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Chapter 6

Asthma and atopy in school children from different socioeconomic backgrounds in Makassar: a study on environment factors, nutritional status and helminth infections

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Abstract

Investigations of risk and protective factors associated with variation in the prevalence of allergic disorders in developing countries are limited. A better understanding of these factors might help to control the allergic march. To this end, the current study was conducted in two schools where children from families with different socioeconomic status, attended. In total, 262 children from a low-socioeconomic status (SES) and 330 from a high-SES schools were studied. The prevalence of asthma and atopy, as determined by skin prick test (SPT) positivity and specific IgE, was assessed and information on environmental factors, nutritional status and helminth infections was collected. Whereas the prevalence of SPT positivity was significantly lower in low-SES school children, prevalence of asthma, as determined by core ISAAC questionnaire, was equivalent in the two schools. A further categorization of the socioeconomic status in each school revealed that in high-SES school, a lower category of socioeconomic, decreased the risk of atopy by 50%, (for SPT positivity OR 0.46 [0.26-0.84], for specific-IgE positivity OR 0.53 [0.28-0.99]) but had not effect on asthma. A lower nutritional status tended to be associated with a decreased risk of SPT positivity in both schools whereas in the high-SES school, a lower nutritional status decreased the risk of having high levels of IgE by 65% (OR 0.35 [0.15-0.81]). There was no significant effect of family size, exposure to animals, presence of smoker in the house and helminth infections on the allergic outcomes measured in the low-SES school but some of these tended to associate with allergic outcome in the high-SES school.

Introduction

It has long been known that allergic disorders cluster within families and this is likely to be due to genetic predisposition. However, a host by environmental factors may modulate expression of clinical allergy. A higher prevalence of allergic disorders in developed countries compared to developing ones [214], and the great differences in prevalence between urban and rural populations particularly in developing countries [165;166;169;170;249;350;351] has clearly shown how important the influence of environmental factors is on the expression of allergic disorders.

The worldwide ISAAC study has revealed Indonesia as a country with lowest prevalence of allergy in the world (ISAAC) [214]. However, this study was done in only one centre in Java. A similar study which was conducted in 10 centres in India showed a large variation in the prevalence of asthma (ranging from 3% to 17%) in different centres indicating that the information on allergic disorders in Indonesia reported by the ISAAC study published in 1998 may not be representative of the whole country.

Several factors related to western lifestyle such as increase in exposure to outdoor pollutants [174;374], increased indoor allergen load [176], altered diet [177;178] and

changes in exposure to infections/microbial products [179;180] have been hypothesized to explain the increase in allergic disorders. However, how these factor influence allergy and atopy in Indonesia has never been addressed.

To investigate this, we initiated a study at two schools with children from different socioeconomic backgrounds in an urban area in Makassar, in Sulawesi, to measure the prevalence of asthma as well as atopy. Several factors such as parental education, number of siblings, exposure to animals, presence of smoker in the house, nutritional status and helminth infections were also measured to see how these factors influence the allergic phenotype in the study population.

Materials and Methods

Study area and population

The study population consisted of children that attended two elementary schools in Makassar, an urban centre, the capital city of South Sulawesi. One was a school (SD Cambaya) where children from families with low-SES were sent to and another school (SD Mangkura) where children from families with a high-SES attended. In total, 262 children from the low-SES and 330 from high-SES were included in the study. Data on asthma symptoms was obtained using a slightly modified ISAAC asthma core questionnaire (see in a paper earlier (Wahyuni *et al.* submitted)) was answered by parents. Children were identified to have asthma if wheezing in the past 12 months reported by parents was confirmed as asthma by a health worker (HW). Additional questions regarding variables of interest such as parental educational background, parental occupation, the number of siblings, the presence of animals (cat or dog or both) in the house and the presence of a smoker in the house were also included in the questionnaire. A month prior to the start of the study, the parents of children in both schools from third to sixth grades were sent a letter informing them of the study and asking them to sign an agreement letter if they agreed for their child to participate in the study. Only children who returned the signed agreement letters were included in the study. The study was approved by the ethics committee of the Faculty of Medicine, Hasanuddin University, Indonesia.

