

The relationship of parasites to asthma

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Relevance of parasitic infection for the study of asthma genetics

Parasitic infection has been associated with a linkage study suggesting that susceptibility to *Schistosoma mansoni* infection is controlled by a locus on chromosome 5q31-q33 [1]. This is the same locus that is thought to be related to total serum IgE level and possibly bronchial responsiveness. This is further supported by a segregation analysis which suggests a major gene influencing control of interleukin-5 production in humans infected with *S. mansoni* [2]. In addition, Palmer *et al.* have suggested a link between the FC ϵ receptor on chromosome 11 and total serum IgE levels in endemically parasitized Australian Aborigines [3]. These papers suggest that parasitic infection may be linked to various atopy and asthma phenotypes and, hence, may be relevant to the study of asthma as the disease and, specifically, to asthma genetics.

Relationship of parasites to asthma

Masters and Barrett-Connor summarized a number of cross-sectional and case-control studies which investigate the relationship of parasites to asthma [4]. Ecological data support an inverse relationship between countries with a high prevalence of parasitic infection having very low asthma rates and countries with high asthma rates having very low rates of parasitic infection.

The data summarized by Barrett-Connor do remain equivocal. In particular, small case control studies failed to substantiate such a relationship although statistical power to detect a relationship is weak in these investigations.

Immunological mechanisms by which parasites might protect against asthma

At least three theories have been developed to suggest how immunologically parasitic infection might protect against the development of asthma. Ogilvey *et al.* hypothesized that high levels of polyclonal IgE would bind to mast cell FC receptors, effectively cross-linking the mast cell and preventing binding for allergen specific IgE [5]. Other potential mechanisms include the secretion of mast cell inhibitory

factors and decreased cholinergic sensitivity [6,7]. It is, however, well known that certain helminthic parasites such *Ascaris lumbricoides* and *Ankylostoma duodenale* have a lung phase associated with respiratory symptoms. *Ascaris* infection is well known as a model for inducing allergy and asthma in mammalian models of the disease. Suffice it to say that it remains unknown whether parasitic infection is associated with the development of asthma or whether parasitic infection is potentially protective for the development of this disorder. The third possibility is that parasitic infection is merely a marker for an increased number of bacterial and viral as well as parasitic infections in early childhood, hence, in general stimulating immune function and resistance to the development of asthma.

What remains unique and intriguing about parasitic infection is that it induces a relative TH₂ response associated with high levels of total and parasite specific IgE skin test reactivity to parasites, yet the absence of hay fever and asthma symptoms at least with high levels of infection. Lynch *et al.* have demonstrated the importance of socio-economic status, and nutrition as important environmental modifiers of the host parasite relationship [8]. Lynch *et al.* have also demonstrated in a longitudinal cohort that intensive treatment of parasites is associated with the development of skin-test reactivity to common aeroallergens. They have also demonstrated that the clinical improvement of asthma after anti-Helminth treatment [9]. In this study 89 childhood asthmatics were treated with Albendazole 400 mg monthly for 1 year and asthma medications were continued. Spirometry, methacholine challenge tests, skin test, total and specific IgE levels were monitored. Treatment for helminthic parasites, specifically *T. trichiura* and *A. lumbricoides* resulted in clinical improvement in allergy phenotypes and in asthma.

Issues requiring further investigation

A longitudinal cohort study is clearly needed to investigate whether parasitic infection is indeed related to asthma incidence. In addition, the influence of age of onset of the parasitic infection, the presence of multiple infections and the relationship of these infections to asthma and intermediate phenotypes to Type 1 hypersensitivity are deserving of further investigation.

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The parasite/asthma relationship has been hypothesized for a number of years and never completely investigated. It is, clearly, worthy of further attention.

References

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