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RESEARCH NEWS

Peanut Allergy: Recent Advances

A review of: Leung DYM, Sampson HA, Yunginger JW, *et al.*, for the TNX-901 Peanut Allergy Study Group 2003 Effect of anti-IgE therapy in patients with peanut allergy. N Engl J Med 348:986–993; and Lack G, Fox D, Northstone K, Golding J, for the Avon Longitudinal Study of Parents and Children Study Team 2003 Factors associated with the development of peanut allergy in childhood. N Engl J Med 348:977–985

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The number of infants, children, and adolescents who are at risk for systemic anaphylaxis is increasing; in one geographic area, 1.44% of the pediatric population has had epinephrine dispensed for first-aid, out-of-hospital treatment (1). In young patients, peanut allergy is the most common food trigger of anaphylaxis, and it is also the most common overall trigger, accounting for up to 50% of all anaphylaxis episodes in this age group (2). Recent articles on peanut allergy in *The New England Journal of Medicine* give reason for cautious optimism about prevention of peanut-induced allergic *reactions* by injecting the anti-IgE antibody TNX-901 (3), and about the possibility of prevention of *sensitization* to peanut by avoidance of newly identified risk factors for peanut allergy (4).

Leung et al explored the novel approach of injecting a humanized IgG1 monoclonal anti-IgE antibody, TNX-901, in a Phase II, multicenter, randomized, double-blind, placebo-controlled, dose-ranging study lasting 3–4 months. They investigated 81 patients age 13-59 years with a total serum IgE level ranging from 11-1017 IU/mL (mean 273 IU/mL), positive epicutaneous test to peanut, and positive double-blind, placebo-controlled oral challenge to peanut flour (mean baseline threshold sensitivity of 331 mg (range 1–2000), equivalent to 1/2–1 peanut). TNX-901 150, 300, or 450 mg, or placebo was injected subcutaneously every 4 weeks for a total of four doses.

TNX-901 injections led to substantial reduction in serum free IgE levels in all the active treatment groups. Approximately 3 weeks after the last injection, compared with unchanged tolerance in the individuals receiving placebo, those receiving TNX-901 450 mg had increased tolerance to peanut flour ($p < 0.001$), expressed as the mean threshold of sensitivity of 2805 mg (approximately 8–9 peanuts), and there was a trend for a dose response to TNX-901 ($p < 0.001$). Some allergen-specific IgE remained. Most individuals receiving TNX-901 developed mild local reactions at the injection sites. Systemic allergic reactions to the peanut flour challenges were not completely prevented and required termination of the challenge and treatment with oral charcoal, epinephrine, antihistamines, and corticosteroids, as appropriate. No individual developed anti-TNX-901 antibodies.

Anti-IgE antibodies work by binding with high affinity to an epitope in the CH3 domain of IgE and forming small, discrete complexes with free IgE in the serum, thus masking the region responsible for binding to the Fcϵ receptor (IgE receptor I) on mast cells and basophils (3). Due to the fact that anti-IgE antibodies do not interact with receptor-bound IgE on these cells to trigger the release of histamine, tryptase, and other mediators, they do not trigger anaphylaxis. Anti-IgE antibodies also reduce the number of IgE receptors on basophils and bind to the constitutive IgE expressed by differentiated B cells, the precursors of IgE-secreting plasma cells. They do not bind to structurally unrelated IgE-binding receptors (IgE receptor II) expressed on lymphocytes and monocytes.

Additional anti-IgE antibody studies are needed in children less than 13 years of age, and in patients with more severe peanut allergy who cannot tolerate *any* ingestion of peanut before treatment. In individuals with greatly elevated total serum IgE levels (>1000 IU/mL) and those with large body mass, it might be difficult to inject an adequate anti-IgE antibody dose. Injections might be needed indefinitely in many peanut-allergic patients, since sensitization to peanut is rarely lost (5). Although IgE appears to be involved in most humans with anaphylaxis, the possibility of non-IgE-dependent anaphylaxis occurring in some individuals, as documented in other mammalian species (6), cannot be ruled out. Moreover, subacute or chronic food allergy symptoms are generally mediated by T cells rather than by IgE (5).