The educational level

The parental educational background ranged from illiterate, elementary school, junior high school, academic level, university degree, masters degree to doctorate. These educational backgrounds were then categorized into elementary (from illiterate to completed elementary school), secondary (from junior to completed senior high school) and tertiary (from academic/university to doctorate level). To analyze the influence of parental educational background on allergy/atopy, it was dichotomized into low if parental

educational background was \leq elementary school, and high if parental educational background was $>$ elementary school.

The socioeconomic level

The socioeconomic status of the children in the two schools did not overlap at all and therefore they were categorized separately. Within the low-SES school, the status was classified into category 1 when parents had manual jobs that needed no skills, category 2 when parents had skilled jobs such as tailor, teacher, sales person in a traditional market or governmental clerk. In the high-SES school, the parents who has professions such as physicians, lawyers, bankers or those with executive governmental or private company positions were classified into category 2, while parents who did not have jobs listed under category 2 but earned enough money to send their child to the school were put into category 1.

The nutritional status

Nutritional status was determined by measuring body mass index (BMI) with reference to age- and sex specific parameters provided by the Centre for Disease Control and Prevention (CDC) growth reference standards [375]. The percentage of BMI was defined as the ratio of BMI observed in a child to the BMI median of the reference data for the same age and sex. Children were classified as severely malnourished if the BMI was $<$ 70% of the reference median (<-3 Z-score), moderately malnourished if the BMI was between 70%-80% of the reference median (-3 to -2 Z-score), mildly malnourished if the BMI was between 80%-90% of the reference median (-2 to -1 Z-score), normally nourished if the BMI was between 90% -120% of the reference median (-1 to $+2$ Z-score) and over nourished if the BMI was $>$ 120% of the reference median ($>$ $+2$ Z-score). When dichotomized data were needed, the cut off point of 90% of reference median (-1 Z-score) was used to categorize children into low- and normal-nutritional status.

Parasitological examination

Stool samples were collected using 5x5x5 pots. The children were instructed to fill the pot carefully using wooden spatula without water or urine contamination. The time of stool passed had to be recorded and the stool had to be stored in a cool area if it stayed overnight in the house before delivery to school. Only stools that arrived in the lab not more than 12 hours after passage were examined. The eggs from intestinal helminth such as *Ascaris lumbricoides*, *Trichuris trichuria* and hookworm were quantified using the Kato Katz methods [376]. To study the effect of helminth infections on asthma, SPT and specific-IgE, children was considered positive for helminth infections, if their stool was positive for one or more of *Ascaris*, *Trichuris* or hookworm eggs.

Skin prick test (SPT)

SPT was performed if children were free from anti-histamine, anti asthmatic or corticosteroid drugs for at least 7 days. SPT reactivity for aeroallergens was tested with extracts of *Dermatophagoides pteronyssinus*, *Dactylis glomerata* grass pollen, and *Blatella germanica* preparation (HAL Allergen Laboratories, the Netherlands). Histamine chloride (10mg/ml) was used as the positive control and allergen diluents as the negative control (HAL Allergen Laboratories, The Netherlands). SPT was done on the volar side of the child's lower arm, using separate skin prick lancets. The results for each child were measured after 15 minutes. Skin prick reactivity was determined to be positive if the longest diameter plus the diameter perpendicular of wheal size divided by two was at least 3 mm [362]. SPT was considered to be positive if there was a positive reaction to either mite or cockroach. The same investigator performed the SPT for all children in the study.

Allergen specific-IgE

Serum level of mite- and cockroach-IgE was determined by radio allergosorbent test (RAST) as described previously [363]. Briefly, 50 μ l serum was incubated overnight with 1.5 mg of Sepharose-coupled allergen in a final volume of 300 μ l PBS, 3% BSA, 0.1% Tween-20. After washing away non-bound serum components, radiolabelled sheep antibodies (Sanquin, Amsterdam, Netherlands) directed to human IgE, were added. After overnight incubation and washing, bound radioactivity was measured. The outcomes were expressed as % binding. To convert these values into IU/ml, the results were plotted to a non-linear regression curve of chimaeric monoclonal IgE antibody dilution series against the major house-dust-mite allergen, *Der p 2*, and Sepharose-coupled mite extracts [304]. The cut off of the assay was 0.3 IU/ml and subjects were considered to have high levels of specific-IgE when the value was more than 1.0 IU/ml. To study the effect of multiple variables on specific-IgE outcome, specific IgE was determined to be positive if the level of specific-IgE was >1 IU/ml in response to mite, cockroach or both.

