

Ascaris-specific IgE and allergic sensitization in a cohort of school children in the former East Germany

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Background: Helminthic infections induce an IL-4-dependent polyclonal stimulation of IgE synthesis. It is still unclear, however, what role helminths play in allergic sensitization.

Objective: We sought to determine the relationship between *Ascaris*-specific IgE and allergic sensitization in a nontropical country.

Methods: In 2 consecutive cross-sectional surveys in 1992-1993 and 1995-1996, data from school entrants (age range, 5 to 7 years), third graders (age range, 8 to 10 years), and sixth graders (age range, 11 to 14 years) were collected. The 2 younger groups were reexamined in the second survey. Data for about 2300 children, including a cohort of 700 subjects, were analyzed. *Ascaris* IgE and total and specific IgE to inhalant allergens were measured, and skin prick tests were performed. Information about asthma and allergic rhinitis was collected by a questionnaire.

Results: Children who were *Ascaris*-IgE seropositive (>0.35 IU/mL) in both surveys had 10-fold higher levels of total IgE (451 IU/mL vs 45 IU/mL, $P < .001$) and higher prevalence rates of allergen-specific IgE seropositivity (56.3% vs 26.6%, $P < .001$). They also had a higher prevalence of allergic rhinitis (12.6% vs 3.7%, $P < .001$) and asthma (5.7% vs 1.6%, $P < .05$). In subjects who were *Ascaris*-seronegative in the first survey but seropositive in the second survey, total and specific IgE increased markedly. Sensitization to *Dermatophagoides pteronyssinus* increased nearly 3-fold in this group. In contrast, in children who became *Ascaris*-seronegative, total and specific IgE decreased.

Conclusions: Contact with low doses of helminthic antigen is associated with an increase of total and specific IgE production. Helminthic infections in East German children are not

the cause for a low prevalence of allergies in the former East Germany. (*J Allergy Clin Immunol* 1998;102:414-20.)

Key words: Allergy, asthma, IgE, parasites, *Ascaris*, helminthic infection

Because of the similarities between the immune response against helminthic parasites and IgE-mediated allergic disease, there has been an intense discussion about the relationship between parasites and allergy.¹⁻³ There are at least 5 possibilities: (1) worms are protective, (2) worms cause allergies, (3) allergic persons are more resistant to worms, (4) allergic persons are more susceptible to worms, or (5) there is no causal relationship. Although it is well known that helminthic infection can cause a polyclonal stimulation of the synthesis of IgE, which is dependent on IL-4 production,^{4,5} it is still unclear which role helminths play in allergic sensitization. Results of different studies indicate that a mild infection with a moderate IgE synthesis increases the allergic reactivity,^{6,7} whereas a heavy infection with an extensive IgE response may be suppressive.^{8,9}

Until now the association between helminths and allergies/asthma has been studied for the most part in tropical areas where worms are endemic and almost all children have been infected at least once in their lifetime. Observing a cohort population in a nontropical country offers the opportunity to investigate the role of sporadic and mild intestinal helminthic infections on allergy-related immune response in comparison with children who were probably never infected in their life.

Compared with the former West Germany, higher total serum IgE levels,^{10,11} but lower rates of allergic diseases, have been reported in the former East Germany.¹²⁻¹⁴ Because of the hypothesis that worms prevent allergies, it has been suggested^{10,15} that the higher prevalence of enteral parasitic infections among children in the former East Germany could be responsible for the lower rates of allergic diseases. To evaluate the role of helminthic infection in relation to allergic sensitization in an ongoing cohort study with East German school children, *Ascaris* IgE was measured together with allergen-specific IgE and skin prick test (SPT) reactivity. Information about

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Abbreviation used

SPT: Skin prick test

asthma and allergic rhinitis was collected by a questionnaire. Because of cross-reactivity^{16,17} with other helminths and persistent levels after infection,¹⁸ *Ascaris*-specific IgE is not specific for an ongoing infection but is more likely a general marker for the contact with helminthic antigen and its immune response.

