

Risk factors for atopy among school children in a rural area of Latin America

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Summary

Background Infection with common childhood infectious diseases including geohelminth infections may provide protection against the development of atopy and allergic disease. Few studies have investigated risk factors for atopy among children living in rural areas of Latin America.

Objective To identify risk factors associated with atopy among school-age children in a rural area of Latin America.

Methods Analytic cross-sectional study of school-age children conducted in seven rural schools in Pichincha Province in Ecuador. Detailed risk factor information was obtained by questionnaire, stool samples were collected for identification of geohelminth parasites, and Mantoux testing was performed to determine tuberculin sensitization.

Results A total of 1002 children from seven rural schools were recruited. The prevalence of geohelminth infections was high (70.1% were infected with at least one geohelminth parasite) and the prevalence of allergic sensitization was high (20.0% had evidence of aeroallergen sensitization). Factors associated with significant protection against atopy in multivariate analyses were the presence of overcrowding in the child's home, low socio-economic level, and infection with geohelminth parasites, and the protective effects of the three factors were statistically independent.

Conclusion Low socio-economic level, overcrowding and geohelminth infection, are independently protective against atopy among school-age children living in a rural area of Latin America.

Keywords atopy, children, geohelminths, overcrowding, socio-economic level

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Introduction

Allergic sensitization to environmental aeroallergens or atopy is an important determinant for the development of allergic disease, and is thought to be under the control of genetic and environmental factors [1]. The large international differences in the prevalence of allergic diseases [2], and the low prevalence of allergic disease reported from rural areas of the Tropics [3, 4] has generated considerable interest in the identification of the environmental factors that influence the development of atopy in such regions.

Many recent studies have focused on the potential modulatory role of childhood infectious diseases in the development of atopy [5]. Several infectious diseases, including measles [6] and hepatitis A [7] have been associated with a reduced prevalence of atopy. There is growing evidence that helminth parasites including geohelminths may be protective against atopy [8, 9] and symptoms of asthma [10].

We have demonstrated recently that geohelminth infections are protective against atopy among school children living in a

tropical area of rural Ecuador, and that the protective effect was primarily associated with infections with ascariasis [11]. While there is considerable epidemiological information available on correlates of atopy in industrialized countries, few published studies have examined risk factors for atopy in rural areas of the Tropics, and information is even scarcer from rural areas of Latin America. To identify potential correlates of atopy in the context of communities heavily exposed to geohelminth infections, we performed an analytic cross-sectional study among school children living in a rural area of Tropical Ecuador.

Methods

Cluster sampling was used to select seven schools out of a sampling frame of 158 schools in the Cantons of Pedro Vicente Maldonado, Puerto Quito, and San Miguel de Los Bancos in a tropical area of Pichincha Province, Ecuador. Informed verbal consent was obtained from the parent or guardian of all children. The ethical committees of the Hospital Pedro Vicente Maldonado and St George's Hospital Medical School approved the study.

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All children attending the seven schools and aged between 7 and 17 years underwent the following procedures: (1) administration of a questionnaire of risk factors for atopy, (2) examination for evidence of a BCG vaccination scar, (3) administration of a Mantoux skin test, (4) skin prick testing using seven relevant aeroallergens, (5) collection of a single stool sample, and (6) measurement of weight and height.

The questionnaire was administered to the parent or guardian in the presence of the child. The questionnaire was modified from the International Study of Asthma and Allergic disease in Childhood (ISAAC) phase II allergy symptom and risk factor questionnaires [12] after pre-testing and validating in two schools in Canton Puerto Quito. The questionnaire collected information about: history of anti-helminthic treatment; maternal and paternal occupation and educational history; type of house construction; family possession of material goods; access to water, electricity, and sanitation; indices of household crowding; birth order; receipt of breast milk and period of breastfeeding; attendance at a day-care facility; paternal and maternal history of allergic disease; vaccination history; history of major infectious diseases (measles, whooping cough, tuberculosis, and ascariasis); family history of tuberculosis; presence of animals inside and outside the house; family member smokers; and type of cooking materials used.

