The Journal of Allergy and Clinical Immunology

2.1. RESUMOS

2.1.1. 886 Cutaneous Prick Testing with DuoTip-Test

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Cutaneous prick testing (CPT) is an important method for determining the specific etiology of a patient's allergy symptoms. The DuoTip-Test® has not been previously compared to other available methods for performing cutaneous prick testing. We examined the DuoTip-Test® skin testing method with our present method using a sterile smallpox needle in 30 allergy patients. CPT with histamine, codeine, saline, short ragweed and dermatophagoides pteronyssinus were performed with both methods, on the paraspinal area of the back, by a single medical assistant. After 15 minutes a single blinded observer measured wheal and flare reactions. Patient preference for DuoTip-Test® versus needle was also elicited. Difference in reproducibility between the two techniques was tested with a two-tailed, paired t-test. No significant differences were seen at the 0.05 level for any test agent. The reproducibility was evaluated as the coefficient of variation (CV=SD/mean area). The CVs found with either method were similar across all test agents. This indicates that the variations with regard to the mean area are similar with both methods. Using a test of binomial probability, the DuoTip-Test® method was highly statistically significantly better tolerated.

2.1.2. 993 Developmental Cytokine Response Profiles and Their Relationship to the Expression of Allergic Sensitization and Asthma in Early Life

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RATIONALE: To determine if developmental differences during early childhood in cytokine response profiles are associated with allergic sensitization and/or asthma at age 6 years.

METHODS: Allergic sensitization (skin prick test) at age 5 years of life was compared to cord blood, age 1, 3, and 5 year cytokine response profiles in children enrolled in the Childhood Origins of ASThma (COAST) project. Phytohemaglutinin (PHA)-induced mononuclear cell cytokine response profileswere evaluated for interferon (IFN)-g, interleukin (IL)-5, and, IL-13.
Skin prick tests were performed on 203 children at age 5 years utilizing the Multi-Test_ II method (Lincoln Diagnostics, Inc.) The children were categorized into four groups: No asthma and SPT negative, no asthma and SPT positive, asthma and SPT negative, and asthma SPT positive.

RESULTS: At birth, age 1, and 3 years, therewere no significant differences between the four groups for the PHA-induced mononuclear cell cytokine responses for IFN-g, IL-5, and IL-13. There were no significant differences at any age between the asthma groups. However, by 5 years of age, the SPT positive groups had increased IL-13 (409 vs. 345 pg/ml p 5 .04), IL-5 (324 vs. 244 pg/ml p 5 .02), and a trend toward a significant difference for IFN-g (355 vs. 287 pg/ml p 5 .07) response profiles.

CONCLUSION: In early life, the pattern of cytokine response profiles differs in children with allergic sensitization but not asthma. However, these differences are not significantly apparent until 5 years of age.
Funding: NIH Grants MO1 RR03186, R01 HL61879, and P01 HL70831

2.1.3. 458 Epicutaneous Testing Using Peanut Extracts Prepared by a Variety of Cooking Methods

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RATIONALE: The incidence of peanut allergy is higher in the United States than in other countries, such as China, despite equal consumption. This is theorized to occur, in part, because of differences in the way peanuts are prepared: roasted versus boiled and/or fried. Since cooking peanuts has been shown to change IgE binding in-vitro, we examined epicutaneous testing responses to peanuts prepared by a variety of cooking methods.

METHODS: Extracts of dry roasted, boiled 20 minutes and one hour, oil roasted, fried, and raw peanuts were prepared. Each extract contained an equal amount of protein. Thirty peanut allergic patients were skin prick tested with each peanut extract using a Multi-test_ apparatus. Wheal size was measured and compared using two-tailed T test.

RESULTS: Skin test reactions to oil roasted (p50.01), boiled one hour and 20 minutes (p50.03, p50.003), and dry roasted (p50.001) peanuts were significantly less than those to raw peanuts. Other comparisons were not significantly different.

CONCLUSION: We observed that peanut extracts prepared by a variety of cooking methods decreased skin test reactivity as compared to raw peanut extract. This suggests that the preparation of peanuts by various cooking methods may not contribute to the higher incidence of peanut allergy in the United States.

2.1.4. 734 Comparison of Two Single-Headed and Two Multiheaded Prick Skin Test Devices

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RATIONALE: Allergen skin test devices continue to be developed with a trend towards producing multiheaded devices. Data on the performance of these devices is limited.

METHODS: Two single-headed devices (Greer Pick®, Duotip-Test®) and two multiheaded devices (Multi-Test II®, OMNITM®) were tested in a prospective blinded fashion looking at pain, wheal and flare reactions using histamine and glycerol-saline on the arms and back. Differences among devices in pain, wheal, and flare reactions were noted. Sensitivity, specificity and intradevice variability were calculated.