Statistical analysis

Standard statistical analyses were performed in SPSS for windows version 10. The prevalence of clinical allergy, SPT and specific-IgE between low- and high-SES schools was compared using Pearson *chi-square*. Statistic agreement between parent-answered questionnaire and HW confirmed diagnosis was estimated using the kappa statistic. Kappa value of 1 indicates perfect agreement, whereas kappa value of 0 indicates there is no agreement. Binary logistic regression adjusted with sex, age and interaction of sex and age was used to study the association between clinical allergy and SPT as well as specific-IgE to mite and cockroach. Odds ratios (OR) > 1 indicate a positive association of variable and the outcome, whereas an OR < 1 indicates a negative association. Outcomes of statistical tests were considered significant when two tailed p-values were smaller than 0.05.

Results

Comparison of children from low and high SES schools

As shown in table 1, the proportion of parents with elementary education was higher in low- compared to high-SES, whereas those with secondary and tertiary education were more often found in the high-SES school. In the high SES school the families were smaller. There were no differences in dog or cat ownership between the families in the two schools whereas presence of a smoker in the house was more often reported in the families from low-SES school. Using BMI to estimate nutritional status, there was a significant difference

	Low- SES school (n=262)	High-SES school (n=330)	p
Allergy/atopy			
Asthma (%)	6.1	7	0.67
SPT positivity (%)	5.7	16.4	<0.01
Specific-IgE >1 IU (%)*	24.6	20.7	0.29
Mite-IgE (IU/ml) (GM and IQR)*	0.35(0.15-0.64)	0.45(0.15-0.81)	0.19~
Cockroach-IgE (IU/ml) (GM and IQR)*	0.37(0.15-0.55)	0.20(0.15-0.22)	<0.01~
Parent educational back ground (%)			
Elementary	76.3	6.4	<0.01~
Secondary	21.8	43.3	<0.01
Tertiary	1.9	50.3	<0.01
Number of siblings (%)			
0	5.7	3.9	<0.01~
1	12.6	19.7	<0.01
2	16.8	37.9	<0.01
>=3	65.1	38.5	<0.01
Animal in the house (%)	14.9	16.1	0.69
Smoker in the house (%)	71.4	51.8	<0.01
Nutritional status (%)			
Severe malnourished	3.1	0.3	<0.01~
Moderate malnourished	5.7	2.7	<0.01
Mild malnourished	32.1	21.2	<0.01
Normal nourished	55.3	62.4	<0.01
Over nourished	3.8	13.3	<0.01
Intestinal helminth infection			
<i>Ascaris lumbricoides</i> (%)	77.9	6.1	<0.01
<i>Trichuris trichuria</i> (%)	88.5	19.7	<0.01
Hookworm (%)	3.1	0.3	<0.01
Any helminth infection (%)	92	23	<0.01
<i>Ascaris</i> epg (GM and IQR)#	8990(3072-28416)	715(282-1314)	<0.01~
<i>Trichuris</i> epg (GM and IQR)#	2085(792-5748)	204(102-330)	<0.01~

Table 1. Description of children in low- and high-SES schools. The difference of prevalences were tested using Pearson *chi-square* and Mann-Whitney test for continuous variables.

*available sera

~continuous variable

#infected children

between the two schools. Proportion of children categorised as malnourished (severe, moderate, mild) was higher in the low-SES school compared to children from high-SES. Regarding infections, the prevalence and the intensity of helminth infections (*Ascaris*, *Trichuris*, hookworm) was significantly higher in low- compared to high-SES school.

The differences in asthma, SPT positivity and specific IgE are also shown in table 1. The prevalence of SPT positivity was significantly higher in high-SES school while no difference was seen in the prevalence of asthma. The level of mite-IgE was not different in the two schools, but significantly higher levels of cockroach-IgE were measured in low- compared to high-SES school

Association of environmental factors, nutritional status and helminth infections with allergic disorders

As shown in table 2, further categorization of socioeconomic status in low-SES school indicated no influence of the two categories on asthma, SPT positivity or specific IgE positivity. In high-SES school, we found that those who scored lower in socioeconomic status, had about 50% lower risk of being SPT positive or having a high specific-IgE to aeroallergens (table 3). Although the parental educational status did not show any association with allergic disorders recorded in the two schools, it was noted that in the high-SES school, none child from families with low educational background had asthma. The family size (number of siblings) did not have any influence on allergic outcomes measured in either school. As shown in table 2, there was no association between the presence of animals in the house and asthma/SPT positivity/specific-IgE in low-SES school but in high-SES school a significant negative association between the presence of animal in the house to SPT positivity (table 3) was found. Although presence of a smoker in the house did not seem to affect allergy in children from low-SES school (table 2), we were surprised to note that children from high-SES school tended to have negative SPT when there was a smoker in the house (table 3).

