

Zoonoses and Asthma

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Type I hypersensitivity is characterized by an immunological response mediated by Th2 lymphocytes and involving the synthesis of immunoglobulin E (IgE) proteins and eosinophils. This pathogenic response of Th2 is crucial in the development of allergic disease.¹ Bronchial asthma is more common in developed countries than in developing ones, suggesting the presence of environmental factors related to socioeconomic and health conditions that favor the appearance of atopy and asthma.² In populations living in less economically favored parts of the world, particularly in rural areas, atopy and asthma rates are very low.³ The International Study of Asthma and Allergy in Childhood revealed marked differences in the prevalence of allergic disease symptoms between countries.⁴ The fact that certain environmental factors can influence the appearance of clinically apparent lung inflammation associated with allergic sensitization has been recognized for years. The increase in allergic diseases has been attributed to the so-called hygiene hypothesis⁵ which proposes that natural or programmed exposure to infectious agents at an early age converts the immune system into producing predominantly Th1 lymphocytes, lowering the intensity of the Th2 response and the likelihood of developing atopic disease.⁶ Many infectious diseases such as parotiditis or hepatitis A protect against the development of atopy. Early exposure to infectious agents has also been found to protect against asthma.

Intestinal helminth infections (or geohelminths) are the most prevalent childhood infections in much of the world to the extent that over 1 billion people are infested by at least 1 geohelminth or parasite.⁷ *Ascaris lumbricoides*, *Trichuris trichiura* and *Necator americanus* are the most common. The possible association between geohelminth infections and atopy⁸⁻¹⁰ and the presence of respiratory symptoms such as wheezing¹¹⁻¹³ has been under investigation for many years.

An increasing incidence of atopy, which is a clear risk factor for asthma, is an observation made in industrialized countries^{14,15} but not in developing countries.^{9,16-18} Endemic parasitic infestation, clinically apparent in developing regions, could be responsible for the dissociation between allergic sensitization and the expression of allergic disease.¹³ Some authors hold that helminth intestinal infections, endemic in tropical countries, induce a polyclonal stimulation of IgE synthesis, thereby modulating the kinetics of the FCεRI mastocyte receptors and conditioning the expression of allergic reactivity in these populations.¹⁸⁻²⁰ The chronic exposure to helminths then, particularly helminths with a systemic phase in their life cycle, such as *A lumbricoides*, could have an antiinflammatory effect and thus suppress the allergic inflammation provoked by IgE in the respiratory tract.¹³ This hypothesis was proposed in the late 1960s and early 1970s.^{21,22}

In a clinical trial in Venezuela in the early 1990s, Lynch et al²³ evaluated a 22-month anthelmintic treatment and found a marked increase in sensitization to *Dermatophagoides*—from 17% to 68%—compared with a control group of untreated patients whose sensitization to *Dermatophagoides* decreased from 26% to 16%. In a similar study carried out in Gabon, *Schistosoma* infestation in children was associated with reduced risk of skin sensitization to dust mites, an effect apparently attributable to interleukin-10 rather than IgE inhibition.²⁴ Reduction of allergic sensitization in adults infested with helminths in Gambia has also been described.⁹

Interest in the role parasitic infections have in allergic processes, particularly asthma, waned in the middle 1990s but has revived recently. Despite the increased rate of sensitizations to common inhaled allergens, Lynch et al²³ obtained a substantial improvement in asthma among patients treated with antiparasitics, improvement which disappeared 2 years after cessation of treatment. In a very recent study in Ecuador, Cooper et al²⁵ found that intestinal parasites protected against allergic sensitization and bronchospasm induced by exercise but not against other allergic symptoms.

Evidence pointing to a possible relation between parasitic infections and wheezing or asthma is even less

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conclusive. In the above-mentioned study in Gabon,²⁴ information on symptoms was not given, while another study in Brazil²⁶ found that asthma was less intense in *Schistosoma*-infected children. Children infected with *Enterobius* in Taiwan were less likely to be diagnosed with asthma (allergic sensitization was not reported) suggesting that this type of infection has a protective effect.²⁷ Similarly, Cooper et al²⁵ observed that parasitic infestation was associated with a marked reduction in the risk of exercise-induced wheezing but not of other allergy symptoms such as asthma, rhinitis, or eczema.

A study carried out in Gambia, however, did not reveal any association between helminth infection and wheezing⁹ while another in China found that *Ascaris* infection was associated with a higher incidence of asthma and allergy sensitization, although in the latter study patients came from a highly selected population.²⁸ In Venezuela severity of asthma was improved by the eradication of parasites in asthmatic children.²³ A study in Ethiopia found differing results:¹³ an intense and marked reduction of the risk of wheezing related with the presence of parasitic infection in both adults and children; at the same time, despite an increased risk of *Dermatophagoides pteronyssinus* sensitization in parasite-infested adults from rural regions, this population did not show higher risk of wheezing. Among the children, however, no relation was found between allergic sensitization and parasitic infection or wheezing.

Several explanations can account for the clear discrepancies between the studies. Firstly, there is the possible existence of false positives and negatives, propitiated in some studies by the use of epidemiological questionnaires that were not validated. Secondly, all the cited studies looked for associations with an apparently dominant endemic parasite but none analyzed the role of possible concomitant parasites; moreover, none of the studies examined the environmental importance of other factors such as exposure to endotoxins, allergens, hepatitis A virus, or any factors associated with asthma, all of which can modify clinical and immunological responses. Thirdly, some of the effects might be parasite-specific and contradictory results could be attributable to the simultaneous presence of more than one parasitic infestation. We consider this explanation to be one of the more plausible as the predominant antigen would modify the main immunological response of the population exposed to it.

In developed countries, where the predominant antigens are aeroallergens, allergic sensitization constitutes one of the main risk factors of asthma.^{14,15} Furthermore, risk is proportionally greater wherever allergen concentration is higher,²⁹ explaining why the rate of asthma in our region (the Canary Islands), where house dust mites are prevalent and persistent, is double the rate of mainland Spain.^{30,31} Our group studied the possible association between asthma and the parasite *Toxocara canis* in a population in Gran Canaria with high exposure to this parasite. We found that asthmatics presented significantly higher titers of IgG-precipitating antibodies

against *T canis* than did the nonasthmatics in the control group^{32,33} and that these differences diminished with age. The presence of such antibodies does not seem to protect against the development of atopy or asthma, at least in our region where the environmental allergen concentrations are particularly high. Consistent with this hypothesis, Selassie et al³⁴ found high titers of IgE specific to *Ascaris* and to *Dermatophagoides* in asthmatics in urban districts of Ethiopia.

Given that allergic sensitization is an important risk factor of asthma in most developed countries, the absence of this association in many tropical populations deserves close analysis. The confirmation of the inverse relation between them suggested by several studies would have important implications for the theory of T cell immunity polarization in allergic disease pathogenesis. Given that eradicating parasite infestations is a universal health care concern, it is important to know the consequences that eradication might have.

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