

Allergic Symptoms, Atopy, and Geohelminth Infections in a Rural Area of Ecuador

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Geohelminth infections may affect the expression of allergic disease. To investigate the relationship between geohelminth infections, atopy, and symptoms of allergic disease, we studied 4,433 schoolchildren from 71 schools in a rural tropical area in Ecuador. Information was collected on allergic symptoms, allergen skin test reactivity, and presence of geohelminth infections. Allergic symptoms were of low prevalence (2.1% had recent wheeze), but prevalence of skin test reactivity was relatively high (18.2%). The presence of geohelminth infections was protective against allergen skin test reactivity (odds ratio 0.62, 95% confidence interval 0.50–0.76, $p < 0.001$) and symptoms of exercise-induced wheeze (odds ratio 0.59, 95% confidence interval 0.40–0.87, $p = 0.008$) but not against other wheeze symptoms or symptoms of allergic rhinitis or atopic eczema. Infection intensity with *Ascaris lumbricoides* or *Trichuris trichiura* was associated with a reduction in the prevalence of allergen skin test reactivity but not with allergic symptoms. There was no evidence of interactions between geohelminth infection and allergen skin test reactivity on the risks of allergic symptoms. The results suggest that geohelminth infections do not explain the low prevalence of allergic symptoms in the study population.

Keywords: allergy; atopy; geohelminths; schoolchildren

The International Study of Asthma and Allergy in Childhood (ISAAC) has revealed large differences in the prevalence of self-reported symptoms of allergic disease among different countries (1). Environmental factors may influence the expression of clinically apparent inflammation of the lungs associated with allergic sensitization, and there has been increased interest as to the potential role of infectious diseases in determining the expression of allergic disease (2).

Several infectious diseases including measles and hepatitis A have been associated with protection from atopy (2), and there is evidence also that early exposure to childhood infectious disease may protect against the development of asthma (3). Intestinal helminth (or geohelminth) infections are among the most prevalent infections of children in many regions worldwide, and greater than 1 billion humans are infected with at least one geohelminth parasite (4). *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworm are the most prevalent geohelminth infections. Inverse associations have been reported between geohelminth infections and both atopy (5–7) and symptoms of wheeze (8–10).

Evidence of allergic sensitization to common environmental aeroallergens is a consistently strong risk factor for allergic

disease in epidemiologic studies conducted in industrialized countries (11, 12). Studies conducted in the less-developed regions of the world have shown that atopy is either a weak risk factor for allergic disease or not a risk factor at all (6, 13–17). The dissociation between allergic sensitization and the expression of clinically apparent allergic disease may be modulated by parasite infection (10). Chronic exposure to geohelminth parasites, particularly those that have a pulmonary phase of larval migration (e.g., *A. lumbricoides* and hookworm), may have antiinflammatory effects and suppress allergic inflammation in the airways (10).

To investigate the risks of symptoms of allergic disease associated with geohelminth infections and atopy (by measurement of allergen skin test reactivity) and to explore the relationship between atopy and geohelminth infection on the risk of allergic disease symptoms, we conducted an analytic cross-sectional study among school-age children attending rural schools in a tropical region of Ecuador.

METHODS

Study Area

The study area covered schools in adjacent districts in the provinces of Pichincha and Esmeraldas. The area is subtropical/tropical rain forest at altitudes of 50 to 1,000 m above sea level. Economic activities in the area are centered largely on agriculture and cattle. The study area consists of small (15–100 houses) and homogeneous (in terms of economic means, lifestyle, and living conditions) communities interconnected by dirt roads. General features of housing are wood or breeze-block walls, corrugated iron roofs, and uncovered wooden or cement floors. Cooking is with propane or wood. All children attending the schools were eligible to participate. Informed verbal consent was obtained from the parent or guardian of all children. The study was approved by the ethical committees of the National Institutes of Allergy and Infectious Diseases, National Institutes of Health, United States; St George's Hospital Medical School, London, United Kingdom; and the foundation Salud y Desarrollo Andino (SALUDESA), Quito, Ecuador.