RESULTS: No significant differences were observed in wheal and flare reactions between the Greer Pick® (7.1mm X 28.4mm) and the Duotip- Test® (7.2mm X 28.6mm). Multiheaded devices were significantly different in wheal and flare reactions compared to each other and the singleheaded devices (Multi-Test II®, 5.4mm X 20.4mm; OMNITM®, 3.3mm X 14.3mm). Pain was generally mild but was greater for the multiheaded devices than the single-headed devices. The single-headed devices were significantly more sensitive (100% each) than the multiheaded devices. The Multi-Test II® was significantly more sensitive (83%) than the
OMNITM® (57%). There was significant intradevice variability for the multiheaded devices with the corner heads being significantly more sensitive than the interior heads. Specificities for all devices were equally good (>93%).

CONCLUSIONS: Single-headed devices are more sensitive than multiheaded devices. The Multi-Test II® is more sensitive than the OMNITM®. In multiheaded devices, corner heads are more sensitive than interior heads. All of these factors can guide the Allergist in choosing the best skin test device for any individual situation.
Funding: Department of Clinical Investigations, Walter Reed Army Medical Center

2.1.5. 1208 Agreement Between Results of an In Vitro Assay for Plasma Allergen-Specific IgE and Skin Testing in a High-Risk Birth Cohort

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RATIONALE: Radioallergosorbent tests (RAST) and skin prick testing are both commonly used to test for allergic sensitization. However, information about how the results of the two tests agree is limited, particularly for preschool children.

METHODS: Children enrolled in the Childhood Origins of ASThma (COAST) project underwent both a peripheral blood draw and percutaneous skin testing at age 5 years. Plasma allergen-specific IgE results were evaluated by fluoroenzyme immunoassay (Unicap® 100, Pharmacia Diagnostics) for the following antigens: *D. farinae, D. pteronyssinus, Alternaria alternata,* dog epithelium, cat dander, grass, birch, and ragweed. Skin prick testing was performed utilizing the Multi-Test® II method (Lincoln Diagnostics, Inc.). Agreement between the two tests was evaluated through calculation of a correlation coefficient and kappa statistic.

RESULTS: The prevalence of skin prick test positivity was higher than the prevalence of RAST positivity for cat dander (23% vs. 14%, p=0.0004), dog epithelium (19% vs. 14%, p=0.08), *D. farinae* (20% vs. 15%, p=0.04)*, D. pteronyssinus* (19% vs. 15%, p=0.09), and grass (12% vs. 8%, p=0.07). For other allergens, the prevalences of skin prick test and RAST positivity were comparable; agreement between the tests was substantial for *Alternaria* (kappa=0.71), oderate for birch (kappa=0.56) and fair for ragweed (kappa=0.39).

CONCLUSIONS: In preschool children, for most allergens, positive results to skin prick testing occurred more frequently than positive RAST results, which could reflect dependence of the skin test response on immune-mediated mechanisms in addition to IgE antibody.
Funding: National Institute of Health

2.1.6. 992 Parental Allergic Sensitization is Associated With a Variable Pattern of Offspring Allergic Sensitization

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RATIONALE: Allergic disease has a strong familial inheritance pattern, and we therefore evaluated allergic sensitization patterns in offspring compared to their parent's to determine their specificity in relationship to parent and to allergen.

METHODS: Children enrolled in the Childhood Origins of ASThma (COAST) project underwent both a peripheral blood draw and percutaneous skin testing at age 5 years. Parents underwent percutaneous skin testing at time of enrollment and a peripheral blood draw within a year after enrollment. Plasma total IgE results were evaluated by fluoroenzyme immunoassay (Unicap_100_, Pharmacia Diagnostics). Skin prick testing was performed utilizing the Multi-Test_ II method (Lincoln Diagnostics, Inc.).

RESULTS: Elevated (above median) total IgE levels in one or both parents were associated with higher IgE levels in children (median 89 for both parents, 43 for mother only, 41 for father only and 20 for neither, $p < 0.01$). In contrast, elevated risk of sensitization to allergens was only observed in children when both parents were sensitized to dog (50% vs. 16%, p 5 0.003), ragweed (29% vs. 12%, p 5 0.04), Alternaria (43% vs. 15%, p 5 0.07) and cat (36% vs. 19%, p 5 0.08).

