Allergic Status of Children in an Indonesian Village*

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SUMMARY **Skin tests to 13 common aero-allergens and to *Ascaris lumbricoides*, clinical studies and blood and faecal examinations were performed on a random sample of primary school children in an Indonesian village. All the children were parasitised, and most had elevated total IgE levels and eosinophilia. Thirty-six per cent had positive skin tests to two or more of the aeroallergens and 47 per cent had positive skin tests to *Ascaris lumbricoides*. No child had a history of allergic rhinitis, atopic dermatitis or urticaria, but 3.7 per cent had mild asthma which was apparently not related to atopic status. It is possible that parasitic infection is related to the low prevalence of allergic diseases in this population but longitudinal studies of this and of similar ethnic populations that have low levels of parasitism, are needed to determine the role of parasitic infestation.**

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There is a growing literature concerning the possible role of parasitic infection in moderating the allergic response to common allergens in children in developing countries. Little has been published about the allergic status of children living in village communities in Southeast Asia. The severity, prevalence and nature of diseases associated with Type 1 allergy (immediate hypersensitivity) was studied in a childhood village population of an Indonesian village. The data collected included a history of symptoms, skin prick tests with 13 common aero-allergens, physical examination, bronchial challenge test with histamine, eosinophil counts, examination of the faeces for parasite eggs and selected studies of serum IgE and serum specific IgE (RAST).

METHODS AND MATERIAL

Skin prick tests

Prick tests were carried out according to the method of Pepys[1] on the forearm using 13 common aero-allergens plus a positive control (histamine diphosphate 0.1 %) and a negative control (normal saline). In addition, skin tests to an extract or *Ascaris lumbricoides* antigen were also used.

The allergens used included three species of house dust mite *(Dermatophagoides farinae, Dermatophagoides pteronyssinus* and *Tyrophagus putrescentiae),* animal epithelia (horse, dog, cat), feathers, kapok, ragweed, rye grass, timothy grass, *Aspergillus fumigatus* and *Alternaria tenius.* These potential allergens were supplied by Hollister-Stier (USA) except for *D. pteronyssinus* and feathers which were supplied by Dome Laboratories. The *Tyrophagus* and *Ascaris* antigens were produced in the Department of Medicine, University of Sydney. Skin reactions were recorded by measuring the size of the resulting wheals using a template 15 minutes after the prick and were considered positive if a wheal greater than 2 millimetres was observed.

Serum IgE and RAST tests

Blood was taken from each child and the serum was collected and stored at -20°C and later analysed for IgE using the method of Salmon *et al.*[2] The normal range in children is up to 200 K units/L. Measurement of specific IgE to the *Ascaris* antigen and to the 3 house dust mites was carried out on a selected group of sera by the RAST method as described by Wide *et al.*[3] Paper

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disc-coupled allergen from *D. pteronyssinus* was obtained from Pharmacia and coupled *Ascaris* antigen was prepared in our laboratory. The radioactivity count scores representing specific IgE were graded as follows: 4 highly positive; 3 strongly positive; 2 clearly positive; 1 borderline, and 0 negative.

Eosinophil counts

A portion of each blood sample collected was used for an eosinophil count using a counting chamber in the standard way.[4]

Faecal Examination

Each child was asked to bring a specimen of faeces, which was examined in eosin solution for the presence of parasite eggs. The parasites detected in the faeces of these children included *Ascaris, Ancylostoma* and *Trichuris.*

Physical examination

In order to determine the prevalence of allergic rhinitis and productive cough, skin atopy and asthma, each child was questioned and examined briefly. Questions were asked relating to past history of asthma, bronchitis and tuberculosis, and the child was asked if he or she had a cough at the present time. The skin was examined for any obvious abnormalities, the nose was examined for nasal discharge and the child was asked to cough vigorously in order to determine if a loose cough was present. This sign has been well described by Gandevia[5] and indicates the presence of a productive cough at the time of examination.

