

Negative association of *Enterobius* infestation with asthma and rhinitis in primary school children in Taipei

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Summary

Background The relationship between allergy and parasites has been controversial, especially in non-tropical countries. *Enterobius vermicularis* (human pinworm) is the most prevalent intestinal parasite in industrialized countries.

Objective To examine the association between pinworm infestation and allergy in primary school children.

Method Peri-anal tape test for pinworm is routinely performed in Taipei primary schools. We collected data from school records and questionnaires distributed to all children in four primary schools grades 1 through 6 ($n = 3107$).

Results The prevalence of physician-diagnosed asthma (9.3% vs. 14.1%, $P = 0.007$) and allergic rhinitis (27.4% vs. 38.3%, $P = 0.001$) was lower in pinworm-positive compared to uninfested children. Pinworm was not correlated with atopic dermatitis or parent allergy. With logistic regression controlling for sex, parent allergy and lower respiratory infection, current asthma (OR = 0.25, 95% CI 0.10–0.63) and rhinitis (OR = 0.61, 95% CI 0.45–0.84) were negatively associated with pinworm. Among children in grades 3–6 who had no asthma or rhinitis before age 7, those with early infestation (pinworm diagnosis at or before grade 1) had a lower risk of having diagnosis of rhinitis during school years, compared to the uninfested group (5.4% vs. 12.3%, $P = 0.03$; adjusted OR = 0.47, 95% CI 0.21–1.02).

Conclusions We identified a negative association between pinworm infestation and allergic airway diseases, which could in part be attributed to protective effect of pinworm infestation on development of allergic symptoms. Other mechanisms of association could not be ruled out.

Keywords allergy, asthma, *Enterobius*, epidemiology, pinworm, parasites, rhinitis

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Introduction

The relation between parasite infestation and allergic diseases has been difficult to clarify because of inconsistency among studies. Ecologic epidemiology has found an inverse association between parasitoses and allergy, i.e. allergic diseases are more prevalent in affluent countries [1]. However, regional studies have yielded equivocal and sometimes conflicting results, indicating complex interactions between parasite and other modulators of human allergic response. In one study, anti-*Ascaris* treatment reduced serum total IgE level while it increased allergen-specific IgE levels [2], suggesting that the polyclonal stimulation of IgE production by parasites can diminish specific IgE responses and allergic reactivity [3]. In another study, parasite was negatively associated with asthma but not mediated through lowering IgE response to allergens [4]. Still others found either no association between parasite and asthma

[5, 6], or a positive association between IgE and parasites, IgE and allergens, and prevalence of asthma or rhinitis [7, 8]. Thus, the role of parasites in allergic diseases remains unclear.

Although intestinal parasites are uncommon in affluent communities, *Enterobius vermicularis* (human pinworm) is a significant exception. Prevalence in the USA is estimated to be 20–42 million cases, with the greatest rate in children between the ages of 5 and 14 years [9]. About 21% of children 4–10 years old were symptom-free carriers of pinworm in a Swedish town [10]. One study in the UK found no association between pinworm and asthma, but the study included a limited number of cases and controls [11]. Screening for *Enterobius* infestation in primary school children has been routinely carried out in Taipei city for more than two decades. Although the carrier rate has been declining, an average of 5% is still seen in school entrants. On the other hand, the prevalence of asthma in Taipei primary schools has increased from 1.5% in 1974 to more than 10% in recent years [12], and about half of teenagers in this city were sensitive to mite allergens [13]. The screening system for *Enterobius* and the high prevalence of allergy provided the backdrop for this investigation.