Questionnaire

A questionnaire that included the core allergy symptom questions of the ISAAC Phase I studies (1) was administered to the parent or guardian in the presence of the child. Stool samples were collected, and skin prick test reactivity to aeroallergens was performed. Fresh stools were examined by the modified Kato–Katz method as described (18): one slide per person was read, the numbers of helminth eggs were counted, and the number of helminth eggs per gram of feces calculated. Skin prick testing was performed to *Dermatophagoides pteronyssinus* (ALK, Horsholm, Denmark), *Dermatophagoides farinae* (ALK), *Alternaria tenuis* (Greer Laboratories, Lenoir, NC), cockroach (Greer), cat fur (Greer), grass pollen (Greer), and tree pollen (Greer). Allergens were scratched onto the volar side of the forearm using ALK plastic bifurcated lancets, and reaction sizes were recorded after 15 minutes by measurement of the perpendicular diameters of the wheal at each scratch site. Reactions were considered positive if the size (mean of the two perpendicular readings) was at least 3 mm greater than the saline control.

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Statistical Analyses

For statistical analyses, atopy was defined as a positive reaction to any of the aeroallergens tested. Geohelminth infection was defined by the presence of eggs of any of *A. lumbricoides*, *T. trichiura*, or *Ancylostoma duodenale* in stool samples. CIs for prevalences and logistic regressions were computed allowing for clustering by school using robust SEs. All logistic regression analyses were adjusted for age and sex. Interactions between presence of helminths and atopy were tested by adding an interaction term to the logistic model. Analyses were done with Stata 5.0 using the survey and cluster functions. Statistical significance is inferred by *p* value less than 0.05.

RESULTS

Subject Characteristics

A total of 4,433 children were sampled from 71 schools. Response rates to the questionnaire were high: questionnaires were completed on 96.3% of the total eligible population of 4,601; stools were collected from 87.7%; and allergen skin testing was performed on 88.3%. The mean age was 10.4 years (range 5–18 years). The prevalence of geohelminth infections was high, with 63.4% having evidence of infection with at least one of the three geohelminth parasites detected (Table 1). Prevalence of *A. lumbricoides* (49.7%) and *T. trichiura* (43.8%) were high, and the prevalence of *A. duodenale* (2.3%) was low. The geometric mean infection intensities among those infected with *A. lumbricoides* and *T. trichiura* were 6,674 eggs per gram of stool (range 70–327,250) and 355 eggs per gram (range 70–101,640), respectively. The sensitivity of the egg detection method was 70 eggs per gram. No other geohelminth eggs or larvae were detected. The prevalence of skin test reactivity to any allergen was 18.2% (Table 1), and the most commonly recognized allergens were house dust mite (9.3%) and cockroach (9.4%). There was little evidence of reactivity to the remaining four allergens. The results of the questionnaire indicate a low prevalence of allergic symptoms in this population of school-age children (Table 1). The prevalence of recent (within the previous 12 months) symptoms of allergy was: wheeze (2.1%), rhinitis (4.1%), and eczema (3.7%). A more specific question for rhinitis (with itchy eyes) indicated a recent prevalence of 2.7%. Severe forms of wheeze were uncommon in the study group ($\geq$ four attacks in the previous year, 1.0% [43/4433]).

Geohelminths and Atopy

A previous smaller study conducted in the same study area showed a strong protective effect of geohelminth infection against atopy and greater protective effects against atopy of higher parasite burdens with ascariasis and trichuriasis (7). In this larger study group, the presence of any geohelminth infection was strongly protective against atopy (or skin test reactivity), odds ratio (OR) = 0.62 (95% confidence interval [CI] 0.50–0.76, $p < 0.001$) also. The magnitude of the ORs for the protective effects against atopy for individual geohelminth parasites were similar (*A. lumbricoides* [OR = 0.65, 95% CI 0.54–0.78, $p < 0.001$], *T. trichiura* [OR = 0.69 95% CI 0.56–0.86, $p = 0.001$], and *A. duodenale* [OR = 0.67, 95% CI 0.33–1.37, $p = 0.3$]). Similarly, there was evidence for a reduction in prevalence of skin test reactivity with increasing egg burden for *T. trichiura* (OR for a change from the first quartile to the third quartile of egg load, i.e., over the interquartile range, of 0.67 [95% CI 0.53–0.84, $p = 0.001$]) and *A. lumbricoides* (OR = 0.82 (95% CI 0.66–1.01, $p = 0.06$)).

