Initial High-Dose Nasal Allergen Exposure Prevents Allergic Sensitization to a Neoantigen


PURPOSE OF THE STUDY. Epidemiologic studies have suggested that high-dose allergen exposure may protect against primary allergic sensitization—the formation of immunoglobulin E (IgE) after initial antigen exposure. This study uses a human nasal allergic sensitization model to evaluate the effect of the dose of the antigen on the rate of primary sensitization to a neoantigen, keyhole limpet hemocyanin (KLH).

STUDY POPULATION. Fifty-one healthy nonsmoking atopic subjects aged 18 to 55 years. Atopic status was defined by a positive skin-prick test to at least one aeroallergen; the subjects therefore had a propensity to mount an allergic (IgE) response to respiratory antigen exposure.

METHODS. Subjects underwent a 33-day sensitization protocol including initial exposure to 0.1-, 10-, 1000-, or 100 000-μg doses of intranasal KLH as well as later exposure to adjuvant intranasal diesel exhaust particles. At the conclusion of protocol, antigen-specific IgE, IgG, and IgG4 were measured in nasal lavage samples.

RESULTS. The rates of allergic sensitization, defined as detectable KLH-specific IgE, for the 0.1-, 10-, 1000-, or 100 000-μg dose groups were 0, 100, 57, and 11%, respectively. Furthermore, the mean KLH-specific IgE levels decreased with increasing doses of initial antigen exposure. Antigen-specific IgG and IgG4 were produced by all subjects, with the highest levels observed in the high-dose group.

CONCLUSIONS. Initial high levels of respiratory antigen exposure may prevent primary allergic sensitization through induction of an antigen-specific non-IgE humoral immune response.

REVIEWER COMMENTS. In children at high risk of allergic sensitization, a means of preventing primary sensitization and inducing durable allergic tolerance would be of great value. This study found that initial high-dose exposure to a neoantigen, KLH, results in a humoral immune response with high levels of antigen-specific IgG, including IgG4, and low levels of KLH-specific IgE. Whether these findings apply to other respiratory antigens remains unclear. The mechanism underlying this induction of tolerance remains unclear, and it is also not known whether this immune response represents durable allergic tolerance. Future studies investigating these issues are needed to move toward potential primary prevention therapy for allergic disease.
the 9% chance of outgrowing TN allergy may seem low, it may be an underestimate of the actual resolution rate, because a large number of eligible patients declined diagnostic food challenges. The results of this study should encourage regular follow-up of children with TN allergy and consideration, when clinically indicated, for physician-supervised oral food challenges to determine the possibility of resolution. Because these oral food challenges can trigger anaphylaxis, they are generally undertaken under the supervision of an allergist and with immediate access to medications and equipment to treat a significant allergic reaction.

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Prevalence and Outcome of Allergic Colitis in Healthy Infants With Rectal Bleeding: A Prospective Cohort Study

PURPOSE OF THE STUDY. To determine the prevalence of allergic colitis (AC) in a cohort of healthy infants with rectal bleeding. A secondary purpose was to determine if bleeding would resolve in untreated infants with rectal bleeding without biopsy-proven AC.

STUDY POPULATION. There were 22 infants ≤6 months of age with rectal bleeding recruited from the referral area of Cincinnati Children’s Hospital Medical Center (Cincinnati, OH). All subjects had a negative history of bleeding disorders, negative stool cultures, positive hemoccult, and a negative history and physical examination for signs of infection, Hirschsprung disease, and inflammatory bowel disease.

METHODS. AC was defined histologically as colonic mucosa with ≥6 eosinophils per high-power field and/or eosinophils in the colonic crypts or muscularis mucosae. Formula or maternal diet was changed only for infants with histologic findings of AC. Formula-fed infants were switched to an extensively hydrolyzed formula and were rebiopsied at 3 weeks. If the biopsy was normal, they were continued on the formula and managed clinically. Those with continued histologic evidence of colitis were changed to an amino acid–based formula at 6 weeks. Breastfed infants continued breastfeeding while mothers followed a milk-protein–free diet. Those with resolution of bleeding and normal biopsies at 3 weeks continued with breastfeeding and a restricted maternal diet. Those with persistent histologic evidence of colitis were rebiopsied at 6 weeks with no further dietary change. Those with persistent bleeding were changed to hydrolysate and rebiopsied at 6 weeks. Those with persistent bleeding and histologic evidence of AC at 6 weeks were changed to an amino acid–based formula.

RESULTS. Of 22 subjects, 14 (63.6%) had histologic evidence of AC. Five had normal biopsies and 3 had nonspecific colitis. Seven of the 14 with AC were formula fed. Six of the 7 had resolution of bleeding, on average, in 1.8 weeks (range: 1–5 weeks). One of the 7 was changed to an amino acid formula at 3 weeks and had resolution of bleeding at 5 weeks. The remainder of the 14 were breastfed. Six were followed to completion of the study. One had a delayed diagnoses because of development of worsening rectal bleeding and an abnormal biopsy at week 3 despite a normal biopsy at the onset of the study. The infant failed to improve with hydrolyzed formula but had resolution of bleeding by week 8 after initiation of an amino acid formula. Of the remaining 5, 2 had normal histology at week 3 with maternal elimination of cow’s milk. Two had improvement by week 3, and 1 had no change. The average time for resolution in the breastfed group was 5.6 weeks (range: 2–8 weeks). For the 5 infants without histologic evidence of colitis, the average time for resolution of bleeding was 3.25 weeks. In those with nonspecific colitis, 2 had resolution by week 6, and the third was ultimately diagnosed with inflammatory bowel disease.

CONCLUSIONS. A significant proportion of infants with rectal bleeding may not have AC and may undergo unnecessary, expensive formula or maternal diet changes that may discourage breastfeeding.

REVIEWER COMMENTS. This small study provides important insights about the prevalence and natural course of proctocolitis. A much larger prospective placebo-controlled study that compares treatment versus no treatment would be very helpful.

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Food Allergen Sensitization in Inner-City Children With Asthma

PURPOSE OF THE STUDY. To determine the prevalence of food allergen sensitization and its association with asthma symptoms and health care utilization in an inner-city asthma population.

STUDY POPULATION. Random serum samples were obtained from children (n = 544) aged 4 to 9 years (median: 6 years) with asthma living in inner-city areas enrolled in the National Cooperative Inner City-Asthma Study.

METHODS. Information regarding demographics, health history, medication use, health care utilization, and
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