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Materials and methods

Study population and questionnaire

A questionnaire was distributed to all the children in four primary schools (1st to 6th grade, $n = 3110$) in Taipei, which was completed by parents or other guardians. The questionnaire inquired about physician diagnosis of asthma, allergic rhinitis, or atopic dermatitis, and the age of first diagnosis. 'Current asthma' and 'current rhinitis' referred to children with diagnosis and whose symptoms were present in the previous 12 months. 'Parent allergy' was physician-diagnosed asthma or allergic rhinitis in either of the parents. 'Lower respiratory infection' was defined as physician diagnosis of pneumonia, bronchitis, or bronchiolitis before the age of 6. 'House dampness' was defined as the presence of either visible mould growing on walls, paint sloughing, or water damage in the house. The survey was carried out during February and March of 2001. All but three people surveyed completed key questions in the questionnaire ($n = 3107$).

Parasite infestation

All primary school students in Taipei city were examined by peri-anal tape test for *Enterobius* eggs in the 1st, 3rd and 5th grades. Some kindergartens also participated in the screening programme. Early morning presses were made by parents, and the tapes were examined by qualified technicians in the Parasitology Laboratory of Department of Health, Taipei City Government. Parents of *Enterobius* carriers were notified and treatment was given in school. Among the 126 primary schools of Taipei, the *Enterobius* carrier rate in 1st-grade students averaged 5.2% (range 1.7–15%) in the year 2000. Fecal specimen examination was not performed, but the carrier rate of intestinal parasites other than *Enterobius* in Taipei was less than 0.1%. Four schools with relatively high infestation rates were included in this study. The questionnaire inquired whether the child had been diagnosed as an *Enterobius* carrier, and the

age of diagnosis. In two of the four schools, tape-test records in schools were used as the reference for self-reported *Enterobius* carrier status, and the concordance rate was 99.3%. Children first diagnosed of pinworm at or before grade 1 were categorized as 'early infestation' ($n = 359$), while those diagnosed at 3rd grade ($n = 59$) or 5th grade ($n = 6$) as 'late infestation'.

Statistical methods

Characteristics of *Enterobius*-negative and -positive school children were compared by chi-square or Student's *t*-test. The association of pinworm infestation with asthma and allergic rhinitis was examined by logistic regression analysis with stepwise selection procedure. Possible interactions between pinworm and other risk factors in relation to allergy were examined by stratified chi-square and Breslow–Day test for homogeneity of odds ratios (OR). Significance level of 0.05 was used for all tests. All statistical analyses were made using the SAS software (release 8.01, SAS Institute, Cary, NC, USA).

Results

Enterobius infestation was identified in 429 (13.8%) of the school children. Among them, 359 (83.7%) were first diagnosed at or before grade 1. There was no difference in the *Enterobius*-positive and -negative groups in terms of sex, sibling number and parent education level (Table 1). The pinworm-infested children were more likely to have siblings who were also infested. Children who were infested with *Enterobius* were less likely to have a diagnosis of asthma or rhinitis, but diagnosis of atopic dermatitis was not related to pinworm infestation. Atopic status of parents was not related to pinworm in school children. The pinworm infestation rates in children who had no, one, or two allergic parents were 14.3, 12.0, and 15.5%, respectively ($P = 0.25$).

Table 1. Characteristics of *Enterobius* peri-anal tape test-negative and -positive school children

	Enterobius		P-value
	Negative	Positive*	
Number	2678	429	
Male (%)	50.9	53.6	0.29
Sibling number (mean $\pm$ SD)	1.48 $\pm$ 0.97	1.51 $\pm$ 0.93	0.60
Parent education (% college or higher)	26.5	26.2	0.91
Parent asthma (%)	3.5	3.0	0.61
Parent allergic rhinitis (%)	26.7	24.7	0.39
Sibling allergic rhinitis (%)	20.6	19.4	0.55
Lower respiratory infections (%)	19.5	19.1	0.85
Otitis media (%)	19.3	22.1	0.16
Sibling <i>Enterobius</i> positive (%)	2.1	13.8	0.001
Asthma diagnosis ever (%)	14.1	9.3	0.007
Asthma with current symptoms (%)	5.6	2.8	0.015
Age of asthma diagnosis (mean $\pm$ SD)	4.18 $\pm$ 2.54	4.13 $\pm$ 2.16	0.88
Allergic rhinitis diagnosis ever (%)	38.3	27.4	0.001
Rhinitis with current symptoms (%)	29.0	20.3	0.001
Age of rhinitis diagnosis (mean $\pm$ SD)	4.95 $\pm$ 2.33	5.06 $\pm$ 2.19	0.61
Atopic dermatitis (%)	9.8	9.6	0.88

*Positive in any of the three surveys at the 1st, 3rd, and 5th grade.