Bronchial challenge testing

To determine the prevalence of asthma and bronchial hyperresponsiveness, a histamine inhalation test was performed in all children. The methods and results of this part of the study have been published.[6,7] Briefly, each child had lung function tests performed with both peak expiratory flow rate and spirometric function. Following this, a dose of normal saline was given to determine nonspecific responsiveness. Increasing doses of histamine were then delivered from De Vilbiss No. 40 hand-held nebulisers and the spirometric results were recorded 60 seconds after each inhalation. The challenge was stopped when the highest dose (8 μmol of histamine) had been given or when the FEV_1 had fallen by 20 per cent. For children in which a fall occurred, the per cent change in FEV_1 from the post saline value was plotted against the dose of histamine to give a dose-response curve. The dose causing a 20 per cent fall in $FEV_{0.5}$ (PD_{20} $FEV_{0.5}$) was used as the index of the degree of bronchial hyperresponsiveness.

Sampling of children

Class lists were obtained from the four primary schools in the village and from the junior high schools. A random sample of 2/3 of the children in each class was selected from these schools to participate in the study. A smaller number of children from some of the junior high schools were also asked to attend in order to determine if atopic status was age-related. The prevalence figures for atopic status in this paper relate only to the primary school children who were aged 8-13 years, with a few 7, 14 and 15 years old.

Protocol

Each child was asked to bring a specimen of faeces and on arrival was given an identification number. The child was then questioned about cough, etc. The skin test was then performed and blood taken. Finally, lung function tests were performed followed by the histamine inhalation test. Children whose resting lung function was abnormal had their lung function response to bronchodilator aerosol documented. A few children were asked to bring samples of house

Table 1. Number of elementary school children by sex and age who were skin tested and number with 1,2,3 and 4 tests positive

Age (yr)	Sex	No. tested	No. positive				
			Aero-allergens				*Ascaris* antigen
			1	2	3	4	
8	M	14	3	2	1	2	not tested
	F	9	2	2	0	1	not tested
8	M	8	0	2	1	0	5
	F	14	1	2	1	2	6
9	M	26	4	4	0	5	13
	F	15	0	0	2	4	11
10	M	23	1	2	5	5	12
	F	23	4	1	3	5	12
11	M	25	8	1	4	3	11
	F	26	5	1	2	7	12
12	M	25	1	2	1	2	12
	F	19	3	0	0	7	8
13	M	26	3	3	1	2	13
	F	17	5	5	2	1	7
14	M	20	5	1	3	0	10
	F	16	1	3	1	1	6
14	M	8	0	1	0	2	4
	F	3	0	0	1	1	3

dust which were collected in plastic bags and frozen for later examination. Housedust mite numbers per gram of dust were counted.[8]

RESULTS

Population

Table 1 gives the age and sex composition of the population examined. Out of a total of 514 children enrolled in the primary schools, 336 were selected at random for testing and 325 attended and were tested.

Skin Tests

Aero-allergens

Table 1 shows the number of children who had positive reactions to 1, 2, 3 and 4 or more aero-allergens (excluding *Ascaris*) by age and sex. Only 317 children had skin test results recorded. Overall, 36 per cent of the children gave positive responses to two or more allergens. This did not vary with age or sex. Figure 1 shows the percentage of children who had positive reactions to each of the aero-allergens tested. Of all the aero-allergens tested, the 3 species of housedust mites gave the highest percentages of positive results, and of the mites, *D. farinae* gave the highest number of responses (26% of males and 31% of females). Feathers were the next commonest cause of skin positivity.

Of the 306 children tested with *Ascaris* antigen, a positive reaction was found in 143 (47%) and a negative reaction in 163 (53%). The responses were not related to sex or age. A greater proportion of children with a positive skin test response to *Ascaris* (60/143) had a positive skin-test reponse to the aero-allergens than those in the *Ascaris*-negative group (38/163; $P < 0.001$, chi-square test). There were no differences in the number or size of skin test responses of children in the four primary schools.

