts and fish.

The skin reactions were first read after 15 min by the assistants and immediately thereafter by the authors in conjunction with the physical examination. The skin test reaction was regarded as positive if it clearly differed from the negative control and if the diameter of the weal produced was 3 mm or more (10, 15, 37). The weal induced by allergen was measured as recommended by Aas et al. (3): $(D+d)/2$. But in this article the reactions are indicated as being positive or negative, and only the proportion of reactions for each allergen equating the histamine reference in size is expressed. The authors made the physical examination after the skin test. Special attention was paid to symptoms and manifestations indicative of allergy. The lungs were auscultated during normal breath-

ing and forced expiration. The peak expiratory flow rate was measured by a Wright's peak flow meter; the same meter was used throughout the trial and the best of three blows was registered.

Asthma was defined as an episodic disorder associated with shortness of breath, wheezing and difficulty in expiration. Allergic rhinitis (seasonal or perennial) was defined as episodic rhinorrhea usually associated with nasal stuffiness and sneezing in response to a known or suspected allergen(s) and often accompanied by lacrimation. If there was no known or suspected allergen the rhinitis had to be associated with asthmatic symptoms, wheezing or atopic dermatitis in order to be accepted as "allergic". Atopic dermatitis was defined as pruritic dermatitis often accompanied by dry skin and white dermographism whether the offending allergen was known or not. Allergic urticaria was defined as periodic, localized, pruritic oedema associated with a known or suspected allergen. Those with contact dermatitis were excluded. The use of diagnostic terms such as asthma, allergic rhinitis and atopic dermatitis indicates that the diagnosis was made earlier by a physician or by the authors on the basis of the definitions outlined. The physical examination facilitated the diagnosis but it was primarily made regardless of the result of the skin test.

RESULTS

At least one positive skin test reaction was observed in 147 cases (50%). The number of positive reactions caused by the different extracts, the weal sizes compared with histamine reference reflecting the biological activity of the extracts, and the biological activity in HEP units derived from the immunochemical analysis are indicated in Table 1. Those with a positive skin test had five reactions on average; 15% had only one positive reaction and 12% 10 reactions or more.

If we had used only the house dust extract from Bencard, 69% of those with at least one

Table 1

Results of skin prick testing in 295 young men aged 18–19 years. Biological potency of the allergen extracts is expressed by comparing the average weal diameters produced with the histamine reference (10 mg/ml), as well as in HEP units obtained from direct RAST assays. These results (Au/ml) were converted to HEP units using coefficients derived from a previous study in which the concentration for histamine reference was also 10 mg/ml (8)

Allergen extract		No. positive reactions	Percentage positive reactions in all subjects	Percentage positive reactions in skin test positive subjects	Percentage reactions as large or larger than histamine	Allergen activity in HEP units
House dust	(B)	101	34	69	40	—
Cat dander	(B)	95	32	65	41	4
Timothy grass	(D)	58	20	39	74	10
Orchard grass	(D)	58	20	39	90	30
Mugwort	(D)	52	18	35	65	2
House dust	(D)	49	17	33	29	—
Horse dander	(B)	42	14	29	24	20
House dust mite	(B)	40	13	27	40	0.2
Birch	(D)	39	13	27	82	7
Alder	(D)	38	13	26	79	5
White oxeye	(D)	38	13	26	39	2
Cat dander	(D)	30	10	20	37	0.3
Dog dander	(B)	24	8	16	21	0.1
House dust mite	(D)	23	8	16	17	0.1
Fish	(B)	18	6	12	28	—
Dog dander	(D)	10	3	7	0	0.7

B = Bencard

D = Dome

positive reaction in the test battery of 16 allergens would have been revealed. With seven appropriately chosen allergens, all of the positive reactors would have been found (Table 2).