Mantoux testing was performed as follows: 5 tuberculin units (TU) of tuberculin (Evans Medical Ltd, Sussex, UK) was injected intradermally into the flexor surface of the upper forearm using a 1 mL syringe with 25-gauge needle. The size of two perpendicular diameters of the induration was measured in mm after 48 to 72 h. Tuberculin Responses were graded as negative (0–4.5 mm) or positive (≥ 5 mm).

Skin prick testing was performed using the following allergens and controls: glycerol/saline control (Greer Laboratories Inc., Lenoir, NC, USA), *Dermatophagoides pteronyssinus* (ALK, Horsholm, Denmark), *Dermatophagoides farinae* (ALK, Denmark), grass pollen mix ('9 Southern grass mix', Greer), tree pollen mix ('11 North American tree mix', Greer), American cockroach (Greer), *Alternaria tenuis* (Greer), cat (Greer), and histamine control (10 g/L; ALK). Allergens were scratched onto the volar side of the forearm using ALK plastic bifurcated lancets, and reaction sizes were recorded after 15 min by measurement of the weal sizes. Reactions were considered positive if the mean weal size diameter was at least 3 mm greater than the saline control.

Fresh stools were collected and examined by both the modified Kato Katz method and formol–ethyl acetate concentration method as described [13].

Atopy was defined as a positive reaction to any of the seven allergens tested. Geohelminth infection was defined as the presence of eggs or larvae in stools examined by Kato-Katz and formol–ethyl acetate concentration methods. All statistical analyses were performed using Stata 7 software (Stata Corporation, College Station, TX, USA). Estimates of risk were calculated using logistic regression. Socio-economic status was divided into quartiles based on a score derived from maternal and paternal educational level and occupation, and the number of material goods in the house. The variable overcrowding measured as the number of persons per sleeping room of the house was divided into tertiles for analysis. Body mass index ($\text{weight}/\text{height}^2$) was divided into quartiles for analysis. Dose–response relationships between

exposures and risk of skin test reactivity were examined using χ^2 tests for trend excluding those in the baseline group. Hierarchical analyses were performed to assess the role of different exposures as intermediate factors in causal pathways for atopy—in this approach, controlling for an intermediate factor in the causal mechanism would be expected to decrease the estimate of effect for skin test reactivity towards unity.

Results

Study subjects

A total of 1002 (99.8%) of 1004 children present on the study days at the seven schools were included in the study. School lists of absent children were not available, although we estimate absentee rates to be less than 5% from a current survey. The sex and age distributions of the 1002 children are shown in Table 1. All 1002 children were assessed by questionnaire. Refusal rates for skin prick testing, stool samples, and Mantoux testing were 0 (0%), 1.5% (15), and 4.3% (43), respectively.

Prevalence of atopic sensitization

The prevalence of atopy to the allergens tested was: *D. pteronyssinus* (9.1%), *D. farinae* (6.0%), grass mix (2.0%), tree mix (1.5%), cockroach (11.6%), *Alternaria* (0.1%), and cat (0.2%). Sensitization to any of the two house dust mite extracts was observed in 10.5% of children. Positive skin test reactions to any allergen were observed in 200 (20.0%) subjects.

General risk factors for atopy

Table 1 shows the relationship between various risk factors and atopy after univariate and multivariate analyses. Female sex was associated with a reduced risk of atopy, and the risk increased with increasing age. A reduced risk was observed among children from the poorest families (socio-economic level IV). Because a reduced risk of atopy was associated only with the lowest quartile, the variable was recoded as a binary categorical variable (quartiles I–III ('Moderate') vs. IV ('Poor')) for inclusion as a confounding factor in multivariate analyses (risk of atopy associated with level IV vs. levels I–III, OR 0.40, 95% CI 0.23–0.72, $P = 0.002$). None of the exposures assessed were significantly associated with risk of atopy including paternal agricultural occupation, type of house construction, breast-feeding as infants, parental history of allergy, parent smokers, and type of cooking fuel (Table 1).