Table 2. Association of *Enterobius* infestation with current asthma and allergic rhinitis after adjustment for personal and family factors

	Asthma		Allergic rhinitis	
	OR	95% CI	OR	95% CI
Male versus female	–	–	1.78	1.46–2.18
Parent asthma	4.44	2.40–8.22	2.09	1.30–3.36
Parent allergic rhinitis	1.56	1.05–2.32	3.84	3.12–4.72
Atopic dermatitis	1.70	1.01–2.87	2.34	1.68–3.26
Lower respiratory infection	5.83	3.97–8.57	2.68	2.11–3.41
Otitis media	–	–	1.68	1.32–2.15
House dampness	1.49	1.02–2.17	–	–
<i>Enterobius</i> infestation	0.25	0.10–0.63	0.61	0.45–0.84

Initial variables were sex, age, number of elder siblings, number of residents in the house, *Enterobius* infestation, parent education (categorized into two groups), parent asthma, parent allergic rhinitis, lower respiratory infection before age 6, otitis media before age 6, house dampness and atopic dermatitis. Stepwise selection was used to select variables into the final model with significance level of less than 0.05. –, Not selected in the final model.

Table 3. Diagnosis of asthma or rhinitis during school years in grade 3–6 children according to three groups of *Enterobius* infestation

	Diagnosis of <i>Enterobius</i>			<i>P</i> -value
	Never	Early	Late	
Parent asthma or rhinitis (<i>n</i> , %)	762/2678 (28.5)	90/359 (25.1)	17/65 (26.2)	0.38
Asthma diagnosis (<i>n</i> , %)	41/1577 (2.6)	3/196 (1.5)	0/59 (0.0)	0.31
Rhinitis diagnosis (<i>n</i> , %)	146/1187 (12.3)	9/166* (5.8)	7/49 (14.3)	0.029

**P* = 0.009 compared with the 'Never' group.

Table 4. Prevalence of *Enterobius* infestation according to age of diagnosis of three atopic diseases

	Diagnosis of atopic disease			<i>P</i> -value
	Never	Before or at age 2	After age 2	
Asthma (<i>n</i>)	2689	125	293	0.026
% <i>Enterobius</i>	14.5	9.6	9.6	
Allergic rhinitis (<i>n</i>)	1965	158	984	0.001
% <i>Enterobius</i>	15.9	8.2	10.5	
Atopic dermatitis (<i>n</i>)	2804	132	171	0.92
% <i>Enterobius</i>	13.8	14.4	12.9	

We examined the relationship between pinworm infestation and asthma/rhinitis cases who had symptoms within the past 12 months. *Enterobius* infestation was negatively associated with current asthma and allergic rhinitis in logistic regression analysis with adjustment for familial and personal risk factors (Table 2). By stratified analysis, we did not find interactions between pinworm and other risk factors in relation to asthma, such as parent history of asthma, lower respiratory infection, otitis media and house dampness.