The correlations between allergic symptoms and skin test reactions are shown in Table 3. Clinical symptoms indicating past or present asthma, bronchial wheezing, or an allergic condition were recorded in 106 cases (36%). Seventy-six young men (24%) had experienced some symptom during the preceding year. In cases where symptoms were or had been present the skin test was positive in 72% whereas it was positive in 37% of asymptomatic subjects. On the other hand, 52% of those subjects with a positive skin test had experienced symptoms at some time; the figure was 20% in subjects with a negative skin test.

Active asthma was detected in five young

men (1.7%); in addition three subjects had experienced asthmatic symptoms in childhood. The cumulative prevalence of asthma was thus 2.7%. On the whole asthma or recurrent bronchial wheezing had occurred in 35 youths (12%). Bronchial wheezing was stated to have been provoked during the last year under the following conditions: only occasionally without any obvious extrinsic factor (six), associated with respiratory infections (eleven), with physical exertion (five), with both conditions (three), with allergen exposure (one), with respiratory infections/physical exertion and allergen exposure (three). If asthma or bronchial wheezing was the only complaint, the skin test was positive in 38%. This figure was doubled (77%) among those subjects whose bronchial symptom was associated with allergic rhinitis and/or atopic dermatitis.

Table 2

Effect of increasing the number and quality of allergen extracts in skin prick testing on the ability of the test to reveal a skin-positive subject (= a subject with at least one positive reaction in the test battery of 16 extracts)

Allergen extract	Cumulative number and percentage of reactions produced by different allergens in skin test positive subjects		
		<i>n</i>	<i>n</i> ₀
House dust	(B)	101	69
Timothy grass	(D)	+17	+11
Cat dander	(B)	+16	+11
Mugwort	(D)	+7	+5
Birch	(D)	+3	+2
House dust mite	(B)	+2	+1
Orchard grass	(D)	+1	+1
Total		147	100

B = Bencard

D = Dome

Allergic rhinitis (including allergic conjunctivitis) was observed in 60 subjects (20%); 36 (12% of all the subjects) suffered from pollen allergy and 26 (9%) associated their symptoms with animals and/or house dust. Six subjects (10% of those with rhinitis) had noted a spontaneous recovery. Thirty-three subjects out of 60 had received some kind of therapy; 11 had been hyposensitized and only one subject thought that the therapy had failed. In the author's opinion injection treatment was indicated for 11 additional subjects suffering from hay fever. The skin test was positive in all but one subject, with allergic rhinitis as the only complaint. The skin test positivity was less frequent (77%) among those subjects with rhinitis accompanied by asthma, bronchial wheezing and/or atopic dermatitis.

Atopic dermatitis (including allergic urticaria) was observed in 58 subjects (20%); in 28 cases the symptom had not appeared during the preceding year. In six subjects dermatitis had disappeared, but rhinitis had developed instead; in one case asthma had occurred. Twenty-six subjects had received long-term topical treatment. Food allergy had been observed by 12 subjects with a skin allergy. The skin test was positive in 57% of the subjects with atopic dermatitis; the figure was much higher (80%) among those with bronchial and nasal manifestations as well.

The group with past or present symptoms and a positive skin test had much higher atopic status, according to the number of positive skin test reactions, than the asymptomatic group with a positive skin test: 61% of the symptomatic subjects had four skin reactions or more compared with the 38% of the asymptomatic subjects. The same tendency was observed in subjects with multiple allergic symptoms compared with those with only one symptom (the corresponding figures were 72% and 49%).

Thirty-six per cent of those with a positive skin test had family members with allergic disorders; 39% of the symptomatic group and 32% of the asymptomatic group reported hereditary allergy. For those with a negative skin test and no symptoms this figure was 26%.