Risk of atopy associated with pets and animals inside and outside the house

Most study subjects reported having dogs (71.4% or 715/1002) and many had cats (34.7%). Dogs and cats were generally kept out of doors. Relatively few children lived with dogs or cats inside the house. Most children lived in households that had farm animals living outside the house (e.g. 86.2% had chickens). The presence of either intra- or extra-domiciliary pets and extra-domiciliary animals was not associated with risk of atopy (Table 2). The exception was the presence of pigs outside the house that was associated with an increased risk in univariate and multivariate analyses.

Table 1. Univariate and multivariate logistic regression analysis of general risk factors for atopy

Risk factor	Total (n = 1002)	Atopic (n = 200)	OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Sex						
Male	532 (53.1%)	121 (22.7%)	0.69 (0.50–0.94)	0.02		
Female	470 (46.9%)	79 (16.8%)				
Age						
7–9	315 (31.4%)	53 (16.8%)	1	0.02†		
10–12	477 (47.6%)	91 (19.1%)	1.17 (0.80–1.69)	0.42		
13–17	210 (21.0%)	56 (26.7%)	1.80 (1.17–2.76)	0.007		
Socio-economic level* ¹⁷⁷						
I	313 (37.9%)	71 (22.7%)	1			
II	130 (15.8%)	29 (22.3%)	0.98 (0.60–1.60)	0.93		
III	244 (29.6%)	50 (20.5%)	0.88 (0.58–1.32)	0.53		
IV	138 (16.7%)	14 (10.1%)	0.39 (0.13–0.71)	0.002		
Body mass index (kg/m ²)* ⁴						
11.8–14.6	249 (24.9%)	39 (15.7%)	1	0.34†	1	0.95†
14.6–15.6	250 (25.1%)	53 (21.2%)	1.45 (0.92–2.29)	0.11	1.39 (0.88–2.21)	0.16
15.7–17.4	248 (24.8%)	45 (18.2%)	1.19 (0.75–1.91)	0.46	1.03 (0.63–1.68)	0.90
17.4–31.4	251 (25.2%)	62 (24.7%)	1.77 (1.13–2.76)	0.01	1.45 (0.86–2.44)	0.16
Agriculturist* ¹⁰⁹						
No	274 (30.7%)	62 (22.6%)	1.22 (0.86–1.72)	0.27	1.07 (0.74–1.56)	0.72
Yes	619 (69.3%)	120 (19.4%)				
House construction						
Wood	486 (48.5%)	91 (18.7%)	1		1	
Mixed wood/cement	121 (12.1%)	25 (20.1%)	1.13 (0.69–1.80)	0.63	0.92 (0.53–1.58)	0.75
Cement	395 (39.4%)	84 (21.5%)	1.17 (0.84–1.63)	0.35	0.82 (0.55–1.23)	0.34
Electricity						
No	131 (13.1%)	20 (15.3%)	1.14 (0.87–2.39)	0.15	1.39 (0.77–2.50)	0.28
Yes	871 (86.9%)	180 (20.7%)				
Breast milk						
No	22 (2.2%)	4 (18.2%)	1.13 (0.38–3.36)	0.83	0.98 (0.27–3.56)	0.98
Yes	980 (98.0%)	196 (20.0%)				
Maternal allergy* ³⁹						
No	901 (93.6%)	181 (20.1%)	0.95 (0.50–1.83)	0.89	0.87 (0.41–1.87)	0.73
Yes	62 (6.4%)	12 (19.4%)				
Paternal allergy* ⁵³						
No	910 (95.9%)	184 (20.2%)	1.18 (0.55–2.54)	0.66	1.17 (0.52–2.67)	0.70
Yes	39 (4.1%)	9 (23.1%)				
Parent smokers						
No	536 (53.5%)	107 (20.0%)	1.00 (0.73–1.36)	1.00	1.00 (0.71–1.42)	0.98
Yes	466 (46.5%)	93 (20.0%)				
Cooking material						
Propane gas						
No	20 (2.0%)	1 (5.0%)	4.83 (0.64–36.40)	0.09	3.91 (0.51–29.90)	0.19
Yes	982 (98.0%)	199 (20.3%)				
Wood						
No	581 (58.0%)	127 (21.9%)	0.75 (0.54–1.03)	0.08	0.78 (0.54–1.13)	0.19
Yes	421 (42.0%)	73 (17.3%)				
Carbon						
No	963 (96.1%)	193 (20.0%)	0.87 (0.38–2.01)	0.75	0.91 (0.39–2.13)	0.83
Yes	39 (3.9%)	7 (18.0%)				