Size of skin test reaction

Overall, the size of the skin test wheals to the aero-allergens averaged smaller than those to histamine, while reactions to *Ascaris* antigen were larger. The mean size for histamine was 4.9 ± 1.20 mm (SE) for *D. pteronyssinus* 3.6 ± 0.76 mm, for *D. farinae* 3.4 ± 0.96 mm, *T. putrescentiae* 3.7 ± 0.93 mm, feathers 3.7 ± 0.10 mm, horse 3.6 ± 0.5 mm and *A. lubricoides* 5.2 ± 1.97 mm. Only 16 children had reactions to aero-allergens equal or greater in size than that produced by histamine.

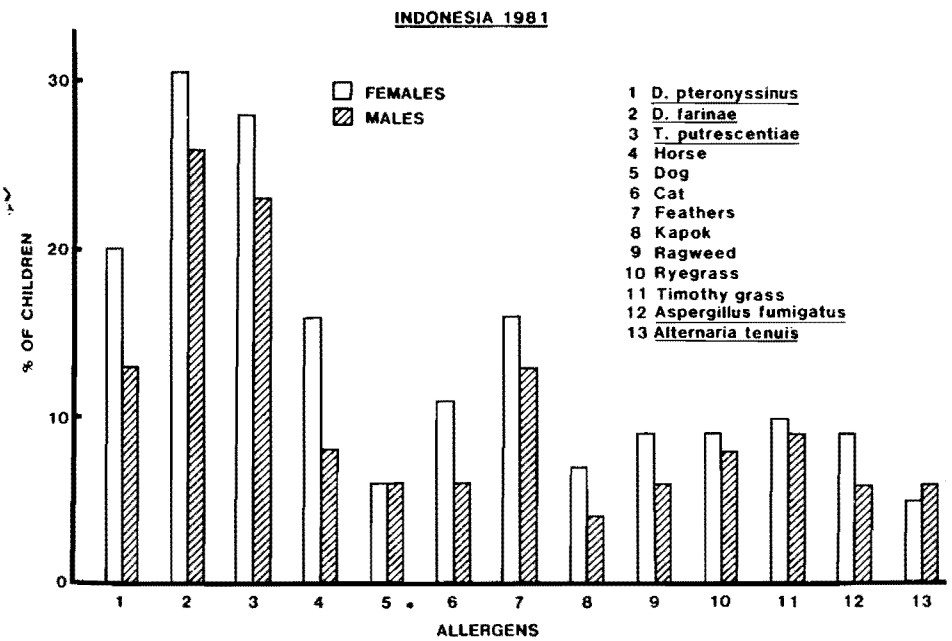

Fig. 1 The proportion of primary school boys and girls with positive skin test responses to 13 common allergens.

There was no relationship between the RAST count and the size of the skin test reaction to *A. lumbricoides*, although those with the largest skin tests (9 mm and above) tended to have the highest RAST counts.

Age and sex distribution of allergic status

Approximately equal numbers of males and females had positive skin tests to both *D. farinae* and *A. lumbricoides* (Figs. 2 and 3). All children tested were included in these figures and there was no significant change with age from 8 to 16 years. Insufficient children over the age of 16 years were studied to allow valid analysis of the results.

History and physical examination

No child gave a clear cut history of allergic rhinitis or of skin allergy. Nasal discharge was present in 45 (14%) children and a loose cough was present in 79 (24%), while 21 (6%) children had both. Fifteen children gave a history of having had asthma in the past. Overall 12 children were considered to have asthma, defined as increased bronchial hyperresponsiveness and a history of breathlessness.[7] The details of these children are given in Table 2. Nine of them had abnormal resting lung function as measured by the peak expiratory flow rate (PEFR). After bronchodilator aerosol, almost all increased their flow rates and only two children remained with obviously abnormal lung function. Seven of the children had a cough at the time of examination. Five of the asthmatic children were allergic, as measured by the skin tests, and seven responded to the *Ascaris* antigen. Thus, as a group, they were not different from the non-asthmatic children in relation to the frequency of skin test responses to the aero-allergens or to *Ascaris* antigens. The PD_{20} $FEV_{0.5}$ was not related in any way to the degree of atopy to aero-allergens or to *Ascaris* antigens.