Forty per cent of the young men were regular smokers; one third of them had been smoking for at least 5 years. The symptoms of two subjects (0.7%) fulfilled the criteria of chronic bronchitis (5). Nineteen per cent of the smokers suffered from prolonged respiratory infections and cough; the figure for non-smokers was 15%. Those subjects with asthma, bronchial wheezing and allergic disorders had experienced susceptibility to respiratory infections and coughed much more often (in 29%) than the asymptomatic subjects (in 9%). The result of skin testing (negative or positive) did

Table 3

Cumulative occurrence of allergic disorders and bronchial wheezing and the immediate skin test reactivity in 295 young men aged 18-19 years

Symptoms	Skin test-negative		Skin test-positive		Total	
	n	%	n	%	n	%
Bronchial wheezing	8	5	5	3	13	4
Bronchial wheezing, allergic rhinitis	3	2	7	5	10	3
Bronchial wheezing, atopic dermatitis	1	1	4	3	5	2
Bronchial wheezing, allergic rhinitis, atopic dermatitis	1	1	6	4	7	3
Allergic rhinitis	1	1	24	16	25	9
Allergic rhinitis, atopic dermatitis	4	2	14	10	18	6
Atopic dermatitis	12	8	12	8	24	8
Allergic urticaria	0	0	4	3	4	1
Total	30	20	76	52	106	36
No symptoms	118	80	71	48	189	64
Total	148	100	147	100	295	100

not itself influence the susceptibility to respiratory infections.

The mean height of these young Finnish men aged 18-19 years was 178.3 cm (s.d. = 6.0 cm). The mean PEF value was 571 l/min (s.d. = 56.2 l/min). The skin test result, smoking habits, susceptibility to bronchial wheezing or respiratory infections did not influence the values. Not even those 36 subjects who had smoked for at least 5 years had lower values (561.2 l/min).

DISCUSSION

The prevalence of skin test positivity in the population studied was high. It does, however, correlate with some previous observations on this subject (16, 20, 31, 40). In these studies the skin test methods, extracts used, interpretation of the results and populations examined varied; nevertheless about half of the subjects tested experienced positive immediate skin reactions. In our previous study (17) 31% of

the 214 adolescents reacted positively when challenged with eight common allergens. This result approaches the figures obtained by Godfrey Griffiths (15) and Johnsen & Mygind (21) in more or less comparable reports. It is obvious that the quantity and quality of the extracts influence the prevalence figures. The house dust and animal dander allergens from Bencard reacted much more readily than the corresponding products from Dome Laboratories. It is suspected that the non-dialysed extracts contain low molecular weight compounds which could induce positive reactions without immunological specificity (1); this was quite obvious with some dust and dander extracts. Multiple positive skin reactions are, however, an indication of atopic disposition whether clinical symptoms are present or not (30). The epidemiological view of immediate skin reactivity does not change much when dialysed, purified and well-standardized allergens from Allergologisk Laboratorium, Copenhagen, and Pharmacia, Sweden are used (18).

According to the Scandinavian recommendations (2), the extracts used in skin prick testing should produce in moderately sensitive patients an average weal size equivalent to that obtained by histamine hydrochloride 1 mg/ml. Many of the allergens applied in our study had quite a high activity when determined by the direct RAST titration method (Table 1). Subjects with low sensitivity might have reacted as a result.

Both dog dander extracts had a low activity in the immunochemical analysis and the skin reactivity was also relatively slight. It was strange, however, that the extract with lower activity produced more skin reactions. The same observation was made earlier (8), but remained unexplained. This phenomenon could be due to irritants in the less potent extract, but it also indicates that the biological method (skin testing) and immunochemical assays should be used together to permit definite conclusions about the allergenic potency of different extracts. This is also recommended by Aas et al. (3).

Seventy-two per cent of the subjects with asthma, bronchial wheezing, allergic rhinitis and atopic dermatitis had at least one positive reaction. This figure was 59% in our previous report (17), but the skin testing was more concise. Hagy & Settippene (19) found that 64% of their series of college students with respiratory allergy had positive reactions in scratch tests. The figure for skin test positivity in asymptomatic subjects has varied between 9% and 49% in a few epidemiological studies (12, 15, 19, 27, 40). In the present study it was found to be 37%. However, the atopic status seems lower in asymptomatic than in symptomatic subjects, if judged by the number of positive skin reactions (this study) or by what is termed the reactivity index (7).