Total shows number (and percentage) of children in each exposure category. Multivariate odds ratios (adjusted ORs) are adjusted for age, sex, and socio-economic level. Socio-economic status is quartiles of increasing poverty (from I to IV).

*Number of missing values. †Test for trend.

95% CI, 95% confidence intervals.

Risk of atopy associated with indicators of infection or infection risk

A number of variables that might provide an indication of the 'burden of exposure' to infectious diseases were

assessed in this study. A total of 694 (70.1%) children had evidence of infection with any geohelminth parasite. Infection rates with the individual geohelminths were: *A. lumbricoides* 52.0% (515), *T. trichiura* 51.8% (513), *Ancylostoma duodenale* 7.5% (74), *Strongyloides stercoralis* 3.1% (31),

Table 2. Univariate and multivariate logistic regression analysis of risk of atopy associated with intra- and extra-domiciliary animals

Risk factor	Total (<i>n</i> = 1002)	Atopic (<i>n</i> = 200)	OR (95% CI)	<i>P</i> -value	Adjusted OR (95% CI)	<i>P</i> -value
<i>Animals inside house</i>						
<i>Dogs</i>						
No	966 (96.4%)	193 (20.0%)				
Yes	36 (3.6%)	7 (19.4%)	0.97 (0.42–2.24)	0.94	0.91 (0.36–2.29)	0.84
<i>Cats</i>						
No	904 (90.2%)	183 (20.2%)				
Yes	98 (9.8%)	17 (17.4%)	0.83 (0.48–1.43)	0.50	0.70 (0.38–1.29)	0.25
<i>Others</i>						
No	924 (92.2%)	179 (19.4%)				
Yes	78 (7.8%)	21 (26.9%)	1.53 (0.91–2.60)	0.11	1.62 (0.93–2.83)	0.09
<i>Animals outside house</i>						
<i>Dogs</i>						
No	315 (31.4%)	58 (18.4%)				
Yes	687 (68.6%)	142 (20.7%)	1.15 (0.82–1.62)	0.41	1.15 (0.79–1.67)	0.47
<i>Cats</i>						
No	745 (74.4%)	145 (19.5%)				
Yes	257 (25.6%)	55 (21.4%)	1.13 (0.79–1.60)	0.50	1.11 (0.75–1.63)	0.60
<i>Horses</i>						
No	802 (80.0%)	173 (20.3%)				
Yes	200 (20.0%)	27 (18.0%)	0.86 (0.55–1.35)	0.52	0.88 (0.54–1.45)	0.62
<i>Cattle</i>						
No	911 (90.9%)	186 (20.4%)				
Yes	91 (9.1%)	14 (15.4%)	0.71 (0.39–1.28)	0.25	0.70 (0.36–1.37)	0.29
<i>Pigs</i>						
No	507 (50.6%)	85 (16.8%)				
Yes	495 (49.4%)	115 (23.2%)	1.50 (1.10–2.06)	0.01	1.42 (1.00–2.01)	0.05
<i>Chickens</i>						
No	138 (13.8%)	29 (21.0%)				
Yes	864 (86.2%)	171 (19.8%)	0.93 (0.60–1.44)	0.74	1.09 (0.64–1.84)	0.75
<i>Others</i>						
No	648 (64.7%)	136 (21.0%)				
Yes	354 (35.3%)	64 (18.1%)	0.83 (0.60–1.16)	0.27	0.85 (0.59–1.22)	0.37