METHODS

Subjects and setting

The study was conducted in an area of the former German Democratic Republic. *East German* or *West German* is used analogously with *from the former East Germany* and *from the former West Germany*, respectively. The main goal of the study was to determine the influence of environmental factors on respiratory health and allergic disease. This analysis uses data from the first (1992-1993) and second (1995-96) cross-sectional surveys. In each survey 3 age groups of school children formed the study population: school entrants (age range, 5 to 7 years), third graders (age range, 8 to 10 years), and sixth graders (age range, 11 to 14 years). The school entrants and the third graders from the first survey were reexamined in the second survey and form the cohort group. Nearly all participants (99.6%) are of German nationality. All school children in these age groups in the cities of Zerbst and Hettstedt and of a randomly selected subgroup of schools in the city of Bitterfeld were invited to participate. Approval of the study protocol was granted by the University of Rostock Ethics Committee. Informed consent was obtained from all parents.

Questionnaire

Letters explaining the study and questionnaires were distributed to the children by the class teacher and recollected 1 week later. The parents of 89.1% (1992-93) and 74.7% (1995-96) of the children filled out the questionnaires. The questionnaire had 72 items and was developed by using questions previously tested in several national and international studies¹⁹ adapted to address East German living conditions. *Asthma* was recorded if the parents gave a positive response to the question of whether a physician ever diagnosed asthma or asthmoid bronchitis. Physician-diagnosed hay fever was considered allergic rhinitis. Additional questions addressed socioeconomic factors, housing characteristics, nutrition, and indoor and outdoor environmental exposures. The highest school or professional degree of both parents was taken as a marker of socioeconomic status. In the second survey the same questionnaire was used with some additional questions (75 items). A question of whether the child ever had a worm infestation was only present in the second survey.

Total and specific IgE

Serum samples were drawn from more than 80% of the children, all of whom consented, and were immediately frozen and stored at -80° C until they could be analyzed together at the end of the second survey. Specific serum IgE was determined in the Pharmacia laboratory (Freiburg) with the RAST technique (Phar-

TABLE I. Description of the study population: First and second survey

	First survey (1992-1993)	Second survey (1995-96)	Cohort* (1995-96)
Target population	2773	3765	1565
Response to questionnaire (%)	2470 (89.1)	2814 (74.7)	1082 (69.1)
Sex			
Boys (%)	1247 (50.5)	1499 (53.3)	546 (50.5)
Girls (%)	1223 (49.5)	1315 (46.7)	536 (49.5)
Age groups			
5-7 yrs (%)	769 (31.1)	725 (25.8)	
8-10 yrs (%)	796 (32.2)	961 (34.2)	531 (49.1)
11-14 yrs (%)	905 (36.6)	1128 (40.1)	551 (50.9)
SPT (%)	2188 (88.6)	2437 (86.7)	842 (77.8)
Total IgE (%)	2149 (87.0)	2327 (82.7)	802 (74.1)
<i>Ascaris</i> -specific IgE (%)	1916 (77.6)	2323 (82.6)	719 (66.5)

*Cohort exists of 5 to 10 year old children in the 1992 to 1993 survey who were 8 to 14 years old in the 1995 to 1996 survey. Their data are also in the first 2 columns. Number and frequency of available data of IgE values and SPTs in both surveys are shown.

macia and Upjohn Diagnostics AB, Uppsala, Sweden). The following antigens were tested: *Ascaris* p1, grass g6, *Der-matophagoides pteronyssinus* d1, cat e1, and birch t3. Levels greater than or equal to 0.35 IU/mL (level 1 on the RAST scale) were considered to be a positive antibody concentration. Total IgE was also determined by Pharmacia with a detection limit of 2 IU/L and an upper limit of 2000 IU/L.

SPT

SPTs were done between 8 AM and 1 PM at school or kindergarten (school entrants) with standardized lancets and allergens. An SPT result was defined as positive if the diameter of the elevated skin reaction on the right forearm was at least 3 mm 15 minutes after puncturing the skin. Tested and analyzed allergens were mixed grass, birch (*Betula verrucosa*), hazel (*Corylus avellana*), ribwort (*Plantago lanceolata*), mugwort (*Artemisia vulgaris*), mites (*D pteronyssinus* and *D farinae*), animal epithelia (cat), fungi (*Aspergillus fumigatus*), and food antigens (milk and egg). A positive control (histamine chloride) and a negative control (dilution of sodium chloride) were also examined but not included in the analysis. In the second survey only 8 reactions to the positive control were smaller than 3 mm, and only 2 children had a reaction to the negative control. None of these 10 children had a reaction to one of the tested allergens.