As shown in table 2 and 3, in both low- and high-SES schools, children with lower nutritional status (BMI < 90% of the reference value) tended to have negative SPT to aeroallergens. In the high-SES school lower nutritional status was associated with a significantly lower risk of mounting high IgE responses to aeroallergens. When multivariate analysis was used with socioeconomic status and nutritional status as variables in the models, the significant association for both variables and allergic outcomes remind significant indicating independent effect (result was not shown)

Infection with helminths (either one or more of *Ascaris*, *Trichuris* and hookworm infections) has no significant effects on any of the allergic parameters measured in the low-SES school (table 2). However, children who were no infected with helminths tended to have more asthma (table 3).

	Asthma			Skin prick test			Specific IgE					
	Pos	Neg	OR (95% CI)	p	Pos	Neg	OR (95% CI)	p	Pos	Neg	OR (95% CI)	p
Socioeconomic												
category 1	7	100	1.15(0.41-3.22)	0.79	6	101	1.02(0.35-2.98)	0.98	26	70	1.14(0.62-2.09)	0.67
category 2	9	146			9	146			33	105		
Parent formal education												
low	13	187	1.38(0.38-5.03)	0.62	12	188	1.27(0.34-4.70)	0.72	43	135	0.81(0.41-1.60)	0.55
high	3	59			3	59			16	40		
Number of siblings												
>=3	12	202	0.38(0.08-1.91)	0.24	11	203	0.36(0.07-1.85)	0.22	48	143	0.81(0.23-2.80)	0.74
0	2	13			2	13			4	9		
Animals in the house												
positive	3	36	1.29(0.34-4.80)	0.70	1	38	0.34(0.04-2.27)	0.31	8	27	0.93(0.39-2.11)	0.86
negative	13	210			14	209			51	148		
Smoker(s) in the house												
positive	10	177	0.61(0.21-1.79)	0.37	10	177	0.76(0.25-2.38)	0.64	39	127	0.72(0.37-1.37)	0.32
negative	6	69			5	70			20	48		
Nutritional status												
% of median < 90	8	99	1.45(0.52-4.06)	0.49	3	104	0.31(0.08-1.16)	0.07#	19	74	0.70(0.37-1.32)	0.27
% of median >= 90	8	147			12	143			40	101		
Helminth infection												
positive	15	226	1.33(0.16-10.69)	0.79	14	227	1.25(0.15-10.21)	0.84	55	160	1.50(0.47-4.82)	0.49
negative	1	20			1	20			4	15		

Table 2. The effect of multiple variables on asthma, SPT positivity and specific-IgE positivity in low-SES schoolchildren. Odds ratio and 95% confidence intervals are given.

* Statistically significant $p < 0.05$

Trend for statistical significance $p = 0.05-0.10$

	Asthma			Skin prick test			Specific IgE					
	Pos	Neg	OR (95% CI)	P	Pos	Neg	OR (95% CI)	P	Pos	Neg	OR (95% CI)	P
Socioeconomic												
category 1	12	212	0.53(0.22-1.25)	0.15	29	191	0.46(0.26-0.84)	0.01*	32	147	0.53(0.28-0.99)	0.05*
category 2	11	95			25	81			24	63		
Parent formal education												
low	0	21		0.75	1	20	0.26(0.03-2.01)	0.20	4	13	1.22(0.38-3.96)	0.73
high	23	286			53	256			52	197		
Number of siblings												
>=3	17	235	0.41(0.08-2.09)	0.29	42	210	2.34(0.29-18.64)	0.42	47	158	2.7(0.33-22.27)	0.35
0	2	11			1	12			1	9		
Animals in the house												
positive	1	52	0.23(0.03-1.74)	0.15	4	49	0.35(0.12-1.02)	0.05*	5	35	0.48(0.18-1.30)	0.15
negative	22	255			50	227			51	175		
Smoker(s) in the house												
positive	14	157	1.48(0.62-3.58)	0.39	22	149	0.57(0.32-1.04)	0.07#	28	106	0.94(0.52-1.71)	0.85
negative	9	150			31	127			28	104		
Nutritional status												
% of median < 90	8	72	1.59(0.63-3.97)	0.32	8	72	0.49(0.22-1.11)	0.09#	7	60	0.35(0.15-0.81)	0.01*
% of median >= 90	15	235			46	204			49	150		
Helminth infection												
positive	2	74	0.28(0.06-1.24)	0.09#	8	68	0.53(0.24-1.18)	0.12	14	48	1.12(0.56-2.24)	0.74
negative	21	233			46	208			42	162		