Total shows number (and percentage) of children in each exposure category. Multivariate odds ratios (adjusted ORs) are adjusted for age, sex, and socio-economic level.

95% CI, 95% confidence intervals.

Enterobius vermicularis 0.5% (5), and *Hymenolepis nana* 1.6% (16).

The results of univariate and multivariate (adjusting for age and sex) analyses are shown in Table 3. In univariate analyses the use of a latrine was associated with a significantly increased risk of atopy, while evidence of overcrowding (upper tertile vs. lower tertile, OR 0.47, 95% CI 0.32–0.71, $P \leq 0.001$) and the presence of any geohelminth infection were associated with a reduced risk. There was evidence of a trend with greater protection associated with greater levels of overcrowding.

The presence of a BCG vaccination scar or evidence of sensitization to tuberculin was not associated with atopy in this study group. Even when all children without BCG scars were excluded from the analysis, the lack of association with atopy remained (OR 0.97, 95% CI 0.64–1.46, $P = 0.87$).

Multivariate analyses controlled for age and sex – socio-economic level was not adjusted for because the 'burden' of infectious disease is likely to be an intermediate factor in the causal pathway between socio-economic level and atopy. In multivariate analyses that controlled for age and sex, overcrowding and infections with any geohelminth infection

(Table 3) or with ascariasis (adjusted OR 0.65, 95% CI 0.47–0.91, $P = 0.01$) or trichuriasis (adjusted OR 0.67, 95% CI 0.49–0.92, $P = 0.01$), remained significantly protective against atopy. Greater parasite burdens with ascariasis (test for trend, $P < 0.001$) or with trichuriasis (test for trend, $P = 0.007$) were associated with greater protective effects. Infections with other geohelminth parasites were not significantly protective in univariate or multivariate analyses.

For hierarchic analyses to assess the statistical relationship between these three protective factors, overcrowding (un-adjusted OR for risk of atopy for 0.4–2.8 persons/room vs. 3–13 persons/room 0.49, 95% CI 0.35–0.70, $P < 0.001$; age- and sex-adjusted OR 0.51, 95% CI 0.36–0.72, $P < 0.001$) and socio-economic level (age- and sex-adjusted OR 0.39, 95% CI 0.22–0.70, $P = 0.002$) were analysed as binary categorical variables. The effects of mutual adjustments for these factors in multivariate models of the risk of atopy are shown in Table 4. Inclusion of geohelminth infection in logistic regression models of the effect of socio-economic level or overcrowding on the risk of atopy had no impact on the estimates of risk for these factors. Further, adjustment for overcrowding had no effect on the estimate of effect for socio-economic level. The

Table 3. Univariate and multivariate logistic regression analysis of indicators of infection on the risk of atopy