Because of better standardization, the manufacturer of SPT dilutions was changed from Allergopharma (Reinbeck, Germany) to Alk (Horsholm, Denmark) between the first and second survey. Therefore the SPT results of the 2 surveys are not comparable and are not analyzed in the cohort group. Results from the second survey are reported.

Analysis

Questionnaire data were entered twice and checked before merging with the serologic and SPT data. All subsequent statistical analyses were performed with SAS (Statistical Analysis Software 6.08, Cary, NC). IgE values were normalized by logarithmic (base 10) transformation for statistical analysis. Statistical significance was estimated with Student's *t* test and the chi-square test. Logistic

TABLE II. Total IgE and prevalence (95% confidence intervals) of history of helminthic infection, specific IgE seropositivity, allergic rhinitis, and asthma in a cohort of 668 children, grouped by *Ascaris* seropositivity in first and second survey

	Group 1 (n = 515)	Group 2 (n = 31)	Group 3 (n = 35)	Group 4 (n = 87)	Total (n = 668)
<i>Ascaris</i> IgE (1992-1993)	Negative	Negative	Positive	Positive	
<i>Ascaris</i> IgE (1995-1996)	Negative	Positive	Negative	Positive	
II Helminthic infection (%)	17.3 (14.0-20.5)	22.6 (7.9-37.3)	25.7 (11.2-40.2)	31.0 (21.3-40.8)	19.8 (16.7-22.8)
II With <i>Ascaris</i> † (%)	7.4 (5.1-9.6)	6.5 (2.2-15.1)	2.9 (0-8.4)	16.1 (8.4-23.8)	8.2 (6.1-10.3)
I Total IgE, geometric mean (IU/mL)	41 (37-45)	165 (118-229)	192 (140-262)	478 (385-592)	65 (58-72)
II Total IgE, geometric mean (IU/mL)	45 (40-50)	265 (188-373)	114 (78-167)	451 (357-570)	69 (61-77)
I Allergen-specific IgE* (%)	25.8 (22.0-29.6)	38.7 (21.6-55.9)	54.3 (37.8-70.8)	55.2 (44.7-65.6)	31.7 (28.2-35.3)
II Allergen-specific IgE* (%)	26.6 (22.8-30.4)	58.1 (40.7-75.4)	40.0 (23.8-56.2)	56.3 (45.9-66.7)	32.6 (29.1-36.2)
I Grass (%)	18.3 (14.9-21.6)	32.3 (15.8-48.7)	22.9 (8.9-36.8)	44.8 (34.4-55.3)	22.6 (19.4-25.8)
II Grass (%)	16.3 (13.1-19.5)	35.5 (18.6-52.3)	17.2 (4.7-29.6)	47.1 (36.6-57.6)	21.3 (18.2-24.4)
I <i>D pteronyssinus</i> (%)	8.9 (6.5-11.4)	16.1 (3.2-29.1)	48.6 (32.0-65.1)	28.7 (19.2-38.2)	13.9 (11.3-16.5)
II <i>D pteronyssinus</i> (%)	12.2 (9.4-15.1)	45.2 (27.6-62.7)	31.4 (16.0-46.8)	36.8 (26.6-46.9)	18.0 (15.1-20.9)
I Allergic rhinitis	2.3 (1.0-3.6)	3.2 (0-9.4)	5.7 (2.0-13.4)	10.3 (3.9-16.7)	3.6 (2.2-5.0)
II Allergic rhinitis	3.7 (2.1-5.3)	9.7 (0-20.1)	11.4 (0.9-22.4)	12.6 (5.7-19.6)	5.5 (3.8-7.3)
I Asthma	2.1 (0.9-3.4)	3.2 (0-9.4)	5.7 (0-13.4)	4.6 (0.2-9.0)	2.7 (1.5-3.9)
II Asthma	1.6 (0.5-2.6)	3.2 (0-9.4)	8.6 (0-17.8)	5.7 (0.9-10.6)	2.5 (1.4-3.7)

I, First survey (1992-1993); II, second survey (1995-1996).