Table 3. The effect of multiple variables on asthma, SPT positivity and specific-IgE positivity in high-SES schoolchildren. Odds ratio and 95% confidence intervals are given.

* Statistically significant $p < 0.05$

Trend for statistical significance $p = 0.05-0.10$

Discussion

This study investigated children aged 7-13 years attending two elementary schools in Makassar, one where children from low-SES families and another where children from high-SES families attended. The schools differed in socioeconomic status of the families whose children were enrolled at the schools. The prevalence of asthma in this urban area was found to be 6.1% in the low-SES and 7% in the high-SES school, slightly higher than the prevalence of asthma measured by ISAAC and reported in 1998 which was 5% in Bandung, Indonesia [214].

ISAAC studies have indicated that SES may influence prevalence of allergic disorders in the world whereby countries with the lowest quartile of gross national product (GNP) per capita have the lowest positive responses to all the questions on symptoms of asthma, rhinitis and eczema [365]. However, several studies that been carried out in developed countries reported asthma to be more prevalent in low-SES children [377-379]. In the current study we did not find a significant difference between the prevalence of asthma in children from low- or high-SES schools, but we did find a significant difference in the SPT positivity to aeroallergens which was higher in children from high-SES. Within the high-SES school, there was also a significant difference in SPT positivity and IgE positivity when socioeconomic status was subdivided into lower and higher categories, with the ones with higher socioeconomic status (category) being more often positive. The fact that we did not find a difference in asthma prevalence as a function of SES, raises the question whether diagnosis of asthma is reliable via the questionnaire that we used. This issue has been discussed extensively in a paper earlier (Wahyuni *et al*, submitted). No association between asthma and SES was also reported from New Zealand [380] and Spain [381] while another study reported fewer asthma cases in those who had higher education and those who owned cars [382]. However, effect of SES on SPT positivity seen here, is in agreement with data from Italy [383], England [384] and Chili [382]. Interestingly, when specific IgE was considered, no significant differences were found between the two schools. From this result one may assume that children from low- and high-SES in this urban area were exposed and responded similarly to aeroallergens. However, it is clear that unlike studies in western/developed countries, IgE positivity does not always, in a linear fashion, lead to SPT positivity. In developed countries such as the Netherlands, having high IgE to aeroallergens is a strong risk factor for SPT positivity (OR=39) (van der zee, unpublished). Here in high-SES school with low intensity of helminths we found having positive IgE to allergens had a strong predictive value for having SPT (OR=29). In children with no helminth infection, the OR was even higher (OR=34). In the low-SES school, IgE to allergens had no predictive value for SPT positivity. It is possible that the higher prevalence of helminth infections in the low SES school, leads to detection of allergen specific IgE that is of low affinity which is not capable of leading to mast cell degranulation [271].

Nutrition has been known to play an important role in regulating immune responses. A study carried out in young children reported that undernourished individuals had

abnormalities in their cell-mediated immunity, complement system, phagocytes, mucosal secretory antibody response, and antibody affinity [385]. Another study showed that immune reactions to incoming pathogens was also lower in malnourished individuals [386]. Although we have no data on detailed nutritional status, we used BMI to categorize children into different nutritional states. The low-SES school had higher proportion of children with malnutrition compared to high-SES school, and SPT positivity was also significantly lower in low-SES school. When we analysed the effect of nutritional status in the two schools separately, only in the high-SES school we found a significant negative association between nutritional status and SPT or IgE positivity while in the low SES school, although there was a trend, this did not reach statistical significance, possibly due to smaller number of SPT positives. With respect to asthma, no association was found between asthma and nutritional status in either school. Whether this is because asthma is more related to obesity than malnutrition as shown in a number of cross-sectional studies (reviewed in [387]) or as already mentioned before on diagnosis of asthma via questionnaire is not optimal, is not clear.

