

Differences in asthma between rural and urban communities in South Africa and other developing countries

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Studies on wheezing or asthma in Africa have consistently shown low levels in the villages and increasing prevalence with urbanization.¹⁻⁴ In many of those studies, the authors focused on differences in helminth infection to explain the changes in the prevalence of wheezing.^{2,5-7} The arguments for this approach are that infestation is common, helminths are known to induce IgE responses, and children in rural Africa generally have high total serum IgE levels despite a low prevalence of allergic symptoms.^{2,4} In contrast, helminths might be less common in many towns because of greater access to sanitation and anthelmintic drugs.^{2,4}

Ascaris lumbricoides is the prototypical geohelminth that infects more than a billion persons worldwide and could influence allergic disease in several ways. First, the larval form of *Ascaris* passes through the lungs, which can give rise to wheezing with or without the infiltrates of Loeffler's syndrome.⁸ Second, increased serum IgE levels might act to inhibit binding of specific IgE to mast cells. Third, the inflammatory or other systemic effects of this worm might inhibit the production of IgE antibodies to inhalant allergens, such as dust mite. Given the possible range of effects of these parasites, it is not surprising that the results of studies investigating the effects of helminths on wheezing have been inconsistent.^{2,5-7} A meta-analysis of cross-sectional studies showed that "asthma" was inversely associated with the presence of hookworm infection but positively associated with *Ascaris* infection.⁹ The latter finding is supported by recent studies showing a positive association between asthma symptoms or severity and ascariasis measured either by the presence of eggs in the stool or specific IgE levels.¹⁰ However, studies of the effects of removing helminths by means of antihelminthic treatment on wheeze have shown very different results.^{6,7}

The article from Drs Calvert and Burney¹¹ in the current edition of the *Journal* addresses the effects of *Ascaris* on exercise-induced bronchospasm (EIB) and atopy in a case-control study of schoolchildren in urban and rural areas of South Africa. The results show that *Ascaris* infection, as judged by the presence of infection but not by sensitization (data for IgE specific for *Ascaris*

are not presented), can be positively associated with EIB independent of the association between EIB and sensitization to inhalant allergens.¹¹ However, their results suggest equally that *Ascaris* infestation can have negative effects on skin test reactivity to inhalant allergens, a finding consistent with previous studies.¹² The positive data relating *Ascaris* infection to EIB (odds ratio, 1.64) contrasts with the absence of any association between EIB and the presence of *Trichuris trichiura* eggs in the stool (odds ratio, 0.99). Whether this reflects differences in the lifecycle of *T trichiura* or uncontrolled confounding by factors associated with ascariasis is not clear. Data from a cross-sectional study in rural Ecuador of more than 2000 school-aged children in whom the prevalence of *Ascaris* infection was similar (approximately 55%) showed no association between *Ascaris* or *T trichiura* infection and EIB measured in the same way. Therefore the results certainly support the authors' conclusion that the effects of helminth infection are complex but do not resolve whether the association between *Ascaris* and EIB or asthma is causal. A number of prospective interventional and observational studies starting in early life before the first infection with helminths are now in progress, and these should provide stronger evidence for or against causality.

In studies on "urbanization" in Africa, it is often assumed that the urban children have a cleaner environment and that the increased asthma incidence is in some way in keeping with the hygiene hypothesis. However, neither the informal settlements in Khayelitsha in South Africa nor the towns of Kumasi in Ghana or Jimma in Ethiopia are comparable with towns in North America or Europe^{2,3,9} and cannot be assumed to be "cleaner" than rural communities. The report in this issue of the *Journal*¹¹ found the same prevalence of helminth infection in the urban and rural schools. Some years ago, Eugene Weinberg and his colleagues¹³ reported that the urban children they studied had a much higher prevalence of *Ascaris* infection than children in the Transkei villages. Nonetheless, asthma was much less common in the villages. Therefore the question is what other changes associated with urbanization could contribute to the increase in asthma. Urbanization leads to differences in diet and lifestyle, including physical activity and housing, as well as changes in infections. Furthermore, it is clear that the effects of bacterial (*Escherichia coli*) and viral (hepatitis A) infections, as well as other parasites, should all be considered. Interestingly, Dr Weinberg subsequently speculated that the physical activity in the villages (ie, regularly running for miles) could have had a beneficial effect on the lungs of these children (E.G. Weinberg, personal communication, 2002).

Buried in the online supplement of the article in the current edition of the *Journal* (see Table E3 in that article's Online Repository at <http://www.jacionline.org>)¹¹ are data showing that serum IgE antibodies to cat allergens were present in sera from 200 children who had negative skin test responses to cat allergen. Indeed, unlike the other allergens tested, there was no significant

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relationship between serum IgE antibodies and skin test responses to cat. We reported a very similar finding when studying a village in Kenya, and at that time, we were equally unable to offer an explanation for the results.⁴ Recently, we have identified a cross-reactive carbohydrate determinant of mammals, and preliminary evidence suggests that this cross-reactive carbohydrate determinant could explain the “false-positive” IgE results for cat found in some African villages.^{14,15} At the moment, it is not clear whether this IgE antibody is induced by a helminth other than *Ascaris* or by an ectoparasite, such as ticks or scabies. Perhaps more interestingly, this IgE antibody does not appear to be related to wheezing. We would argue that the effects of ectoparasites should not be excluded in considering the effects of parasites on allergic disease.

The study reported by Calvert and Burney¹¹ evaluated a large number of children with serum markers, skin tests, and stool microscopy. Nonetheless, there are limitations to their study that illustrate some of the problems in trying to interpret changes in allergic disease in Africa. The problems with using EIB as the surrogate for asthma in countries where the air is humid are well known, but they might have other problems using 6 minutes of “free running” as the exercise. Children who run for long distances as part of their normal lives not only might have altered lung function, but also this will also influence their speed of running in the free running test.¹⁴ There are studies in Africa in which many of the children with physician-diagnosed asthma did not have EIB and other studies in which many of the children with EIB had no other evidence of asthma. Thus ideally one would evaluate symptomatic asthmatic subjects in the same community, if there were a significant number. Equally, it would help to have other evidence for airways inflammation, such as exhaled nitric oxide levels, which would now be possible. *Ascaris* and *T trichiura* are dominant nematodes in some parts of Africa, but there are many other infections or parasites that could be relevant.

Finally, it is clear that there are major changes in lifestyle that have occurred with urbanization in Africa, as well as over the last 50 years in westernized countries.¹⁶ It is important not to forget how much lifestyle has changed and how poorly equipped we are to monitor changes in physical activity or breathing patterns during a child's daily life.¹⁷ In Africa, there have been major increases in the prevalence of “wheezing.” However, this does not necessarily translate into the severe asthma that is now so common among children in western countries. Thus we still need to understand the factors that leave some rural villages with no significant asthma compared with the increased prevalence of wheezing that has appeared associated with urbanization and the perhaps additional factors that lead to severity that are

common in western countries and cause significant morbidity and mortality among minority populations in the United States.¹⁸

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