Risk factor	Total (n = 1002)	Atopic (n = 200)	OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Consumption of river water						
No	259 (25.8%)	46 (17.8%)				
Yes	743 (74.2%)	154 (20.7%)	0.83 (0.57–1.19)	0.30	0.78 (0.54–1.13)	0.19
Use of latrine						
No	41 (4.1%)	3 (7.2%)				
Yes	961 (95.9%)	197 (20.5%)	3.27 (1.00–10.72)	0.04	3.20 (0.97–10.50)	0.06
Overcrowding						
0.4–1.8	304 (30.4%)	75 (24.7%)	1	<0.01‡	1	0.003‡
2–2.8	319 (31.8%)	74 (23.2%)	0.92 (0.64–1.33)	0.67	0.93 (0.64–1.35)	0.71
3–13	379 (37.8%)	51 (13.5%)	0.47 (0.32–0.71)	<0.00	0.49 (0.33–0.73)	<0.001
Birth order						
1–2	411 (41.0%)	86 (20.9%)	1	0.65‡	1	0.30‡
3–4	274 (27.3%)	49 (17.9%)	0.82 (0.56–1.12)	0.33	0.49 (0.58–1.27)	0.44
5–6	162 (16.2%)	36 (22.2%)	1.08 (0.70–1.68)	0.73	1.14 (0.73–1.78)	0.56
≥7	155 (15.5%)	29 (18.7%)	0.87 (0.54–1.39)	0.56	0.83 (0.52–1.33)	0.44
Day care						
No	777 (77.5%)	161 (20.7%)				
Yes	225 (22.5%)	39 (17.3%)	0.80 (0.54–1.18)	0.26	0.81 (0.55–1.19)	0.28
BCG scar* ¹						
No	117 (11.7%)	25 (21.4%)				
Yes	884 (88.2%)	175 (19.8%)	0.91 (0.57–1.46)	0.69	0.89 (0.55–1.43)	0.63
Positive Mantoux* ⁴³						
No	776 (80.9%)	156 (20.1%)				
Yes	183 (19.1%)	36 (19.7%)	0.97 (0.65–1.46)	0.90	0.92 (0.61–1.38)	0.68
Family history of tuberculosis						
No	915 (91.3%)	186 (20.3%)				
Yes	87 (8.7%)	14 (16.1%)	0.75 (0.41–1.36)	0.35	0.78 (0.40–1.32)	0.30
Childhood vaccines†* ²⁴⁶						
No	22 (2.9%)	4 (18.2%)				
Yes	734 (97.1%)	154 (21.0%)	1.19 (0.40–3.58)	0.75	1.20 (0.40–3.64)	0.74
History of measles* ³⁴						
No	784 (81.0%)	151 (19.3%)				
Yes	184 (19.0%)	41 (22.3%)	1.20 (0.81–1.78)	0.36	1.14 (0.76–1.70)	0.52
Cold-like illnesses (number/year)† ¹						
0	127 (12.7%)	26 (20.5%)	1	0.59‡	1	0.19‡
1–2	490 (49.0%)	93 (19.0%)	0.91 (0.56–1.48)	0.70	0.92 (0.56–1.50)	0.73
≥3	384 (38.3%)	81 (21.1%)	1.04 (0.63–1.71)	0.88	1.07 (0.65–1.76)	0.79
Geohelminth infection						
No	294 (29.7%)	72 (24.5%)				
Yes	695 (70.3%)	126 (18.1%)	0.68 (0.49–0.95)	0.02	0.65 (0.47–0.91)	0.01

Total shows number (and percentage) of children in each exposure category. Multivariate odds ratios (adjusted ORs) are adjusted for age and sex. Overcrowding expressed as the number of persons per room is divided into tertiles.

*Number of missing values. †Receipt of at least one dose of oral polio vaccine or diphtheria–pertussis–tetanus. ‡Test for trend.

95% CI, 95% confidence intervals.

data indicate that geohelminth infection, socio-economic level, and overcrowding, are statistically independent.

Discussion

We have investigated the potential risk factors associated with atopy in a group of school-age children living in rural communities in a tropical region of Latin America. The findings extend our previous observations among school children living in the same rural region of Ecuador that provided evidence for a strong protective effect of active

geohelminths (i.e. positive stool samples for geohelminth ova) against atopy [11] to explore the relationship between other potential correlates of atopy in the context of endemic geohelminth infection. Our findings show that few factors normally considered protective against atopy in industrialized countries (e.g. farming occupation and domestic pets) were protective in this rural population, but that both socio-economic level and overcrowding were strongly and independently protective against atopy in multivariate analyses that controlled for age and sex. Further, the protective effects against atopy of increased overcrowding and reduced socio-economic level could not be explained by a higher prevalence of geohelminth infection.