Number of siblings, first reported by Strachan [211] to influence risk of developing hay fever, has been assumed to be an indicator of exposure to infections during early childhood. Although several studies have reported no association between number of siblings and asthma/wheezing [388-390], a large number of studies carried out in developed countries have found a negative association between number of siblings and allergic disorders (reviewed in [391]. Here in an urban area of a developing country, we found no association between larger family size (siblings ≥ 3) and any of the allergic outcomes measured. These results suggest that the size of the family (no siblings versus sibling ≥ 3), as a possible estimate of microbial exposure, does not associate with allergic disorders in developing countries where microbial exposure is high.

The inhalation of environmental tobacco smoke or passive smoking has been found to be associated with asthma in children [392;393]. In our data, we found no association between asthma and the presence of a smoker in the house. Furthermore, in high-SES school there was a tendency to be SPT positive when the child had no exposure to tobacco smoke in the house. To make sure this is not a finding by chance, more studies are needed. The result so far have been variable with respect to the association between exposure to tobacco and SPT positivity; one study reported a significant higher prevalence of aeroallergen sensitization among children who were regularly exposed to tobacco at home (OR= 2.9, 95% CI 1.1 to 7.7)[394] whereas others studies showed no correlation between allergen sensitization and exposure to tobacco at home [395] as in utero [396].

The influence of the presence of animals in the house on allergic outcomes is controversial. Some studies found that exposure to animals appears to protect against asthma [397-401] and reduce sensitization to allergens [397], while others reported no association [402]. Here we found no effect in low-SES school, while in high-SES school SPT positivity

was less frequent in children with animals in the house. One possible explanation for the difference in the two schools is that the presence of animal in the house may mean different things in the two schools. The presence of animal in the house does not necessarily mean close contact with the animal, particularly in low-SES families.

Geohelminths have been reported to be negatively associated with wheeze in Ethiopia [170;251] and with atopy in Venezuela [403], Ecuador [250;259] and the Gambia [249]. Other helminth infections, such as *Schistosoma haematobium* [241] and *Schistosoma mansoni* have been shown to protect from SPT positivity as well as severe asthma [242;243]. Here in high-SES school, a trend for negative association was found between asthma and presence of helminth infection (OR=0.28, p=0.09). This negative trend was not seen in the low-SES school. But it is worth noticing that, in the area where the low-SES school is situated, high prevalence of respiratory infections has been reported by the health authority, (unpublished data from Indonesian local health authority) which may affect the data on reported wheezing.

When we considered helminth infections, in the school where these infections were more prevalent and worm burdens were higher, the prevalence of SPT positivity was significantly lower. However, we found no association between helminth infections and SPT positivity when schools analyzed separately. This is in contrast to other studies with geohelminths [249;250;259]. It might have been difficult to detect any helminth effect in the low-SES school as the transmission intensity is expected to be high and therefore the helminth negative subjects when examined repeatedly may turn out to be infected. In the high-SES school, the prevalence of SPT positivity in helminth infected subjects was lower (10%) than in helminth negative children (18%), but this difference did not reach statistical significance, indicating that other factors than helminths may play an important role in inhibiting skin prick test positivity.

Conclusions

There were large differences between children from low- and high-SES schools with respect to factors that influence allergic outcomes. Although, SPT positivity was significantly lower in the high SES school, the prevalence of asthma was similar in the two schools. Thus either SPT positivity is not a good predictor for development of asthma, or in low-SES schools, children suffer from non allergic asthma. It is also possible that the diagnosis of asthma, via questionnaires, particularly in low-SES schools, is not accurate. Further ranking of socioeconomic status within the high-SES school, indicated that there is protection from SPT and IgE positivity in the relatively lower socioeconomic groups. The findings with nutritional status indicated that in particular in the high-SES schools, lower nutritional status was associated with protection from SPT and IgE positivity, this effect was independent from socioeconomic status (multivariate analysis not shown). Helminth infections, often associated with low nutritional status and low socioeconomic status, had no significant effects on allergic outcomes.