greater reactivity to specific allergens. The protein microarray immunoassay confirmed that Ara h1, Ara h2, and Ara h3 are major peanut allergens and allows for parallel epitope analysis. This has led to the discovery of an additional important epitope of Ara h1 and the recognition of a high degree of patient heterogeneity. This qualitative difference in epitope diversity might provide prognostic information about the patient.

**Conclusions.** The protein microarray immunoassay confirmed that Ara h1, Ara h2, and Ara h3 are major peanut allergens and allows for parallel epitope analysis. This has led to the discovery of an additional important epitope of Ara h1 and the recognition of a high degree of patient heterogeneity. This qualitative difference in epitope diversity might provide prognostic information about the patient.

**Reviewers’ Comments.** Current techniques for mapping large numbers of epitopes by using individual patient sera are relatively time consuming, labor intensive, expensive, and prone to error. However, such studies have been useful, because identification of certain IgE-binding segments correlates with clinical outcomes such as likelihood for an allergy to resolve. Peptide microarray technology is a novel assay that allows characterization of large numbers of individual patient samples simultaneously with minimal amounts of blood. Microarray technology may be a useful diagnostic tool to assess differences in epitope recognition among patients and may provide more prognostic information regarding patients’ peanut allergies. In addition, these assessments of allergens may speed the production of allergy vaccines engineered in the future.

**THE EFFECTS OF A DOUBLE BLIND, PLACEBO CONTROLLED, ARTIFICIAL FOOD COLOURINGS AND BENZOATE PRESERVATIVE CHALLENGE ON HYPERACTIVITY IN A GENERAL POPULATION OF PRESCHOOL CHILDREN**


**Purpose of the Study.** To test whether food additives, specifically a limited number of food dyes and a preservative, have a pharmacologic effect on behavior irrespective of other characteristics of the child.

**Study Population.** This study started with 2878 children who were resident and registered with a general practitioner on the Isle of Wight, United Kingdom, on their third birthday. The dates of birth were between September 1994 and August 1996. After screening and the signing of consent forms, the eventual study population was 397, of which 277 completed most aspects of the study.

**Methods.** There were 2 scales used to assess hyperactivity: the Emotionality, Activity, and Sociability Hyperactivity Scale and the Weiss-Werry-Peters Activity Scale. Atopic status was determined by skin-test reactivity to house dust mites, grass pollen, cat, milk, egg, or peanut. The children were divided into 4 groups and entered into a randomized, placebo-controlled, double-blind, crossover challenge study. The groups were hyperactive and atopic, nonhyperactive but atopic, hyperactive but not atopic, and nonhyperactive and nonatopic. This was a 4-week study period that followed a lead-in week in which the diet was free of artificial colorings and sodium benzoate. During the second or fourth week they received either the placebo or the active challenge diet. During the day they would be required to drink 300 mL of a fruit juice that was placebo or contained a total of 20 mg (5 mg each) of sunset yellow, tartrazine, carmoisine, and ponceau 4R. The juice also contained 45 mg of sodium benzoate. The child’s behavior was assessed weekly in the clinic with validated tests, and the parents also rated behavior. Compliance was assessed and indicated that 81% of the children drank all or nearly all of the challenge drinks. There was also a “snack” diary in which parents reported ingestion of foods that contained artificial color or preservatives. From the original starting group of 397, 30% failed to complete all 4 weeks of the study.

**Results.** All 4 groups of children were similar in terms of gender, age at baseline testing, other behavior problems, and maternal age at leaving full-time education. There was no difference in the activity scores measured in the clinic during any time period of the study. However, parental ratings of behavior showed a reduction in hyperactive behavior when the food additives were removed from the diet. There was a significantly greater increase in hyperactive behavior reported by the parents during the active versus placebo phase of the challenge. These effects were not influenced by the presence or absence of hyperactivity in the child nor by the presence or absence of atopy.

**Conclusions.** There is an effect of artificial food coloring and benzoate preservative on the activity of 3-year-old children that is detectable by the parent but not at all detectable by an assessment of activity in the clinic. Subgroups are not made more vulnerable to this effect by prior level or history of hyperactivity or by atopy.

**Reviewer’s Comments.** This was a very different article to review. The authors have taken the gold-standard model of “testing” and applied it with behavior as the outcome. A potential problem is the fact that this was done at home and over an extended period of challenge and was not done solely in the clinic. Also, there is precious little “allergy” in the article notwithstanding the use of limited skin testing, the mention of IgE, and histamine. What is of note here is a very common issue for pediatricians. Not too infrequently do parents seek allergy referral for behavior issues. This is a vexing problem, and rarely is the issue an IgE-mediated condition. Also of note is that the dyes and preservatives are not available for skin testing. The takehome message that may be of help to a primary care provider includes the fact that being allergic to inhalants did not predispose the child to react to the additives. Another message in this study is that the tools and the situation that is offered in the office to assess behavior do not match the parental observations.

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**ANAPHYLAXIS AND INSECT ALLERGY**

**A POPULATION-BASED STUDY OF THE INCIDENCE, CAUSE, AND SEVERITY OF ANAPHYLAXIS IN THE UNITED KINGDOM**


**Purpose of the Study.** To determine the incidence, severity, and causes of anaphylaxis in the United Kingdom.

**Study Population.** United Kingdom residents born between 1912 and 1999 who were registered in the General Practice Research Database between 1994 and 1999.