Eosinophils

Almost all the children had eosinophilia. The number of eosinophils ranged from 8 to 2,882 per ml. The mean and SD (for 319 children tested) was 885 ± 542/ml. Skin test positivity to *A. lumbricoides* did not affect the eosinophil count.

Total IgE

IgE was measured in 63 serum specimens. The mean value was 3,170 K units/L and the range was 304-10,450 (normal mean in children is less than 200 Ku/L). Insufficient specimens of serum from the children with asthma were analysed to allow a comparison of IgE levels between asthmatic and nonasthmatic children. However, there were differences in levels of IgE in relation to skin-test status. Table 3 lists the mean ± SD values for IgE and eosinophil counts for the 63 children divided into groups according to the skin test responses to *Ascaris* and to the house dust mite allergens. The group of children whose skin tests were negative to both *Ascaris* and mites had lower IgE levels than those with positive reactions to *Ascaris*, housedust mite (HDM) or both. Although children who were positive to both *Ascaris* and HDM had higher eosinophil counts, the range was wide and the value for this group was not significantly different from that of the other groups.

Specific IgE

A relatively small number of RAST tests were done. All children who had tests for *A. lumbricoides* (n = 62) were positive with scores between 2 and 4 regardless of the skin reaction. Twelve sera from

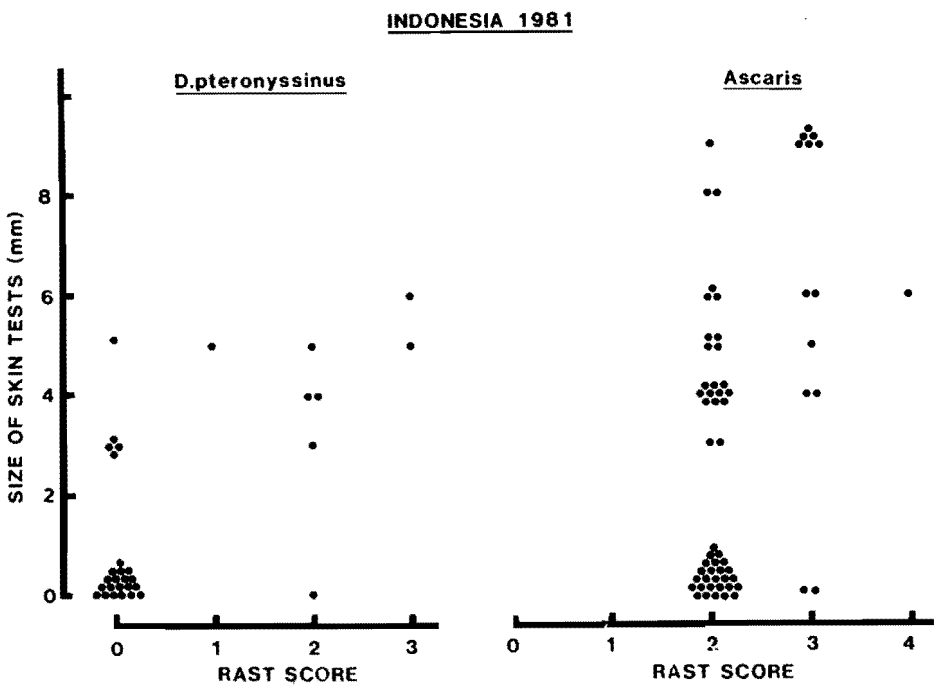

Fig. 2 The relationship between size of skin test wheal and RAST score for *Dermatophagoides pteronyssinus* (n = 33) and *Ascaris lumbricoides* (n = 61). There was no relationship for *Ascaris* and a weak relationship for *D. pteronyssinus.*