*Allergen-specific IgE: at least 1 positive result of 4 tested inhalant allergens (≥ 0.35 IU/mL).

regression analysis was used to study the association (or relations between specific IgE against inhalant allergens and *Ascaris* IgE adjusting for sex, age, number of siblings, education of the parents, and family history of allergies).

RESULTS

Study population

Data from 2470 children in the first survey and 2814 in the second survey (Table I) were available for analysis. Of the 1082 children who took part in both surveys (cohort group), 719 had *Ascaris* IgE measurements. Complete data, including total IgE and inhalant allergen-specific IgE levels and information from the questionnaire about histories of worm infection, asthma, and allergic rhinitis, were available for 668 children in the cohort. There were no significant differences for sex, age, or prevalence of hay fever between children with *Ascaris* IgE measurement and those without it. In the group without *Ascaris* IgE, significantly more children had asthma in both surveys. Parents of the children with asthma more often did not consent with an examination and blood sample of their children but did fill in the questionnaire.

Ascaris IgE

RAST results against *Ascaris* antigen were positive (> 0.35 IU/mL) in 20.1% of the children in the first survey and 15.7% in the second survey. Factors associated with the prevalence of *Ascaris* IgE were analyzed by using data from the second survey. The overall frequency of *Ascaris* IgE seropositivity was significantly higher ($P < .001$) in boys (18%) than in girls (13%) and increased

with age from 9.4% (5 to 7 years) to 15.7% (8 to 10 years) to 19.9% (11 to 14 years). *Ascaris* IgE seropositivity was significantly more prevalent ($P < .001$) in children whose parents had low school education (25.5%) (no more than an eighth-grade education) than in those whose parents had a university degree (11.5%). Increasing family size was also associated with a higher prevalence of *Ascaris* IgE seropositivity, rising from 8.3% with no sibling to 14.9% with 1 sibling, 22.0% with 2 siblings, and 33.7% with 3 or more siblings. Another associated factor was frequent contact with a dog (20.4% vs 14.6%) or cat (20.7% vs 14.7%) in the first year of life. No significant difference was observed by city of residence, parental history of allergic rhinitis or asthma, current contact with a pet, age when child started day-care, years of attending a kindergarten, parental current smoking or maternal smoking during pregnancy, or daily duration of playing outside.

Cohort population

Thirty-one children who were *Ascaris* IgE-seronegative in the first survey became seropositive by the second survey, whereas 35 previously seropositive children became seronegative by the second survey. Eighty-seven children were seropositive in both surveys (Table II). The total IgE level is about 10-fold higher in children who were *Ascaris* IgE-seropositive during both surveys than in *Ascaris* IgE-seronegative children. From the first to second survey, total IgE increased in the group that became seropositive and decreased in the group that became seronegative. However, the group that became

TABLE III. Total IgE levels and prevalence (95% confidence-interval) of helminthic infection, specific IgE seropositivity, SPT, allergic rhinitis, and asthma in the second survey by RAST class of *Ascaris* IgE in the second survey