To better define the effect of pinworm infestation on later development of asthma and rhinitis, we limited the analysis to

grades 3–6 school children who did not have diagnosis of asthma or allergic rhinitis before the age of 7. These children were categorized into three groups by the age of first diagnosis of *Enterobius*: never, early (before or at grade 1), or late (first diagnosed at grade 3 or 5). Among children who have not had asthma diagnosis before age 7, those with *Enterobius* were less likely to have asthma diagnosis in school years, but the difference did not reach statistical significance (Table 3). Among non-asthmatic children who had no allergic rhinitis before age 7, the early infestation group was less likely to have allergic rhinitis in school years compared with the uninfected group. In logistic regression analysis controlling for other risk factors (sex, age, parent asthma, parent rhinitis, lower respiratory infection and house dampness), pinworm was associated with a reduced risk (OR = 0.47, 95% CI 0.21–1.02). There was no significant difference in rhinitis prevalence between the uninfected and the late infestation groups.

We also examined the association between pinworm infestation and having diagnosis of asthma, allergic rhinitis, or atopic dermatitis in early childhood (at or before age 2). Asthma and allergic rhinitis, whether diagnosed before or after age 2, were associated with lower prevalence of *Enterobius*, while atopic dermatitis was not associated with *Enterobius* (Table 4).

Discussion

With the help of the pinworm screening in Taipei primary schools, we identified a negative association between *Enterobius* infestation and allergic airway diseases. The association remained significant after controlling for several risk factors for asthma and rhinitis, such as parent allergy history and early childhood infections. Theoretically, the negative association between asthma/rhinitis and pinworm could be interpreted as either: (i) pinworm infestation protected the individual from developing allergy; (ii) allergic individuals had better defense to pinworms, resulting in eradication of parasites or lower parasite burden; or (iii) the combination of both effects.

To test directly if pinworm could protect against allergic diseases, a follow-up study is required. Relying on the self-reported age of first diagnosis of pinworm infestation, asthma

and allergic rhinitis, we examined the association retrospectively. By excluding children who had diagnosis of asthma or rhinitis before age 7 (Table 3), it could reasonably be assumed that in the early infestation group pinworm infestation occurred before asthma or rhinitis, which developed in school years. Although asthma cases were too few to allow meaningful discussion, the early infestation group had lower occurrence of rhinitis. Thus the data suggested that early pinworm infection could be protective, at least in term of allergic symptoms. On the other hand, the late infestation group had similar rhinitis prevalence to the uninfected group, but the case number was probably less than adequate for definite description. It is possible that the time of infestation was important in modulating the immune system; this was suggested by an East German study which found changes in allergen-specific IgE levels in children who turned from *Ascaris* IgE sero-negative to sero-positive during primary school years [7].

Parasite infestation may protect individuals from developing allergy through polyconal stimulation of IgE production. The non-specific IgE can diminish specific IgE responses, inhibit mast cells and inhibit allergic reactivity [3, 14]. Other mechanisms independent of IgE are also possible, as shown in an Ethiopian population whose mite-specific IgE levels were not associated with either *Ascaris*- or *Necator*-specific IgE [4]. The mechanism for pinworm is more likely to be IgE-independent, because pinworm infestation was not correlated with elevated total serum IgE in either allergic or non-allergic children [11].

It was reported that in populations endemically exposed to helminthes, atopic individuals have significantly lower total IgE levels, higher specific anti-parasite IgE concentrations, and less intense helminth infections than non-atopic counterparts [2]. Asthmatic children also seemed to have fewer symptoms of parasitosis [6]. It is suggested that allergic individuals may have a genetic predisposition to be protected from intestinal parasites [15]. Thus, the negative association in this report could also be interpreted as 'allergic individuals had better defense to pinworms'. We were unable to test this possibility, since the actual time of infestation was unknown. However, if some genetic factor associated with allergy did provide a better defense to parasites, it would be expected that children of allergic parents were less likely to become infested. This was not the case here (Tables 1 and 3), and the finding is suggestive of mechanisms other than genetic factor, by which allergic individuals may have less parasite infestation.

Interestingly, the negative association between allergy and pinworm was seen only for asthma and rhinitis, but not for atopic dermatitis. This was not due to age differences (Table 4), but suggested different patterns of interaction between pinworm and the three diseases. History regarding food allergy in early childhood and serum pinworm- and allergen-specific IgE levels could be helpful to discern different pathways of association. Another limitation in interpreting the data is that the extent of childhood exposure to pinworm eggs was undetermined, making it unknown whether lack of infestation meant lack of exposure or success in eradication.

