

Total and specific IgE (house dust mite and intestinal helminths) in asthmatics and controls from Gondar, Ethiopia

F. G. SELASSIE, R. H. STEVENS*, P. CULLINAN†, D. PRITCHARD‡, M. JONES†, J. HARRIS†, J. G. AYRES§ and A. J. NEWMAN TAYLOR†

Gondar College of Medical Sciences, Gondar, Ethiopia, *Communicable Disease Surveillance Centre, Birmingham Heartlands Hospital NHS Trust, Birmingham, †Department of Occupational and Environmental Medicine, Imperial College (NHLI), London, ‡Department of Life Sciences, University of Nottingham, Nottingham and §Department of Respiratory Medicine, Birmingham Heartlands Hospital NHS Trust, Bordesley Green East, Birmingham, U.K.

Summary

Background The role, if any, of parasitosis in the development of asthma remains incompletely understood; both 'protective' and 'predictive' associations have been reported. We report a study which examined immunoglobulin (Ig) E responses to two common helminths in asthmatics living in Ethiopia.

Objective To compare the frequencies of specific IgE antibodies to *Ascaris* and *Necator* species and to Der p 1 among 84 adult asthmatics and a referent group of nonasthmatics.

Methods A case-control analysis.

Results Total IgE levels were not different between the two groups. The presence of specific IgE to Der p 1 was strongly associated with asthma ($P=0.001$). Raised levels of *Ascaris* ($P=0.010$) and *Necator* ($P=0.001$) specific IgE antibodies were more common among referents; there were no associations between specific IgE production to Der p 1 and either of the two parasites.

Conclusion These findings confirm the association between Der p 1 sensitization and asthma among urban, adult Ethiopians. While they also indicate a negative relationship with two indicators of helminth infestation it appears that this is not mediated through the immunological response to common aeroallergens.

Keywords: Africa, *Ascaris*, asthma, Der p 1, Ethiopia, helminth, *Necator*, specific immunoglobulin E

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Introduction

Studies of the association between infestation with intestinal helminths and asthma have been conflicting, suggesting both predictive and protective roles [1,2]. All have been cross-sectional, often using case-control analysis and taking microscopic evidence of current excretion of ova, or parasite burden after chemotherapy, as indicating helminthic exposure. We report a study in which we have related both house dust mite and helminth serology to clinically verified asthma in a population of adults living in an Ethiopian town.

Correspondence: P. Cullinan, Department of Occupational and Environmental Medicine, Imperial College (NHLI), 1b Manresa Road, London SW3 6LR, U.K.

Subjects and methods

We identified asthmatics from adult (≥ 16 years) outpatients attending the Gondar College of Medical Science (Ethiopia) with recurrent episodes of wheezy breathlessness and in whose case notes was recorded either a diagnosis of, or treatment for, asthma. A referent group of nonasthmatics was assembled from contemporaneous outpatients at the same hospital whose main complaint was non-respiratory and who had no recorded history of asthma or wheezy breathlessness. Although not formally matched, referents were chosen to reflect broadly the age and sex distribution of the case series.

All subjects with a peak flow greater than 60% of that predicted [3] by their age and sex underwent histamine

provocation testing using a deVilbis no. 40 hand held nebulizer. We asked those with a peak expiratory flow of less than 61% predicted to inhale two puffs of salbutamol. Bronchial hyperreactivity was defined by either a $PD_{20} \leq$ a cumulative dose of 4 μ mol of histamine or a >15% increase in peak flow 15 min after salbutamol.

Serum samples were collected from all participants and stored at -20°C . They were transported on ice to the UK where CAP (Pharmacia Upjohn, Uppsala, Sweden) tests were performed for total immunoglobulin (Ig) E concentration and IgE antibody to Der p 1 allergen. ELISA tests for IgE antibody to the excretory-secretory products of *Necator americanus* and *Ascaris lumbricoides* were performed using a previously described method [4]. All laboratory investigations were undertaken without knowledge of case status.

We classified as positive levels of specific Der p 1 IgE antibodies ≥ 0.35 kU/L; and for the helminth-specific IgE, optical densities in the upper quartile of each distribution (≥ 0.35 OD for *Ascaris* and ≥ 0.25 OD for *Necator*). The relationships between categorical variables were assessed by χ^2 tests and between continuous variables using *t*-tests and Wilcoxon's rank sum test. Using logistic regression (Egret, SERC, Seattle, WA, USA) we examined the associations between case status and sensitization to these allergens after adjustment for age, sex and concentration of total IgE.

Results

The average age of the subjects was 40, ranging from 17 to 67 years (Table 1); approximately half were women. Cases and referents were well matched on age and sex. Peak expiratory flow in the cases was, on average, 88% of the value predicted by their age, sex and height; among

referents the average value was 108%. Eighty one percent of cases, but only 4% of controls, had bronchial hyperresponsiveness.

Concentrations of total IgE antibodies in serum were almost uniformly high, with a median of 1345 kU/L (inter-quartile range 537–2577 kU/L). The mean level of total IgE was a little higher in cases but the difference was not statistically significant ($P = 0.26$) (Table 1).

Fifty subjects (33%) had raised levels of specific IgE to at least one helminth, 26 of them to both species. This was unrelated either to age or sex. The distributions of helminth-specific IgE antibodies, expressed as optical densities (OD) by case status, are displayed in Fig. 1. The geometric mean OD for *Ascaris* was lower among cases (0.19) than referents (0.31), a difference which was statistically significant ($P < 0.001$). A similar pattern was observed in the *Necator* measurements (geometric means 0.13 and 0.24, respectively, $P < 0.001$). A positive measurement of *Ascaris*- and *Necator*-specific IgE antibodies was, respectively, 2.1 ($P = 0.01$) and 2.7 times ($P = 0.001$) more common among controls than cases.