	<i>Ascaris</i> IgE RAST class				
	0 (n = 1911)	I (n = 130)	II (n = 170)	≥III (n = 61)	Total (n = 2272)
Helminthic infestation	16.6 (15.0-18.3)	16.9 (10.5-23.4)	28.2 (21.5-35.0)	34.4 (22.5-46.3)	18.0 (16.4-19.6)
With <i>Ascaris</i>	7.1 (5.9-8.2)	7.7 (3.1-12.3)	10.6 (6.0-15.2)	19.7 (9.7-29.6)	7.7 (6.6-8.8)
Total IgE, geometric mean (IU/mL)	43 (41-46)	211 (179-250)	431 (371-501)	1097 (935-1288)	61 (58-65)
Allergen-specific IgE* (%)	24.4 (22.5-26.3)	48.5 (39.9-57.1)	52.4 (44.8-59.9)	65.6 (53.7-77.5)	29.0 (27.1-30.8)
Grass (%)	15.0 (13.4-16.6)	33.1 (25.0-41.2)	38.8 (31.5-46.1)	45.9 (33.4-58.4)	18.6 (17.0-20.2)
<i>D pteronyssinus</i> (%)	11.4 (9.9-12.8)	32.3 (24.3-40.3)	34.7 (27.5-41.9)	47.5 (35.0-60.1)	15.3 (13.8-16.8)
SPT† (%)	27.6 (25.6-29.6)	36.9 (28.6-45.2)	42.4 (34.9-49.8)	42.6 (30.2-55.0)	29.6 (27.7-31.5)
Grass (%)	14.6 (13.0-16.2)	26.2 (18.6-33.7)	29.4 (22.6-36.6)	29.5 (18.1-41.0)	16.8 (15.2-18.3)
<i>D pteronyssinus</i> (%)	10.0 (8.7-11.4)	16.9 (10.5-23.4)	17.6 (11.9-23.4)	21.3 (11.0-31.6)	11.3 (10.0-12.6)
Allergic rhinitis	3.8 (2.9-4.6)	6.9 (2.6-11.3)	12.4 (7.4-17.3)	1.6 (0-4.8)	4.5 (3.7-5.4)
Asthma	2.7 (2.0-3.5)	6.9 (2.6-11.3)	3.5 (0.8-6.3)	8.2 (1.3-15.1)	3.2 (2.4-3.9)

*Allergen-specific IgE: at least 1 positive of 4 tested inhalant allergens (≥0.35 IU/mL).

†SPT: at least 1 positive reaction (>2 mm) of 12 tested allergens.

TABLE IV. Association between *Ascaris* IgE and allergen-specific IgE seropositivity at second survey

	No. of cases/total*	%	Crude OR	Adjusted OR†	95% CI
<i>Ascaris</i> IgE seropositivity					
No	470/1915	24.5	1.0		
Yes	189/359	52.7	3.42	3.65	2.86-4.67
Allergic family history‡					
No	550/2007	27.4	1.0		
Yes	109/267	40.8	1.83	1.9	1.45-2.53
Sex					
Girls	240/1071	22.4	1.0		
Boys	419/1203	34.8	1.85	1.84	1.51-2.23
Age (yrs)					
5-7	152/606	27.3	1.0		
8-10	212/565	25.1	1.12	1.049	0.813-1.35
11-14	295/891	33.1	1.48	1.357	1.06-1.73
Siblings					
None	169/567	29.8	1.0		
1	354/1187	29.8	1.0	0.89	0.70-1.12
2	98/360	27.2	0.88	0.75	0.55-1.03
≥3	38/160	23.8	0.73	0.50	0.32-0.78
Parental education§					
1	36/145	24.8	1.0		
2	313/1131	27.7	1.16	0.97	0.69-1.37
3	180/625	28.8	1.23	1.01	0.70-1.45
4	103/286	36.0	1.70	1.48	0.98-2.22

*Number of children with allergen-specific IgE (at least 1 positive result of 4 tested allergens ≥0.35 IU/mL) versus total number of children in that category.

†Odds ratios (OR) adjusted for all other variables in the table. Adjusted odds ratios were used to estimate 95% confidence intervals (CI).

‡At least 1 parent with asthma or allergic rhinitis.

§Highest educational degree of mother or father: 1, eighth grade or lower; 2, tenth grade; 3, twelfth grade or technical college; 4, university.

newly *Ascaris* IgE-seropositive had a higher total IgE level at the first survey. A similar pattern was observed with the allergen-specific IgE. The prevalence of at least 1 positive RAST result increased in the group that became *Ascaris*-seropositive and decreased in the group that became seronegative. Sensitization to *D pteronyssinus* increased nearly 3-fold in the children with new *Ascaris* IgE seropositivity. The frequencies of a positive allergen-specific IgE were always higher in children who were ever *Ascaris*-IgE seropositive. Allergic rhinitis was most prevalent in the group who were *Ascaris* IgE-seropositive at both surveys. The biggest increase in the prevalence of allergic rhinitis from the first to second survey was observed in the group that became newly seropositive, whereas the association between the prevalence of asthma and *Ascaris* IgE seropositivity was weaker.