The cumulative asthma prevalence was 2.7% and recurrent bronchial wheezing 9% in addition. Alanko (4) reported the prevalence to be 0.5% in boys aged from 10 to 19 years according to the previous observations made by physicians. Prevalence rates from 0.58% to 7.1% have been reported elsewhere at the

same ages (19, 25, 34, 35, 36, 38). It is not, however, always obvious whether the figures obtained indicate active or cumulative disease. The occurrence of asthma has also been studied in conjunction with health surveys for military service (11, 13, 32, 39). In these studies asthma is reported to have caused a rejection in 0.32–0.96%; the prevalence figures are assessed between 0.38 and 0.96%. It is quite impossible to define exactly what is asthma and what is bronchial wheezing, which does not deserve the title of asthma from an epidemiological point of view. The definition is based in practice on the frequency of symptoms and the need for treatment. It is obvious that most the young people with recurrent bronchial wheezing do have hyper-reactive bronchi, which is essential for an asthmatic reaction (28). The occurrence of recurrent bronchial wheezing in children and youths has been 9.9–23.0% in various studies this decade (6, 9, 35). If bronchial wheezing appeared as the only symptom, the skin test positivity rate was no higher than in asymptomatic subjects. The correlation of atopy and bronchial hyperreactivity is far from solved and has been questioned by Woolcock et al. (40) on the basis of an epidemiological survey. In our study only four subjects of the 29 who had experienced their symptom of asthma or bronchial wheezing during the last year had noted that it was provoked by an allergen.

The cumulative prevalence of allergic rhinitis was 20% including the 12% for hay fever. Alanko (4) reported that 2.7% of the boys aged 10–19 years suffered from allergic rhinitis; the figure increased to nearly 10% with advancing age. Malmberg (26) reported that allergic rhinitis occurred in 13% of Finnish schoolchildren aged 7–11 years. The highest prevalence rates, of hay fever 12.7–23.2%, have been obtained in college students (14, 19, 21, 34). The diagnosis of seasonal hay fever is usually easy, but differentiation between extrinsic perennial, intrinsic perennial and vasomotoric rhinitis is in some cases arbitrary. Nevertheless, in this

study the correlation between allergic rhinitis and skin test positivity was remarkably good. The lack of treatment in subjects with nasal allergy was striking.

The cumulative prevalence of atopic dermatitis was 20%; spontaneous recovery was a common feature with advancing age. It is agreed that atopic skin symptoms are common, but relevant figures are hard to obtain. Salo (33) reports that 5.6% of the new recruits have active atopic dermatitis; our figure was 10%. Patients with respiratory allergy suffer from atopic dermatitis in 15–63%, according to several investigators (23, 29); the figure was 38% in this study. On the other hand, we found a respiratory allergy in 52% in patients with dermatitis. Atopic dermatitis correlated quite poorly with skin test positivity; the same observation was made in our former study (17). Jones et al. (22) have stated that when symptoms referring to respiratory allergy are lacking skin test positivity is no more frequent among patients with dermatitis than in a "normal population".

Our study shows that respiratory disorders, generally considered to be essentially allergic in origin, and atopic dermatitis are surprisingly common in Finnish young men. Most of the symptoms are mild and a considerable part disappear with age; nevertheless far too many subjects with atopic disorders have received no treatment or adequate instructions on how to avoid harmful allergens and how important this may be. It is also obvious that the susceptibility to asthmatic reactions and allergic symptoms has been underestimated when judging the capability of a young man to manage compulsory military service. A clear indication of this is that asthma has doubled as a cause for interruption of service over a 4-year period.

The high prevalence of skin test positivity among asymptomatic subjects is an interesting matter for discussion. It has been shown that skin test positivity without atopic manifestations as an apparent risk factor for developing respiratory allergy (30). If the

extracts are satisfactory and the proper technique is used, a positive reaction merely implies that the mast cells in skin contain specific immunoglobulin ready to act when challenged by allergens. Follow-up studies are urgently needed to clarify the role and significance of immediate skin test reactivity (atopic predisposition) for the appearance of new allergic symptoms and development of manifest ones in different populations.

