

Parasites and allergic disease: Another piece of the puzzle

Robert K. Bush, MD *Madison, Wis*

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Immunity to parasitic infections principally involves innate and adaptive T_H2 responses and is accompanied by the development of IgE antibodies to parasite antigens. Epidemiologic and experimental studies suggest that helminth infections can modulate allergic disease,¹ but cross-reactivity between helminth antigens and allergens that induce human allergic disease has been described. Tropomyosin from filarial parasites can induce IgE antibodies that cross-react with house dust mite allergens,² and similarly, IgE responses to tropomyosins from *Ascaris* species cross-react with cockroach allergens.³

In the current issue of the *Journal*, Santiago et al⁴ add an additional piece to the puzzle of the relationship between parasites and allergic diseases. The authors demonstrate that a glutathione-S-transferase (GST) from the filarial parasite *Wuchereria bancrofti* and a major cockroach GST allergen, Bla g 5, share epitopes that bind human IgE. By using computer models of amino acid sequences of the GST from Bla g 5 and *W bancrofti*, 3-dimensional structures of the proteins were determined. Epitope-mapping studies demonstrated that certain peptides binding human IgE were highly conserved between Bla g 5 and *W bancrofti* GST (40% sequence identity). Further studies showed that Bla g 5 and *W bancrofti* GST inhibited IgE binding of cockroach-sensitized human sera and IgE of *W bancrofti*-infected patients equally well. In an animal model the investigators further demonstrated that mice infected with the nematode *Heligmosomoides bakeri* showed skin test reactivity to Bla g 5 but not Bla g 4.

In addition to the present study, immunologic cross-reactivity to Der p 8, a GST from house dust mite, and Bla g 5 has been demonstrated.⁵ Thus the present study by Santiago et al⁴ and the work of others suggest that sensitization to common allergens, such as Bla g 5 and tropomyosins, which are involved in human allergic disease, might result from parasitic infections.

Furthermore, the recent report linking IgE antibodies to galactose- α -1,3-galactose from the bite of the ectoparasitic tick *Amblyomma americanum*⁶ is another example in which a parasite induces IgE antibodies in human subjects with subsequent effects on allergic diseases (anaphylaxis to murine mAb therapeutic reagents and delayed urticaria and anaphylaxis to red meats). Thus not only systemic parasitic infections but also exposure to ectoparasite antigens (eg, tick bites) might lead to allergic

manifestations in human subjects. Other carbohydrate components common to parasites and allergens also might have a role in human allergic diseases.

Although exposure to parasite antigens might directly induce cross-reactive IgE antibodies to human allergens, does molecular mimicry between other environmental exposures and parasite components account for allergic diseases? Chitin is the second most abundant polysaccharide in nature and is found in parasites, fungi, insects, and house dust mites. The potential role of chitin in inducing asthma is suggested by the high prevalence of asthma in occupational settings among persons working with chitinous substances, such as crustaceans and fungi.⁷ In a recent report⁸ cell-wall preparations containing chitin induced eosinophilic airway inflammation in an animal model that was attenuated by enzymatic degradation of chitin. Furthermore, injection of chitin into the skin of mice induced the accumulation of IL-4-expressing innate immature cells.⁹ Although shared by parasites and aeroallergens, the role of chitins in allergic diseases requires further investigation.

A family of proteins, the lipocalins, are important aeroallergens. The major allergens of mice, rats, dogs, and horses belong to this family of proteins.¹⁰ Many of these allergens are very potent inducers of IgE-mediated sensitization and allergic diseases. Twenty percent or more of workers exposed to laboratory animals (mice and rats) become sensitized, many of whom have no personal or family history of atopy. Interestingly, amino acid sequence homology between lipocalins and schistosome antigens has been reported,¹⁰ but cross-reactivity studies similar to the work that Santiago et al⁴ report have not been conducted. Several other sources of lipocalin allergens causing anaphylaxis from insect bites have also been identified. These include a salivary protein from reduviid (kissing) bugs¹¹ and a protein from the pigeon tick *Argas reflexus*.¹² Lastly, the cockroach allergen Bla g 4 is a putative lipocalin family protein.¹³ Although amino acid sequence homology does not predict antigen cross-reactivity with IgE antibodies, additional studies might help us better understand the immune response relationships between aeroallergens and parasitic antigens and whether molecular mimicry is responsible.

In summary, the induction of cross-reactive IgE antibodies to aeroallergens by parasitic infections in the study by Santiago et al⁴ suggests that the immune responses to parasites can induce allergic disease. Other examples in which components common to aeroallergens (chitin, glycans, and proteins) can mimic parasite exposure and induce T_H2 responses have also appeared. Continued research on the innate and adaptive immune responses will help solve the fascinating puzzle of parasite-allergen relationships.

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From the Division of Allergy, Immunology, Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, University of Wisconsin-Madison.

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Corresponding author: Robert K. Bush, MD, Allergy and Immunology, K4/910 CSC #9988, 600 Highland Ave, Madison, WI 53792. E-mail: rkb@medicine.wisc.edu.

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