***Ascaris* IgE RAST class**

An increase in the level of *Ascaris* IgE RAST class was associated with a marked increase in total IgE levels, and the prevalence of specific IgE seropositivity and positive SPT results increased markedly (Table III). A history of a helminthic infection was not higher in children with low *Ascaris* IgE (RAST class 1) than in children with no *Ascaris* IgE, but they had higher total IgE levels and a higher prevalence of specific IgE against inhalant allergens, SPT reactions, allergic rhinitis, and asthma. Of the 61 children with RAST class III and higher, 66% were allergen-specific IgE seropositive, but only one child had allergic rhinitis.

Allergen-specific IgE

The relationship between IgE specific for inhaled allergen and *Ascaris* seropositivity was analyzed with data from the second survey in a logistic regression model (Table IV). *Ascaris* IgE seropositivity is a stronger risk factor than a positive family history of allergies. The incidence of seropositivity of specific IgE to inhalant allergens between the first and second surveys was also analyzed by an analogue model. Because of a lower number of cases (64), a significant risk was only observed with *Ascaris* IgE seropositivity (odds ratio, 2.6; confidence interval, 1.3-5.2).

DISCUSSION

We examined a population of schoolchildren, including a cohort group of about 700 children, from the former East Germany in 2 surveys that were 3 years apart. *Ascaris* IgE seropositivity was strongly associated with higher total IgE levels, specific IgE seropositivity against inhalant allergens, positive SPT reactions, and allergic rhinitis. The incidence of *Ascaris* seropositivity between the first and second survey was correlated with increased total IgE and the prevalence of allergen-specific IgE seropositivity and allergic diseases. A remission of *Ascaris* IgE was associated with decreases of total and specific IgE levels. It

was not possible to determine whether a decrease in the prevalence of allergic diseases also occurred because only lifetime and not point prevalence was determined in the questionnaire. Furthermore, it is likely that a delay in the manifestation of allergic disease after sensitization influences in part the differences in the prevalence of asthma and allergic rhinitis in the different cohort groups. The magnitude of the risk of a positive *Ascaris* IgE result could be estimated by using logistic regression analysis. After adjustment for sex, age, number of siblings, and socioeconomic status, a positive *Ascaris* IgE result was a stronger risk factor for allergic sensitization to inhalant allergens than a family history of allergies.

In the former German Democratic Republic, infection with *Ascaris* and other helminths was not very common, but it was still existent. There are only a few published population-based data about the prevalence of *Ascaris* species, *Toxocara* species, and other helminthic parasites in East Germany. Stool examinations in persons 14 to 20 years of age showed a prevalence of 1.5% for *Ascaris* species and 1.5% for *Trichuris trichiura* infection.²⁰ Other investigations found *Ascaris* eggs in 0.3% to 1% of stool tests.^{21,22} Compared with these studies, the 20.1% prevalence of *Ascaris* IgE seropositivity in the first study and 15.7% in the second study are high. In populations with a low prevalence of helminthic diseases, individual worm burden of infected persons is also very low. An average worm burden of 1 worm per infected, asymptomatic person has been estimated.²³ Thus tests for stool eggs appear to be a better source of diagnosis than an actual *Ascaris* infection, but they fail as tools for the diagnosis of infections with juvenile and male worms alone because they do not produce eggs. Additionally, previous helminthic infections would be missed. Therefore in a population with a low prevalence of helminthic diseases, stool testing markedly underestimates the frequency of worm infections. To investigate the role of sporadic and light intestinal helminthic infections on allergy-related immune response, it is more useful to measure *Ascaris* IgE as marker of helminthic contact.

Because we have no data from West German children about *Ascaris* IgE and allergic sensitization, a direct comparison between East and West German children is not possible. But with lower total IgE levels in West Germany,^{10,11} they have probably a lower prevalence of helminthic infection. Because we could demonstrate that helminthic infections enhance allergic reactivity, the higher prevalence of helminthic infections in East German children could not be the cause of the lower prevalence of allergies in the former East Germany.