ACKNOWLEDGEMENTS

We wish to thank our assistants Ulla Lautala and Irma Liukkonen as well as Docent Fred Björkstén who helped to carry out the immunochemical assays of the allergen extracts. This study was supported by grants from the Finnish Anti-Tuberculosis Association and the Foundation for Allergy Research.

REFERENCES

1. Aas, K.: Standardization of allergen extracts. *Dev. Biol. Stand.* 29, 341–349, 1975.
2. Aas, K. & Belin, L.: Standardization of diagnostic work in allergy. *Acta Allergol.* 27, 439–468, 1972.
3. Aas, K., Backman, A., Belin, L. & Weeke, B.: Standardization of allergen extracts with appropriate methods. *Allergy* 33, 130–137, 1978.
4. Alanko, K.: Prevalence of asthma in a Finnish rural population. *Scand. J. Resp. Dis., Suppl.* 76, 1–64, 1970.
5. American Thoracic Society: Chronic bronchitis, asthma and pulmonary emphysema. *Amer. Rev. Resp. Dis.* 85, 762–768, 1962.
6. Anyon, C. P. & Kiddle, G. B.: The prevalence of wheezy children in lower Hutt. *New Zealand Med. J.* 79, 822–823, 1974.
7. Barbee, R. A., Lebowitz, M. D., Thompson, H. C. & Burrows, B.: Immediate skin test reactivity in a general population sample. *Ann. Intern. Med.* 84, 129–133, 1976.
8. Björkstén, F.: Determination of the potency of allergen extracts by biological and immunochemical method (in Finnish). *Finnish Allergy Research Foundation Year Book*, pp. 10–18, 1977.
9. Broder, I., Higgins, M. W., Mathews, K. P. & Keller, J. B. III: Epidemiology of asthma and allergic rhinitis in a total community, Tecumseh, Michigan. *J. Allergy Clin. Immunol.* 53, 127–138, 1974.