A high proportion of all subjects (111; 73%) had raised levels of specific IgE antibodies to Der p 1. These included all but six cases with asthma (93%), a proportion approximately twice as high as that among controls (48%, $P < 0.001$). This finding was consistent across the age range.

Of those with *Ascaris*-specific IgE antibodies, 68% also had antibodies to Der p 1 a proportion not significantly different ($P = 0.51$) from that among those without evidence of *Ascaris* antibodies. *Necator* and Der p 1 antibodies were similarly unrelated. These findings were also unrelated to age. Analyses using 'continuous' measurements of IgE did not materially alter the observations.

Regression analysis confirmed an independent association between asthma and sensitization to Der p 1 (odds ratio 14.2, 95% CI 5.5–36.9); and inverse associations between asthma and the presence of specific antibodies to *Ascaris* (OR 0.38, 0.18–0.80) or *Necator* antibodies (OR 0.28, 0.13–0.60) or either helminth (OR 0.28, 0.14–0.56). Age, sex and level of total IgE did not significantly confound any of these relationships.

Discussion

Our findings indicate an association between asthma in an urban African setting and specific IgE production to *Dermatophagoides pteronyssinus* — or an immunologically equivalent antigen. In this sense the results echo those from a cross-sectional survey of self-reported asthma in a different Ethiopian town [5]; in that study the slightly lower estimated odds ratio (11.0) may reflect the less stringent criterion used to define asthma, and the wider age range of their studied population. We also found an inverse

Table 1. Details of cases and controls

	Cases	Controls
<i>n</i>	84	69
Mean age (range)	41 (17–66)	39 (18–67)
Female, <i>n</i> (%)	40 (48)	32 (46)
Expected PEF*, mean (SD)	394 (84)	407 (95)
Observed PEF, mean (SD)	360 (110)	452 (84)
Bronchial hyperreactivity, <i>n</i> (%)	68 (81.0)	3 (4.4)
Total IgE, median kU/L	1411	1224
Positive <i>Ascaris</i> IgE, <i>n</i> (%)	14 (17)	24 (35)
Positive <i>Necator</i> , IgE, <i>n</i> (%)	12 (14)	26 (38)
Positive Der p 1 IgE, <i>n</i> (%)	78 (93)	33 (48)

*Peak expiratory flow.

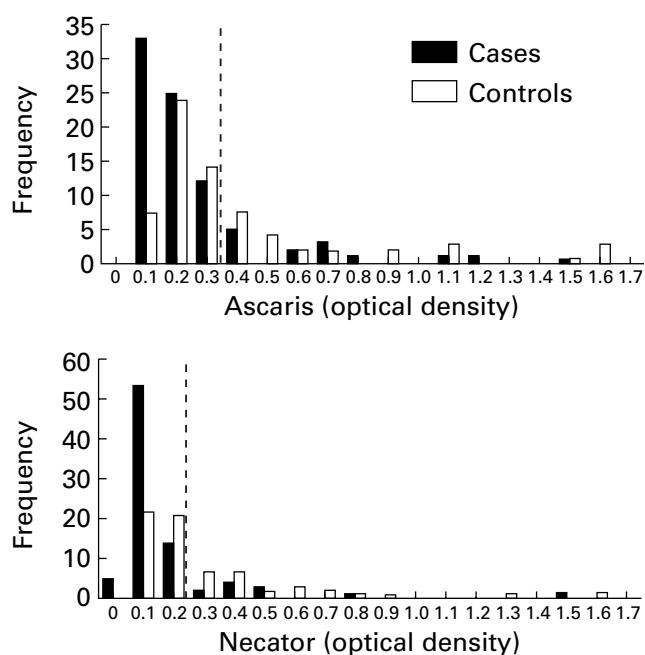


Fig. 1. Distributions of optical densities to *Necator* and *Ascaris* among cases and controls. The dotted lines mark cut-off points between 'positive' and 'negative' levels

relationship between asthma and evidence of infection with *Ascaris* and *Necator* parasites. However, the presence of IgE antibodies to *D. pteronyssinus* in serum was not related to immunological evidence of infection with either *Ascaris* or *Necator*.

To our knowledge, this is the first study of asthma in Africa to employ a serological measurement of helminth infestation. In order to ensure clinical specificity we also confirmed a diagnosis of asthma with physiological measurement of bronchial hyperresponsiveness. By selecting asthmatics and a referent population from the same clinical setting we aimed to avoid major social or economic differences between the two groups; the alternative — comparison with 'community' controls — would have risked confounding by those factors, many inscrutable, which determine hospital attendance in this population. We believe it improbable that our referent group was selected on the basis of disease related to helminth infestation.

The reality of any relationship between parasitosis and asthma, and if present the direction of its effect, remain uncertain [1,2]. Case-control designs such as ours, lack the

ability to distinguish any temporal sequence in the two conditions, a deficit which experimental data suggest may be important [6]. However, we believe that these findings are a useful addition to the debate although their interpretation rests on two premises: firstly, that evidence of immunological sensitization to Der p 1 represents, in this population, the 'atopic' state; and secondly, that the presence of specific IgE antibodies to helminths in adulthood reflects earlier exposure to these parasites, initially in childhood. Under these assumptions, our findings provide support for the hypothesis that the increasing prevalence of asthma reported in many parts of the world is a consequence of improved hygiene and lower rates of childhood infection. However, they also imply that this effect is not mediated through the immunological response to common environmental allergens ('atopy') but by determinants which translate IgE-associated sensitization into asthma.

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Conflicts of interest: none.

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