Because of cross-reactivities with *Toxocara* species, and also to a lesser degree with *Necator americanus* (hookworm)²⁴ and *Trichuris trichiura*,¹⁶ *Ascaris* IgE is not specific for an ongoing *Ascaris* infection but rather a marker for past or present contact with helminths and the resulting immune response. The observed association between contact with cats and dogs in the first year of life and *Ascaris* IgE seropositivity may represent previous *Toxocara canis* or *Toxocara cati* infection. Studies of children in The

Netherlands and Ireland found *Toxocara* IgG antibodies in 7.6% of Dutch children aged 4 to 6 years and in 31% of Irish children aged 4 to 19 years.^{25,26} In East Germany higher prevalence rates have been reported for *Enterobius vermicularis*,²² but threadworms are noninvasive and therefore have little or no effect on IgE synthesis.²⁷

In asthmatic compared with nonasthmatic South African and Nigerian children, a higher SPT reactivity against *Ascaris* antigen has been found.^{6,28,29} These observations in a hyperendemic area suggested that patients who responded immunologically to parasitic infections may be predisposed to asthma. The other interpretation of these results was that asthmatic subjects exposed to *Ascaris* species are more likely to mount a reagenic response to parasite antigens.¹

Analyzing data from a cohort offers the opportunity to examine the influence of a new *Ascaris* seroreactivity on allergic sensitization. The increase in the frequency of specific IgE seropositivity against inhalant allergens between the first and second surveys in the group that became *Ascaris*-seropositive underlines the role of helminthic contact as a real risk factor. The children with incident *Ascaris* IgE seropositivity had high total IgE levels and a high prevalence of specific IgE at the first survey, suggesting that they were predisposed and had a basal higher synthesis of total and specific IgE. Another possibility is that some children were already infected but did not have measurable *Ascaris* antibodies at the time of the first survey.

Data from Venezuelan children^{7,8} also indicate that mild and sporadic intestinal helminthic infections can augment the expression of allergic reactivity. It has been demonstrated in children living in slum areas from Caracas that antihelminthic treatment caused a substantial increase in skin test reactivity and in specific IgE antibodies against house dust.⁷ SPT reactivity and specific IgE against *Ascaris* species also increased substantially. Treatment in this endemic area was interpreted as low-level contact, which causes a stimulation of a polyclonal IgE synthesis. Under conditions of heavy parasitic infections, allergic response could be inhibited by mast cell saturation.⁹ However, passive sensitization of heavily parasitized Indians suggested that the cutaneous mast cells still have free IgE receptors.³⁰ In our study children with high *Ascaris* IgE (RAST class 3 and more) also had a high frequency of specific IgE against inhalant allergens but a very low prevalence of allergic rhinitis, indicating that there could be an inhibiting effect of heavy infections caused by an extensive IgE response. The contradictory results may be explained, at least in part, by a consideration of the frequency, intensity, and type of infection and the time of first infection in life.

It is rare that the role of a potential risk or protective factor causes a discussion with such conflicting hypotheses as those proposed for the relationship between worms and allergies. The main reason is that the physiologic function of the IgE system is still not well understood even if nematode infection has been used extensively as an approach to understanding IgE regulation. How does enhanced IgE synthesis induced by parasite infestation influence the immune response to common inhaled allergens? Infection

of rats with *Nippostrongylus* species³¹ or of guinea pigs and mice with *Ascaris* species³² together with the third-party antigen ovalbumin yielded a potentiated and prolonged IgE response to ovalbumin. The clear involvement of a T_{H2}-type response explains the IgE predominance.⁵ Reactions of PBMCs of helminth-infected persons indicate that helminth-induced serum IgE levels are directly related to an increased capacity of PBMCs to produce IL-4 and inversely associated with IFN- γ production.⁴

From the different possibilities about the relationship between parasites and allergy, our data support best the second hypothesis that worms cause allergies or enhance allergic reactivity. Another possibility is that persons with an allergic predisposition react more likely with an IgE synthesis to all foreign proteins, either inhaled or in the gut. If this is true, one would expect a higher *Ascaris* reactivity in children with a family history of allergies. In our study, however, we found no difference in *Ascaris* seropositivity between children with an allergic family history and those without.

In conclusion, in this investigation we observed that higher IgE levels after *Ascaris* sensitization are associated with allergen-specific IgE seropositivity, positive SPT results, and higher rates of allergic rhinitis. Our findings support the hypothesis that low level contact with helminths enhances allergic reactivity.

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