Table 2. Details of asthmatics

Sex	Age (yr)	Initial PEFR (L/min)	PEFR (% predicted)	PEFR Post-BD (L/min)	Loose cough	Skin tests: aero-allergens No. +ve	Skin tests: aero-allergens mean size (mm)	Skin tests: *Ascaris* antigen mean size (mm)	Eosinophil count (cells/ml)	PD_{20} $FEV_{0.5}$ (μMol)
M	9	130	59	140	yes	5	3	4	1210	4.6
M	9	140	62	240	no	0		7	451	3.2
F	10	295	111	320	no	1	4	0	935	0.67
F	11	190	71	205	no	0		0	550	0.34
F	10	110	56	170	yes	0		0	539	2.2
M	15	160	40	300	no	0		6	440	4.2
M	11	200	83	260	yes	1	3	0	1375	0.86
F	10	155	71	185	yes	0		3	847	2.7
F	10	123	52	205	yes	3	4	6	1353	1.75
F	15	265	76	NT	no	4	3	9	869	0.65
F	9	145	65	150	yes	0		0	451	3.5
M	12	235	85	270	yes	0		9	309	2.6

PEFR = peak expiratory flow rate
post-BD = post-bronchodilator
PD_{20} $FEV_{0.5}$ = provoking dose causing 20% fall in forced expiratory volume in 0.5 second

Table 3. Values (mean ± SD) for IgE and eosinophil count in relation to skin test response to *Ascaris* antigen and three species of housedust mite (HDM)

Skin tests		No. examined	IgE (Ku/L)	Eosinophils (/ml)
Ascaris antigen	HDM			
+ve	+ve	21	3485 ± 2660	1031 ± 602
	-ve	14	4079 ± 2740	713 ± 215
-ve	+ve	14	3600 ± 1641	833 ± 343
	-ve	14	1641 ± 1408*	26 ± 506

*$P < 0.05$ when compared to any of other groups

children who had positive skin tests to *D. pteronyssinus* were tested, and 6 had RAST scores ⩾ 2, while only 1 of 20 with negative skin-test reactivity had a positive RAST score. The sample was too small to determine if a relationship exists between the size of the skin reaction and the RAST score to this mite allergen..

Mite count

Dust was obtained from 13 houses. House dust mites were found in all samples. *Dermatophagoides* species were found in 10 of the samples with counts varying between 20 and 104 mites/g.

Faecal parasite counts

Stools from 309 elementary school children were examined. Eggs were found in every specimen. Of these, 292 or 94 per cent were positive for *Ascaris*, 17 (6%) for *Ancylostoma* and 83 (27%) for *Trichuris*.

DISCUSSION

The children of Banyuatis village enjoy a relatively high standard of living. The average family income is above the average for Indonesia. Almost all the inhabitants are farmers, but 5 per cent are tradesmen and a few are storekeepers. Virtually all children attend school, and are neatly clothed and well washed. There is reticulated water in the village which is connected to 90 per cent of the houses. The children are healthy and very few have serious illnesses. Gastrointestinal and upper respiratory tract infections are common. Asthma and other allergic diseases are almost unknown and no case of childhood asthma was treated at the local health centre, which is staffed by one medical graduate, in the previous 2 years.

In spite of the apparent high standard of living, parasitic eggs were found in the faeces of every child. There seems little doubt that this heavy parasite load accounts for the eosinophilia and high total IgE levels found in virtually every child. The children take no treatment for intestinal parasites, probably because the parasites cause no directly related symptoms and there is thus no reason for treatment.