There was no evidence that the magnitude of the effect on allergen skin test reactivity differed between the three parasites. This was found by comparing each pair of parasites separately. Logistic regression of skin test reactivity was performed for

TABLE 1. AGE-SEX DISTRIBUTION, SYMPTOMS OF ALLERGIC DISEASE, ALLERGEN SKIN TEST REACTIVITY, AND GEOHELMINTH INFECTIONS IN THE STUDY POPULATION

Factor	Number/Total	Percentage	95% CI
Sex			
Male	2,148/4,433	48.5	
Female	2,285/4,433	51.5	
Age, yr			
5–9	1,685/4,433	38.0	
10–14	2,592/4,433	58.5	
15–18	154/4,433	3.5	
Symptoms			
Asthma			
Asthma ever	457/4,431	10.3	8.8–11.9
Wheeze in past year	94/4,433	2.1	1.4–2.9
1–3 attacks	49/4,433	1.1	0.7–1.5
4–12 attacks	39/4,433	0.9	0.5–1.3
≥ 12 attacks	4/4,433	0.1	*
Woken by wheeze in past year	47/4,433	1.1	0.6–1.5
Wheeze limiting speech in past year	20/4,433	0.5	0.1–0.8
Wheeze during or after exercise in past year	93/4,431	2.1	1.5–2.7
Rhinitis			
Rhinitis ever	197/4,429	4.4	2.7–6.2
Rhinitis in past year without colds	182/4,433	4.1	2.5–5.7
Rhinitis in past year with itchy eyes	121/4,443	2.7	1.7–3.7
Eczema			
Eczema ever	188/4,429	4.2	3.0–5.5
Itchy rash affecting flexures in past year	163/4,433	3.7	2.5–4.8
Persistent itchy rash throughout past year	32/4,433	0.7	0.4–1.0
Woken at night by itchy rash in past year	28/4,433	0.6	0.3–1.0
Skin prick reaction ≥ 3 mm			
Any allergen	741/4,064	18.2	16.2–20.2
House dust mite†	377/4,064	9.3	8.0–10.6
Cat fur	31/4,064	0.8	0.5–1.1
Alternaria	21/4,064	0.5	0.3–0.8
Cockroach	380/4,064	9.4	7.9–10.8
Mixed grass pollen	82/4,064	2.0	1.4–2.6
Mixed tree pollen	65/4,064	1.6	1.2–2.0
Geohelminth infections			
Any geohelminth‡	2,558/4,035	63.4	7.4–69.4
Ascaris lumbricoides	2,006/4,035	49.7	3.7–55.8
Trichuris trichiura	1,768/4,035	43.8	7.9–49.7
Ancylostoma duodenale	91/4,035	2.3	1.1–3.4

Definition of abbreviation: CI = confidence interval.

95% CIs are adjusted for clustering.

* Cannot be estimated due to small numbers.

† Dermatophagoides pteronyssinus and Dermatophagoides farinae combined.

‡ Presence of eggs of any of *A. lumbricoides*, *T. trichiura*, and *A. duodenale*. No eggs or larvae of other geohelminth parasites were detected.

children who had only one of the parasites (i.e., were disparate in their infection for the two parasites). The explanatory variable was set to 1 for the first parasite and 0 for the second. If this variable had a significant effect on skin test reactivity, the magnitude of the effects of the two parasites would be significantly different. None of the pairs of parasites differed significantly (*A. lumbricoides* vs. *T. trichiura*, $p = 0.6$; *A. lumbricoides* vs. *A. duodenale*, $p = 0.9$; *T. trichiura* vs. *A. duodenale*, $p = 0.7$).

Geohelminths and Allergic Symptoms

The presence of infection with geohelminths was associated with a lower prevalence of symptoms of allergy. The relationship between the presence of geohelminths and the risk of selected

allergic symptoms is shown in Table 2. Very few of these relationships were statistically significant. Only for exercise-induced wheeze was there strong evidence of a protective effect of infections with any geohelminth or *T. trichiura*. If we test the composite null hypothesis that allergic symptoms are unrelated to geohelminth infection, we should multiply the five p values for any geohelminth by 5, giving for exercise-induced wheeze $p = 0.04$, which remains statistically significant.

Within infected children, the effect of parasite burden on allergic symptoms was estimated by logistic regression on log_e-transformed infection intensity; there was no evidence for a reduction in prevalence of any of the allergic symptoms with increasing infection intensity with either *A. lumbricoides* or *T. trichiura*.