**Methods.** The General Practice Research Database includes demographic and clinical data provided by general practitioners in the United Kingdom. Inclusion criteria for this study were an age of <80 years and having at least 6 months of recorded data in the database. After all cases were identified, 70 cases were selected randomly to undergo a more detailed evaluation that included contacting the general practitioner involved in the case. The investigators defined anaphylaxis as an acute allergic reaction characterized by generalized urticaria, often accompanied...
by swollen tongue, wheezing, flushing, gastrointestinal symptoms, or hypotension. The reaction was considered mild if the symptoms were primarily limited to generalized urticaria and did not require treatment in an emergency department; the reaction was considered to be moderate if a hospital or emergency department visit was initiated for treatment and the symptoms were treated with epinephrine; and the event was considered to be severe if there was hypotension.

Results. A total of 898 patients were identified, and a random sample of 70 (9%) cases with a coded diagnosis and 50 (43%) cases with a comment diagnosis underwent additional evaluation. Relevant information on the diagnosis was available for >90% of these cases. Criteria for anaphylaxis was met in 87 of the 120 cases, so that an estimated 675 cases of the total 783 were estimated to have confirmed anaphylaxis, resulting in an incidence of 8.4 cases per 100,000 person-years. Insect stings were responsible for 32% and medications for 30% of cases. Food was implicated in 22% of cases, and more than half of these were due to a tree nut or peanut. Severity of the cases was as follows: mild, 29%; moderate, 45%; severe, 9%; indeterminate, 17%. One death was identified.

Conclusions. In the United Kingdom, the estimated incidence rate of anaphylaxis was 8.4 cases per 100,000 person-years, and ~10% of these cases were life threatening.

Reviewer’s Comments. Although anaphylaxis is a relatively uncommon event, 10% of cases are characterized by hypotension. The estimated percentage of severe, life-threatening events would have been even higher if lower airway symptoms were considered as a manifestation of severe anaphylaxis. Physicians evaluating patients with suspected allergic reactions should be prepared to treat life-threatening symptoms.

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ANAPHYLAXIS: A 7-YEAR FOLLOW-UP SURVEY OF 46 CHILDREN


Purpose of the Study. To follow children with a previous history of anaphylaxis to determine the clinical course of this syndrome.

Study Population. A total of 76 children referred between 1994 and 1996 with clinical features of anaphylaxis, which included at least 2 indicators (hypotension, inspiratory dyspnea, urticaria/angi-oedema) within 2 hours of exposure of the suspected causative agents.

Methods. After a mean duration of 7 years, 46 (61%) children were interviewed by telephone.

Results. Of the 46 patients, 14 (30%) had experienced a recurrence of anaphylaxis. Ten had single episodes, 2 had 2 episodes, 1 had 3 recurrences, and 1 had 4 recurrences. None of the patients died or experienced biphasic reactions. Patients who were sensitive to at least 1 food allergen were more likely to have recurrent episodes of anaphylaxis than those without food sensitivity (93% vs 56%; \( P < .04 \)). For 14 of the 46 who experienced recurrence of anaphylaxis, no specific cause was clearly associated with the recurrence. Children with atopic dermatitis at initial presentation (95% vs 31%; \( P = .004 \)) and those with angioedema and urticaria at the time of the current study (93% vs 37%; \( P = .0002 \)) were found to be at significantly higher risk for recurrent anaphylaxis.

Conclusions. Patients may have a greater risk for recurrent anaphylaxis if they have atopic dermatitis, angioedema, or urticaria and 1 positive food skin test.

Reviewer’s Comments. This is the first study to help define the natural history of pediatric anaphylaxis. It emphasizes the need for a thorough work-up, education, and provision of autoinjectable epinephrine in all of these patients.

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CLINICAL FEATURES AND ANAPHYLAXIS IN CHILDREN WITH COLD URTICARIA

Alangari AA, Twarog FJ, Shih MC, Schneider LC. Pediatr. 2004;113:e313–e317

Purpose of the Study. To characterize the features of cold urticaria in children, focusing particularly on systemic reactions.

Study Population. Thirty children (chart reviewed) who were evaluated over a 3-year period in an academic allergy program and a private practice.

Methods. Cold urticaria was diagnosed based on the patient’s history and was supported by an ice-cube challenge test using a standard protocol (17 of 30 positive). The degree of symptoms was categorized into 3 types: localized urticaria/angi-oedema, generalized urticaria and/or angioedema without hypotension or respiratory symptoms, or severe systemic reactions with episodes suggesting respiratory distress and/or hypotension.

Results. There were 17 females, and the mean age of patients was 12 years (range: 2–18.5 years). Mean age of onset of cold urticaria was 7 years. The duration of cold urticaria was 3.2 years (range: 0.5–13.5 years). Data on progression were available for 27 of the 30 patients. Symptoms resolved spontaneously in only 2 patients. Swimming was the only trigger in 10 of the 30 patients; touching cold objects triggered urticaria in 9 patients; and cold weather was a trigger for the remaining 11 patients. Six of the patients experienced other causes of urticaria. The rate of atopic disease in the patient’s families was 89.3%. Response to antihistamine was variable, with 24 of 30 patients responding (8 had a poor response, 7 had a moderate response, and 9 had a good response).

Conclusions. Cold urticaria occurs in children and may be associated with anaphylaxis. No secondary causes were found. The primary determinants for reactions were body surface area exposed, temperature, and duration of exposure. All patients with cold urticaria were counseled and received autoinjector epinephrine.

Reviewer’s Comments. The natural history of cold urticaria, which seems to be primarily idiopathic, has not been well defined in children. There seems to be a higher rate of personal atopy and a family history of atopy in the patients. Counseling should include caution regarding aquatic activity, the most common trigger.

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OUTCOMES OF ALLERGY TO INSECT STINGS IN CHILDREN, WITH AND WITHOUT VENOM IMMUNOTHERAPY

A Population-Based Study of the Incidence, Cause, and Severity of Anaphylaxis in the United Kingdom

Elizabeth Matsui

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