Table 4. Hierarchical analyses to assess the role of exposures as intermediate factors in the causal pathway for atopy

Exposure	OR (95% CI) <i>P</i> -value	Geohelminth-adj. OR (95% CI) <i>P</i> -value	Overcrowding-adj. OR (95% CI) <i>P</i> -value	Two factor-adj. OR (95% CI) <i>P</i> -value
Socio-economic level	0.39 (0.22–0.70) 0.002	0.43 (0.24–0.78) 0.005	0.42 (0.24–0.77) 0.004	0.46 (0.25–0.84) 0.01
Overcrowding	0.49 (0.35–0.70) <0.001	0.52 (0.37–0.74) <0.001		0.53 (0.36–0.78) 0.001

All odds ratios (ORs) are adjusted for age and sex. Overcrowding and socio-economic level are analysed as binary categorical variables. The effect of adjusting for potential intermediate factors (geohelminth infection, overcrowding, or both (two factor) are shown). 95% CI, 95% confidence intervals; adj., adjusted.

The major limitations of this study were the cross-sectional design and the use of questionnaires to obtain information on risk factors. The cross-sectional design does not allow us to identify the temporal sequence between the risk factors and atopy, although reverse causality is not a possibility for many of the exposures measured. The use of questionnaires makes the study open to information bias. Atopy (measured by skin test reactivity) and geohelminth prevalence and intensity (measured using standard parasitological protocols) were both objectively measured. Misclassification of exposure is likely to be a problem with this study as we did not identify past infections with specific pathogens but rather used surrogate measures of exposure to estimate infection burden. Because the study was population based, the findings are likely to be generalizable to the population of school children living in rural Tropical regions of Ecuador and to similar areas elsewhere in Latin America.

There has been considerable research interest into the potential protective effects of childhood infections and the development of allergic sensitization and allergic disease, the so-called hygiene hypothesis [14]. Protective effects against atopy have been reported for a number of pathogens [5]. We were not able to detect a protective effect for past measles infection in this study nor for cold-like illness within the previous year. The latter might be explained by the fact that histories were elicited in school-age children: previous studies has shown a protective effect against atopy of mild upper respiratory tract infections but only during the first year 3 years of life [15, 16].

There has been interest also in the potential protective effects against atopy of exposure to mycobacteria [17]. Early observations of an inverse relationship between tuberculin responses and atopic diseases [18] have not been replicated [19–21]. In this study of population of school-age children, 88% of whom had evidence of having received BCG vaccination at birth, we were not able to identify a relationship between the presence of a vaccination scar or evidence of sensitization to tuberculin and risk of atopy. Similar findings have been reported recently from the Gambia [22].

The protective effects of enteric infections against atopy appear to be greater than for respiratory pathogens [23]. Because only a very small proportion (<10%) of families routinely boil water for drinking use, we felt that use of river water would provide a useful, albeit indirect, measure of exposure to enteric infections through a contaminated drinking source. Our findings suggest that consumption of river water was only weakly protective against atopy. These findings are

likely to be significantly affected by misclassification of exposure. Interestingly, use of a latrine that is likely to be associated with cleaner sanitary practices (and perhaps reduced exposure to enteric infections) was associated with an increased risk of atopy.