Atopy and Allergic Symptoms

Atopy (or skin prick test reactivity) was associated with an increased risk of all allergic symptoms (recent wheeze, exercise-induced wheeze, rhinitis with itchy eyes, and itchy rash) (Table 3). An increased risk of recent wheeze was significantly associated with skin test sensitivity to house dust mite, grass pollen, and tree pollen. The only significant association with exercise-induced wheeze was house dust mite. Rhinitis with itchy eyes was associated with house dust mite and tree pollen sensitivity. Itchy rash was significantly associated with cat fur (OR 2.69, 95% CI 1.08–6.68, $p = 0.03$).

Geohelminths, Atopy, and Allergic Symptoms

Analysis of the data from this population of school-age children indicates that geohelminth infections are associated with reduced risk of allergic symptoms, whereas allergen skin test reactivity is associated with an increased risk of allergic symptoms, although the effects were small and statistically nonsignificant for most symptoms. Allergen skin test reactivity and geohelminth infection are quite strongly inversely associated, and the effect of one on symptom prevalence may be the result of the other. Data for geohelminth infection status and allergen skin test reactivity were available for 3,681 of the children. The effect of mutual adjustment for these two exposures is shown in Table 4. The effect of skin test reactivity remained significant for all symptoms except exercise-induced wheeze. After adjustment, the OR for skin test reactivity and itchy rash became statistically significant. The OR were changed little by adjustment for geohelminth infection. Adjustment for skin test reactivity had little

TABLE 2. RELATIONSHIP BETWEEN RECENT ALLERGIC SYMPTOMS AND INFECTIONS WITH GEOHELMINTH PARASITES

Symptom	Parasite	OR*	95% CI	p Value
Wheeze	Any geohelminth	0.78	0.49–1.26	0.3
	<i>A. lumbricoides</i>	0.88	0.58–1.34	0.5
	<i>Trichuris trichiura</i>	1.06	0.70–1.61	0.8
≥4 Attacks	Any geohelminth	0.70	0.32–1.50	0.4
	<i>Ascaris lumbricoides</i>	0.72	0.37–1.42	0.3
	<i>Trichuris trichiura</i>	0.92	0.44–1.93	0.8
Exercise-induced wheeze	Any geohelminth	0.59	0.40–0.87	0.008
	<i>Ascaris lumbricoides</i>	0.69	0.44–1.09	0.1
	<i>Trichuris trichiura</i>	0.60	0.39–0.90	0.02
Rhinitis with itchy eyes	Any geohelminth	0.90	0.56–1.44	0.7
	<i>Ascaris lumbricoides</i>	1.00	0.55–1.79	0.99
	<i>Trichuris trichiura</i>	1.04	0.59–1.85	0.9
Itchy rash affecting flexures	Any geohelminth	0.86	0.51–1.45	0.6
	<i>Ascaris lumbricoides</i>	0.93	0.62–1.40	0.7
	<i>Trichuris trichiura</i>	0.84	0.44–1.62	0.6

Definition of abbreviations: CI = confidence interval; OR = odds ratio.

* All OR are adjusted for age, sex, and clustering by school.

TABLE 3. RELATIONSHIP BETWEEN RECENT ALLERGIC SYMPTOMS* AND ALLERGEN SKIN TEST REACTIVITY

Symptom	Parasite	OR†	95% CI	p Value
Wheeze	Any allergen	2.40	1.54–3.74	<0.001
	House dust mite	2.88	1.69–4.92	<0.001
	Cockroach	1.56	0.91–2.68	0.1
	Grass pollen	2.89	1.15–7.28	0.03
	Tree pollen	6.05	2.69–13.60	<0.001
≥4 Attacks	Any allergen	2.40	1.20–4.81	0.01
	House dust mite	2.34	0.92–5.92	0.07
	Cockroach	1.85	0.79–4.33	0.2
	Grass pollen	3.82	1.10–13.29	0.04
	Tree pollen	6.16	1.70–22.34	0.006
Exercise-induced wheeze	Any allergen	1.58	1.01–2.49	0.05
	House dust mite	2.02	1.01–4.06	0.05
	Cockroach	0.98	0.51–1.86	0.9
	Grass pollen	1.72	0.68–4.35	0.2
	Tree pollen	2.24	0.71–7.01	0.2
Rhinitis with itchy eyes	Any allergen	1.71	1.17–2.52	0.006
	House dust mite	1.94	1.07–3.52	0.03
	Cockroach	1.00	0.57–1.75	0.99
	Grass pollen	0.83	0.18–3.85	0.8
	Tree pollen	3.54	2.05–6.12	<0.001
Itchy rash affecting flexures	Any allergen	1.32	0.95–1.85	0.1
	House dust mite	1.08	0.66–1.78	0.8
	Cockroach	1.19	0.75–1.94	0.5
	Grass pollen	1.25	0.54–2.88	0.6
	Tree pollen	1.18	0.36–3.91	0.8

Definition of abbreviations: CI = confidence interval; OR = odds ratio.