10. Bryant, D. H., Burns, M. W. & Lazarus, L.: The correlation between skin tests, bronchial provocation tests and the serum level of IgE specific for common allergens in patients with asthma. *Clin. Allergy* 5, 145-157, 1975.
11. Cottin, J., Corroller, F., LeRest, F., Prost, A., Delobel, M. & Moreau, A.: Fréquence et étiologie de l'asthme chez le jeune adulte: dans une population de 190 000 jeune adulte. *Poumon* 27, 404-416, 1971.
12. Curran, W. S. & Goldman, G.: The incidence of immediate reacting allergen skin tests in the normal adult population. *Ann. Intern. Med.* 55, 777-783, 1961.
13. Eriksson-Lihr, Z.: Special features in allergy in children. *Acta Allergol.* 8, 289-313, 1955.
14. Freeman, G. L. & Johnson, S.: Allergic diseases in adolescents. I. Description of survey, prevalence of allergy. *Amer. J. Dis. Child.* 107, 549-566, 1964.
15. Godfrey, R. C. & Griffiths, M.: The prevalence of immediate positive skin tests to Dermatophagoides pteronyssinus and grass pollen in schoolchildren. *Clin. Allergy* 6, 79-82, 1976.
16. Grow, M. H. & Herman, N. B.: Intracutaneous tests in normal individuals. *J. Allergy* 7, 108-111, 1936.
17. Haahtela, T.: The prevalence of allergic conditions and immediate skin test reactions among Finnish adolescents. *Clin. Allergy* 9, 53-60, 1979.
18. Haahtela, T. & Jokela, H.: Epidemiology of immediate skin test reactivity. In preparation.
19. Hagy, W. G. & Settignano, G. A.: Bronchial asthma, allergic rhinitis and allergy among college students. *J. Allergy* 44, 323-332, 1969.
20. Herxheimer, H., McInroy, P., Sutton, K. H., Utidjian, H. L. & Utidjian, H. M. D.: The evaluation of skin tests in respiratory allergy. *Acta Allergol.* 7, 380-396, 1954.
21. Johnsen, N. J. & Mygind, N.: Incidence of latent and clinical respiratory tract allergy in medical students (Danish). *Ugeskr. Laeg.* 140, 596-600, 1978.
22. Jones, H. E., Inouye, J. C., McGerity, J. L. & Lewis, G. W.: Atopic diseases and serum immunoglobulin-E. *Br. J. Dermatol.* 92, 17-25, 1975.
23. Kaita, T.: Studies of bronchial asthma in children. I. Statistical observation of bronchial asthma in children. *Hiroshima J. Med. Sci.* 16, 163-168, 1967.
24. Koskenvuo, K. & Kotiranta, E.: The health status of Finnish conscripts in 1976 (in Finnish). *Sotilaslääk. Aikak.* 52, 6-8, 1977.
25. Kraepelin, S.: Frequency of bronchial asthma in Swedish school children. *Acta Paediat. Scand.* 43, Suppl. 100, 149, 1954.
26. Malmberg, H.: Personal communication, 1979.
27. McNicol, K. N. & Williams, H. E.: Spectrum of asthma in children II, allergic components. *Br. Med. J.* 4, 12-16, 1973.
28. Muittari, A.: The value of the metacholine test as a diagnostic method in bronchospastic disorders. *Ann. Med. Intern. Fenn.* 57, 197-203, 1968.
29. Pearson, R. S. B.: Asthma in Barbados. *Clin. Allergy* 3, 289-297, 1973.
30. Pepys, J. & Davies, R. J.: Allergy. In Clark, T. J. H. & Godfrey, S. (eds.): *Asthma*, pp. 126-161. Chapman & Hall, London, 1977.
31. Rackemann, F. M. & Simon, F. A.: Technic on intracutaneous tests and results of routine tests in normal persons. *J. Allergy* 6, 184-188, 1935.
32. Roundtree, L. G., McGill, K. H. & Edwards, T. I.: Causes of rejection and incidence of defects among 18 and 19-year old Selective Service registrants. *J. Am. Med. Assoc.* 123, 181-185, 1943.
33. Salo, H.: Personal communication, 1979.
34. Sherry, M. N. & Scott, R. B.: Prevalence of allergic diseases in freshmen college students: a survey based on predominantly Negro population. *Ann. Allergy* 26, 335-338, 1968.
35. Smith, J. M.: The prevalence of asthma and wheezing in children. *Br. J. Dis. Chest* 70, 73-77, 1976.
36. Smith, J. M., Harding, L. K. & Cumming, G.: The changing prevalence of asthma in schoolchildren. *Clin. Allergy* 1, 57-61, 1971.
37. Stenius-Aarniala, B. S. M., Malmberg, C. H. O., Holopainen, E. E. A. & Björkstén, F.: In vivo tests with pollen extracts previously investigated by means of direct RAST titration allergen assay. *Clin. Allergy* 8, 411-418, 1978.
38. Tips, R. L.: A study of the inheritance of atopic hypersensitivity in man. *Am. J. Hum. Genet.* 6, 328-343, 1954.
39. Williams, D. A.: Social importance of allergic diseases. First International Congress for Allergy, Zürich, 1951.
40. Woolcock, A. J., Colman, M. H. & Jones, M. W.: Atopy and bronchial reactivity in Australian and Melanesian population. *Clin. Allergy* 8, 155-164, 40 1978.
41. Yman, L., Ponterius, G. & Brandt, R.: RAST-based allergen assay methods. *Dev. Biol. Stand.* 29, 151-165, 1975.

Address:

Dr. Tari Haahtela
Dept. of Pulmonary Diseases
Tiuru Hospital
SF-55330 Tiuruniemi
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.