The study was conducted in an area that was highly endemic for geohelminth parasites, and 70.1% of the children had evidence of infection with any geohelminth parasite. Geohelminths, the only enteric infection that we identified directly, were associated with a protective effect against atopy, as demonstrated in previous studies [8, 9, 11]. Strong protective effects against atopy were observed also for overcrowding and socio-economic level. Because overcrowding and geohelminth infection could explain part of the protective effect of socio-economic level, we performed hierarchical analyses to determine if controlling for these factors in models of the relationship between socio-economic level and atopy might explain part or whole of the protective effect of socio-economic level. The results of hierarchical analyses indicated that neither variable contributed to the protective effect of socio-economic level. Likewise, adjusting for geohelminth infection in models of the association between overcrowding and atopy suggested that geohelminth infection could not be an explanation for the protective effect of overcrowding. Overcrowding is likely to reflect a number of factors including socio-economic factors and risk of cross-infection with common childhood infectious diseases.

Interestingly, birth order [14, 24], attendance at day care [25], sharing a bedroom [26] and family history of allergy, that are consistently associated (either positively or inversely) with atopy in industrialized countries, did not affect risk of atopy in this study. The former three factors may be indirect markers of biologically relevant factor/s that are ubiquitous in this study population of school-age children living in a poor region of the rural Tropics. In the case of the latter, parental history of allergic disease could be expected to be a poor measure of the underlying propensity to atopy in a population of children with a low prevalence of allergic disease and where the relationship between atopy and allergic symptoms is weak [27]. A lack of association between atopy and family history of allergy has been reported previously in Africa [9].

We were not able to identify as protective against atopy other exposures that have been strongly associated with atopy in industrialized countries. These factors included farming occupation [28, 29], and presence of household pets such as

cats [30, 31] and dogs [26]. The lack of protective effects of farming could be explained by the fact that in rural communities all children are exposed to a similar degree to protective factors associated with farming: a study in Austria has shown that children who did not live on a farm but who had regular contact with livestock were also protected against atopy [28]. Almost all the children in this study were likely to have regular contact with livestock and poultry. The absence of an association with pets (specifically cats and dogs) may be explained by the essentially different relationship that families in the rural Tropics have with such animals. They have dogs to warn of intruders and cats to control vermin and these animals generally live outside the house and do not have close contact with their owners. Exposure to pet allergens may therefore be low.

An important observation from this study was the high prevalence of atopy observed in this rural study population despite exposure to a large number of potentially protective factors (i.e. overcrowding, geohelminth infections, poor living conditions, and a rural environment [3, 4, 9, 32]). We have reported previously a low prevalence of allergic symptoms (e.g. prevalence of wheeze within previous 12 months of 2.1%) despite a high prevalence of atopy and a relatively weak, although statistically significant, relationship between atopy and allergic symptoms among school children from the same region of Ecuador [27]. A study that compared allergy between a rural and urban area of Kenya speculated that the weak relationship between atopy and allergic symptoms observed in rural areas could become stronger during the process of urbanization [32], and could follow the loss of protective exposures (e.g. geohelminth infections) and acquisition of risk factors (e.g. urban pollution). This hypothesis could be of particular relevance to Latin America that has seen dramatic demographic changes over the last twenty to thirty years associated with massive population migrations from rural to urban areas. If migrant rural populations with a high prevalence of atopy were at increased risk of allergic disease, this could have significant public health consequences for urban populations living in Latin America, and could be reflected in the current estimates of allergic disease prevalence among children in the urban centres of Latin America that are among the highest reported worldwide [2].

In conclusion, we have investigated the relationship between environmental exposures and the risk of atopy among school-age children living in rural communities in a tropical region of Latin America. Our findings indicate strong independent protective effects for socio-economic level, overcrowding, and geohelminth infections, but no association with many factors that have been associated with protective effects in industrialized countries such as farming occupation and household pets. Overcrowding may be a surrogate marker for other protective exposures such as cross-infections within a family. Infections with geohelminth parasites may mediate protection directly or indirectly through association with other enteric infections or other factors that are associated with living in a microbially contaminated environment. Further epidemiological studies are required to investigate risk factors for atopy in urban and rural areas of Latin America, the interactions between different exposures on the risk of atopy and the relationship between atopy and allergic disease.

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