* Within the previous 12 months.

† All ORs are adjusted for age, sex, and clustering by school.

effect on the OR for the association of symptoms and geohelminth infection. For exercise-induced wheeze, the effect of geohelminth infection remained significant and, for this symptom, appeared to have a greater effect than did skin test reactivity (i.e., the OR for geohelminth infection is more different from 1 than the OR for atopy). The interaction between skin test reactivity and geohelminth infection was not significant for any of the symptoms in Table 4 ($p = 0.3, 0.5, 0.9, 0.3$, and 0.4 , respectively).

DISCUSSION

The study findings demonstrate, in a population of school-age children living in a rural area of the tropics where the prevalence of allergic disease is low, that geohelminth infections are strongly

TABLE 4. EFFECTS OF MUTUAL ADJUSTMENT OF ANY GEOHELMINTH INFECTION AND ALLERGEN SKIN TEST REACTIVITY ON THE RISKS OF ALLERGIC SYMPTOMS*

Symptom	Atopy (Adjusted for Geohelminths)			Geohelminths (Adjusted for Atopy)		
	OR [†]	95% CI	p Value	OR [†]	95% CI	p Value
Wheeze						
Any	2.20	1.27–3.80	0.005	0.82	0.51–1.32	0.4
≥4 Attacks	2.31	1.00–5.33	0.05	0.77	0.36–1.65	0.5
Exercise-induced wheeze	1.26	0.72–2.20	0.4	0.59	0.40–0.88	0.01
Rhinitis with itchy eyes	1.74	1.17–2.58	0.006	0.96	0.58–1.57	0.9
Itchy rash affecting flexures	1.47	1.05–2.06	0.02	0.85	0.50–1.46	0.6

Definition of abbreviations: CI = confidence interval; OR = odds ratio.

* Within the previous 12 months.

† All ORs are adjusted for age, sex, and clustering by school.

protective against allergen skin test reactivity but not strongly protective against allergic symptoms except for exercise-induced wheeze.

The major limitations of this study were the cross-sectional design and the use of questionnaires to obtain information on allergic symptoms. The cross-sectional design does not allow us to identify the temporal sequence between the geohelminth infection, atopy, and allergic symptoms. The determination of allergic symptoms using questionnaires makes the study open to misclassification errors, particularly with respect to symptoms of rhinitis and allergic eczema. Misclassification is less likely to be a significant problem for asthma symptoms: previous studies have validated the ISSAC core questions (1) against objective measures of bronchial hyperreactivity and have shown approximately 90% accuracy in diagnosis (19). Atopy (measured by skin test reactivity) and geohelminth prevalence and intensity (measured using standard parasitologic protocols) were both objectively measured. We were not able to control for a number of factors that may have confounded the relationship between geohelminth infections, atopy, and allergic symptoms. Such factors might include overcrowding, other infectious agents including enteric infections, and diet. Data on socioeconomic level were not collected in this study. Because geohelminth infection could be argued to be an intermediate factor in the causal pathway between socioeconomic level and atopy/allergy, it may not be appropriate to adjust for confounding by socioeconomic level in analyses of the association between geohelminth infection and atopy/allergy.

The low prevalence of symptoms of allergic disease in this rural population is comparable with the lowest prevalences of self-reported symptoms among children from the 155 centers in 56 countries that participated in the ISAAC studies (1). Phase I of ISAAC found large variations in the prevalence of asthma ranging from 2.1 to 32.2%, with high prevalences from English-speaking countries and Latin America (1). The prevalence of recent (within the past year) allergic symptoms was low even compared with those reported using parental questionnaires from the low-allergy prevalence country Albania (15). For example, 2.1% of children had symptoms of recent wheeze compared with 4.9% in Albania. The findings also show that rates of allergic sensitization outside the urban centers of Latin America, which had among the highest rates of allergic symptoms of all the ISAAC study centers (1), are as low as those reported from rural regions of Africa (6, 13).