Most allergic individuals have more than one disease phenotype; therefore, a potential advantage of anti-IgE antibody over currently available treatments is that it is not specific for a particular allergy such as peanut allergy, or for a particular allergic disorder such as anaphylaxis. Indeed, the monoclonal anti-IgE antibody omalizumab (Xolair®) reduces asthma and allergic rhinitis symptoms significantly (7, 8).

In another study published in the same issue of *The New England Journal of Medicine*, Lack et al identified previously unreported risk factors for peanut allergy in a geographically defined cohort of 13,971 preschool chil-

dren, 23 of whom had peanut allergy confirmed by double-blind peanut challenge (4). Case children and controls were not matched. A significant independent relationship of peanut allergy was found with: application of skin creams containing peanut oil to inflamed skin (Odds Ratio (OR), 6.8; 95% Confidence Interval (CI), 1.4–32.9); atopic dermatitis (OR, 2.6; 95% CI, 1.4–5.0); oozing, crusted rash (OR, 5.2; 95% CI, 2.7–10.2); and intake of soy milk or soy formula (OR, 2.6; 95% CI, 1.3–5.2), perhaps through cross-sensitization to common epitopes in peanut and soy. There was no evidence that sensitization to peanut was attributable to the maternal diet, either before birth or by transmission of maternally ingested peanut allergens through breast milk.

IgE synthesis and production of pro-inflammatory cytokines are favored by exposure to extremely low concentrations of allergens (9). If these risk factors involving exposure to minute amounts of peanut are confirmed in future studies, new strategies to prevent sensitization in infants at risk for peanut allergy could be developed.

1. Simons FER, Peterson S, Black CD 2002 Epinephrine dispensing patterns for an out-of-hospital population: A novel approach to studying the epidemiology of anaphylaxis. J Allergy Clin Immunol 110:647–651
2. Simons FER, Chad ZH, Gold M 2002 Real-time reporting of anaphylaxis in infants, children and adolescents by physicians involved in the Canadian Pediatric Surveillance Program. J Allergy Clin Immunol 109:S181
3. Leung DYM, Sampson HA, Yunginger JW, Burks AW Jr, Schneider LC, Wortel CH, Davis FM, Hyun JD, Shanahan WR Jr, for the TNX-901 Peanut Allergy Study Group 2003 Effect of anti-IgE therapy in patients with peanut allergy. N Engl J Med 348: 986–993
4. Lack G, Fox D, Northstone K, Golding J, for the Avon Longitudinal Study of Parents and Children Study Team 2003 Factors associated with the development of peanut allergy in childhood. N Engl J Med 348:977–985
5. Sicherer SH 2002 Food allergy. Lancet 360:701–710
6. Strait RT, Morris SC, Yang M, Qu X-W, Finkelman FD 2002 Pathways of anaphylaxis in the mouse. J Allergy Clin Immunol 109:658–668
7. Milgrom H, Fick RB Jr, Su JQ, Reimann JD, Bush RK, Watrous ML, Metzger WJ for the rhuMAb-E25 Study Group 1999 Treatment of allergic asthma with monoclonal anti-IgE antibody. N Engl J Med 341:1966–1973
8. Kuehr J, Brauburger J, Zielen S, Schauer U, Kamin W, Von Berg A, Leupold W, Bergmann KC, Rolinck-Werninghaus C, Grave M, Hultsch T, Wahn U and the Omalizumab Rhinitis Study Group 2002 Efficacy of combination treatment with anti-IgE plus specific immunotherapy in polysensitized children and adolescents with seasonal allergic rhinitis. J Allergy Clin Immunol 109:274–280
9. DeKruyff RH, Fang Y, Umetsu DT 1992 IL-4 synthesis by in vivo primed keyhole limpet hemocyanin-specific CD4+ T cells. I. Influence of antigen concentration and antigen-presenting cell type. J Immunol 149:3468–3476

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