Although 36 per cent of the children gave positive skin test reactions to two or more of the aero-allergens tested, there was little to suggest that these children had any symptoms related to these allergens. The reactions were smaller than those to histamine and *Ascaris*. In addition, the RAST tests done on a selected group of sera from children who had positive skin tests to the mite antigen were frequently negative (Figure 2), suggesting that the specific IgE levels to these allergens were extremely low. The absence of atopic skin disease and allergic rhinitis suggest strongly that aero-allergens are not associated with any overt "allergic" disease in these children.

A small number of children, approximately 3.7 per cent, had mild asthma as defined by symptoms of breathlessness and bronchial hyperresponsiveness. However, compared with the prevalence of asthma in Australia, these rates are low. In addition, the degree of bronchial responsiveness was not severe and may well have been related to persisting bronchial infections since the majority of these children had a loose cough and abnormal resting lung function. Only three (25%) of these children had more than one positive skin reaction to aero-allergens and were thus no more atopic than the overall population.

The studies of the few dust samples obtained indicate that different varieties of housedust mites exist in this village so that the prevalence of allergic reactions to mites could be expected to be similar to that found in other areas where mites are common. This in fact was the case. The prevalence of skin test reactions to mites in these children was similar to that in 8- or 9-year-old children in a coastal area of New South Wales.

A small number of children gave positive reactions, albeit small, to a number of pollens and animals to which they have not been exposed. Ragweed and timothy grass do not grow in this region and positive reactions probably represent cross reactions to similar aero-allergens from animals and pollens in the local environment.

It has been suggested that the high total IgE levels caused by worm infestations may have some effect on the immune system, either in preventing the formation of IgE to the aero-allergens[9,10] or in saturating the appropriate sites on mast cells.[11] Godfrey[9] found no evidence of asthma or allergic rhinitis in rural children in the Gambia. They found children with high total IgE values and attributed this lack of allergic disease to the possible "protective" effect of the high IgE levels. Turner[10] has discussed the likely role of parasitic infections in modulating the prevalence of asthma in detail. Based on his analysis it is likely that parasitic infections repress the synthesis

of IgE.

Warrell *et al,*[12] in 1975, suggested that high IgE levels in apparently healthy Nigerians with helminthic infestation protected them from atopic disease because asthmatics had much lower levels of IgE. In the present study, however, there was no relationship between total IgE and size of skin test reaction. Thus, those children with the largest skin test reactions to aero-allergens did not have lower levels of total IgE. In addition, the suggestion of Warrell *et al.*[12] was not confirmed by Macfarlane *et al,*[13] who identified parasites as frequently in asthmatics as in control subjects. They also found no difference in IgE levels between urban and rural asthmatics, nor was there any correlation in asthmatics or controls between levels of nonspecific IgE and results of skin tests to common environmental allergens.

There are a number of papers which do not support the hypothesis that high IgE levels to parasites protect against the development of allergic disease. Firstly, there was the finding of a fall in prevalence of asthma in Tristan de Cunha over a period of time in which there was a marked reduction in intestinal parasites.[14] In Malaysia, asthma and atopic diseases were found among parasitised children[15] and similarly, Lash,[16] in the Gambia, found asthmatic children who were parasitised. Carswell *et al*[17] found parasites in asthmatic and non-asthmatic children in Tanzanian. Joubert *et al*[18] have suggested that infestations with *Ascaris* may predispose to atopic asthma. Thus, considerable confusion still exists and longitudinal studies on populations such as this one are needed to determine if atopic diseases increase when parasitic infestations decrease.

The findings of the present study suggest that all children in this village were able to mount a response to parasites producing high IgE levels but only half the children had skin reactivity to *A. lumbricoides.* Furthermore, those without a skin test reaction were less likely to be reactive to aero-allergens and, based on a small sample, had lower IgE values. These skin test differences may result from different kinds of mast cells in the skin of some children, or they represent a marker for a different kind of response to the parasite in different children. Clarification of the relationship between these responses and the manifestations of atopic disease awaits more information.

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