In this study, the only allergic symptom for which a protective effect of geohelminth infection was observed was exercise-induced wheeze. Protection against exercise-induced wheeze was associated with infections with both *T. trichiura* and *A. lumbricoides*. The effect of hookworm could not be assessed because no individuals with hookworm had evidence of exercise-induced wheeze. Although there was evidence of a reduced prevalence of symptoms of recent wheeze among children infected with any geohelminth or with ascariasis, the protective effects were not statistically significant in contrast to a recent nested case-control study in Ethiopia that described significant protective effects against recent wheeze (within the previous 12 months) for both hookworm and ascariasis (10). The explanation for a strong protective effect of geohelminth infection against exercise-induced wheeze and not recent wheeze symptoms is not clear but could be a consequence of insufficient power given the low prevalence of allergic symptoms in the study population.

We have demonstrated previously a protective effect of geohelminth infection against allergen skin test reactivity among school-age children in the same study area in Ecuador (7). In this larger study that included some of the schools studied previously, we were able to confirm our previous observations of

a strong protective effect of geohelminth infections against allergen skin test reactivity and greater protective effects with higher infection intensities with ascariasis and trichuriasis (7). Previous studies from other geographic regions have demonstrated protective effects for geohelminth parasites against atopy (5, 6), although some studies have showed increased rates of allergic sensitization among geohelminth-infected populations (20, 21). The differences in the effects of geohelminth infections on allergic sensitization may relate to the endemicity of geohelminth infection between different populations (22, 23). In areas of high geohelminth endemicity as in our study population, immunoregulatory mechanisms that suppress antiparasite immune responses (22) and immune responses to unrelated antigens (22, 24) including aeroallergens (25) causing suppression of allergen skin test reactivity may develop. Alternatively, geohelminth infections may be surrogate markers for another factor(s) that directly mediates protective effects against exercise-induced wheeze. Microbial products including endotoxin appear to be strongly protective against both allergic sensitization and allergic symptoms (26). The presence and intensity of infections with geohelminth parasites are likely to reflect exposure to a microbially contaminated environment and could therefore be surrogate markers for levels of environmental endotoxin.

Skin test reactivity to any allergen or specific allergens was a significant risk factor for recent wheeze, rhinitis (with itchy eyes), and atopic eczema (itchy rash affecting the flexures); however, the magnitude of the effects was relatively small and was much smaller than those reported in a study involving a comparable population of schoolchildren from the United Kingdom (e.g., OR for recent wheeze in United Kingdom 6.7 vs. Ecuador OR 2.4) that used similar methodology (15) and where a similar rate of allergen skin test reactivity was reported (United Kingdom 17.8% vs. Ecuador 18.2%). Our observations show that the risks of allergic disease associated with allergen skin test reactivity do appear to be smaller in a rural area of the tropics compared with those in an industrialized country, despite the likelihood of significant exposure to aeroallergens in both populations.

Our rates of allergen skin test reactivity appear to be higher than those reported from previous studies conducted in schoolchildren in rural Africa (11.2% in Gabon [25] and 10.9% in Kenya [16]) where the prevalence of allergic symptoms were also low. In a geohelminth-endemic area of rural Ecuador, therefore, we find relatively high ("European") levels of allergen skin test reactivity, a low prevalence of allergic symptoms, and a weak association between allergic symptoms and allergen skin test reactivity. A dissociation between atopy and allergic symptoms has been reported previously from rural Africa (13, 16). A study conducted in Ethiopia with a comparable prevalence of skin test reactivity (25%) to this study showed that the risk of recent wheeze was strongly associated with atopy in an urban (OR 9.5) but not a rural (OR 2.0) area and that the weak relationship observed in the rural area could be explained by high-intensity geohelminth infections (10). In this study, geohelminth infections (individually, combined, or by infection intensity) were strongly protective against allergen skin test reactivity but only weakly associated with allergic symptoms and did not appear to explain the dissociation between allergen skin test reactivity and allergic symptoms. Environmental factors other than geohelminth infections may explain the relatively weak association between atopy and allergy in such areas (16).

In conclusion, our data from a cross-sectional study of schoolchildren in a rural area of the tropics provide evidence for a protective role of geohelminth infections against exercise-induced wheeze but only very limited support for a protective effect against other allergic symptoms. Our findings show also that rates of allergic disease symptoms outside the urban centers

of Latin America, which had among the highest rates of allergic symptoms of all the ISAAC study centers (1), are as low as those reported from rural regions of Africa (6, 13).

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