Ecologic epidemiology has suggested a negative association between parasites and allergy, and a handful of studies were supportive of this relationship [2, 16]. Studies done in non-tropical countries have either shown no correlation [5, 6, 11] or positive association between parasites and allergy [7]. It is likely

that different parasites, parasite burden and the age of infestation all had different effects on the immunologic system and the development of allergy. Also, the parasite effect has to be considered in the context of other risk factors, such as other childhood infections, allergen exposure, diet and genetic propensity to atopy. The population in this study lived in a non-tropical area with a lifestyle similar to Western societies. Because pinworm is the most prevalent parasite in industrialized communities, its study bares high relevance to the modern trend in allergic diseases.

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References

- 1 Masters S, Barrett-Connor E. Parasites and asthma- predictive or protective? *Epidemiol Rev* 1985; 7:49–58.
- 2 Lynch NR, Hagel IA, Palenque ME et al. Relationship between helminthic infection and IgE response in atopic and nonatopic children in a tropical environment. *J Allergy Clin Immunol* 1998; 101:217–21.
- 3 Lynch NR, Goldblatt J, Le Souef PN. Parasite infections and the risk of asthma and atopy. *Thorax* 1999; 54:659–60.
- 4 Selassie FG, Stevens RH, Cullinan P et al. Total and specific IgE (house dust mite and intestinal helminths) in asthmatics and controls from Gondar. *Ethiopia Clin Exp Allergy* 2000; 30:356–8.
- 5 Leeman BJ, Cabrera MR. No association found between *Strongyloides* infestation and asthma. *J Asthma* 1995; 32:57–62.
- 6 de Almeida MM, Arede C, Marta CS et al. Atopy Enteroparasites *Allergie Immunologie* 1998; 30:291–4.
- 7 Dold S, Heinrich J, Wichmann HE, Wjst M. *Ascaris*-specific IgE and allergic sensitization in a cohort of school children in the former East Germany. *J Allergy Clin Immunol* 1998; 102:414–20.
- 8 Alshishtawy MM, Abdella AM, Gelber LE, Chapman MD. Asthma in Tanta, Egypt: serologic analysis of total and specific IgE antibody levels and their relationship to parasite infection. *Int Arch Allergy Appl Immunol* 1991; 96:348–54.
- 9 Russell LJ. The pinworm, *Enterobius vermicularis*. *Prim Care* 1991; 18:13–24.
- 10 Herrstrom P, Fristrom A, Karlsson A, Hogstedt B. *Enterobius vermicularis* and finger sucking in young Swedish children. *Scand J Primary Health Care* 1997; 15:146–8.
- 11 Jarrett EEE, Kerr JW. Threadworms and IgE in allergic asthma. *Clin Allergy* 1973; 3:203–7.
- 12 Hsieh K-H, Shen J-J. Prevalence of childhood asthma in Taipei, Taiwan, and other Asian Pacific Countries. *J Asthma* 1988; 25:73–82.
- 13 Huang S-L, Shiao G-M, Chou P. Association between body mass index and allergy in teenage girls in Taiwan. *Clin Exp Allergy* 1999; 28:323–9.
- 14 Bell RG. IgE, allergies and helminth parasites: a new perspective on an old conundrum. *Immunol Cell Biol* 1996; 74:337–45.
- 15 Scott ST. Parasites and asthma/allergy: what is the relationship. *J Allergy Clin Immunol* 2000; 105:205–10.
- 16 van den Biggelaar AHJ, van Ree R, Rodrigues LC et al. Decreased atopy in children infected with *Schistosoma heamatobium*: a role for parasite-induced interleukin-10. *Lancet* 2000; 356:1723–7.