CONCLUSION: Children who have at least one parent with an elevated total IgE have elevated total IgE levels. In contrast, children are more likely to be sensitized to dog, ragweed, Alternaria, or cat only if both of their parents are sensitized.
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Funding: National Institute of Health M01 RR03186, R01 HL61879, and P01 HL70831

2.1.7. 438 Food Allergen Sensitization is Independently Associated with Decreased Lung Function in Children

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RATIONALE: Studies have revealed associations of diagnosed food allergy with asthma, and in small studies, with airway hyper-responsiveness and inflammation. No studies have evaluated whether food allergen sensitization is associated with altered pulmonary function. The bjective was to determine whether food allergen sensitization in children is associated with lung function independently of aero allergen sensitization.

METHODS: This study is a cross-sectional analysis of 919 children aged 10 to 17 years, derived from a population based Chinese twin cohort. Subjects had spirometry performed and skin testing using Multi-test II. Primary outcomes were % predicted FVC and % predicted FEV1. The key predictor was food allergen sensitization on skin testing. The association between lung function and food allergy sensitization was assessed by multiple linear regression analyses, adjusting for age, smoking, and sensitization to aero-allergens. GEE was used to account for intra-twin pair correlations.

RESULTS: There was a modest but statistically significant negative association between food allergen sensitization and decreased FEV1 (beta 5-2.7%, p50.026) and FVC (beta 5 -2.6%, p50.043) in boys but not FEV1/FVC. This association was not observed in girls. No interaction of food and aero-allergen sensitization on lung function was observed.

CONCLUSIONS: In boys, from this clinically asymptomatic population, food allergen sensitization was associated with reduced lung function independently of aero-allergen sensitization. Potential explanations for these findings include that food allergen sensitization in childhood may serve as a risk factor for development of asthma, or that reduced lung volume develops as a result of early nutritional changes due to food allergy.

2.1.8. 434 Prevalence of Sensitization to Food Allergens Among Food Allergy Index and Control Families

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RATIONALE: The prevalence of sensitization to food allergens has not been previously described among family members.

METHODS: The data was derived from an ongoing family-based food allergy study in Chicago, Illinois. This analysis included 102 index children with clinically diagnosed food allergy (age 1-17.5 years), their 129 siblings (age 0.8-20.1 years), 145 mothers and 93 fathers from 181 index families, and 56 children (age 1.3-19.7 years) and 32 parents from 30 control families. Skin prick testing, using Multi-Test II, was performed to food allergens (cow milk, egg white, soybean, wheat, peanut, walnut, fish mix, shellfish mix, sesame seed) with histamine and saline controls. Sensitization was defined as mean wheal diameter 3 mm or greater than the saline control. The prevalence of sensitization was analyzed for index and control family members separately.

RESULTS: The most common sensitizing food allergens were peanut, walnut, sesame, milk, egg, and soy. Among index families, sensitization to at least 1 tested food allergen was observed in 83.3% of index children, 30.2% of siblings, 17.2%of mothers, and 44.1% of fathers; among control families, sensitization was observed in 23.2% of children and 9.4% of parents. Index children and their siblings had significantly higher rates of sensitization to 2 or more food allergens (64.7% and 18.7%, respectively) than children in control families (10.8%).

CONCLUSIONS: Our data showed higher rates of sensitization among siblings and parents of index children than those in control families. However, sensitization to food allergens was common even among children in control families.
Funding: Food Allergy Project, NIH M01 RR-00048

2.1.9. 495 Prevalence of Atopy in Rural China among Children and Adults

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RATIONALE: The prevalence of sensitization to foods and aeroallergens has not been previously described in a large unselected rural Chinese population.

METHODS: The data was derived from a community-based twin study in Anqing, China. Skin prick testing, using Multi-Test II, was performed on 2108 subjects to 9 foods (cow milk, egg white, soybean, wheat, peanut, walnut, fish mix, shellfish mix, sesame seed) and 5 aeroallergens (Alternaria tenius, dust mite mix [D. farinae and D. pteronyssinus], cat hair, dog epithelia, cockroach mix [American and German]) with histamine and saline controls. Sensitization was defined as a mean wheal diameter 3 mm or greater than the saline control. Atopy was defined as sensitization to _1 allergen. The analysis was stratified by gender and age (children [11-17 years] and adults [_18 years]).

RESULTS: The analysis included 927 same-gender twin pairs (n 5 1854 subjects); 58.2% were male (n 5 1080). Ages ranged from 11 to 70 years; 44.4% were children (n5824). Atopy was observed in 46.7% (n5866) of the total subjects, with 65.3% (n5556) of the atopic subjects sensitized to 2 allergens. The most common sensitizing food allergens were shellfish (16.2%, n 5 301) and peanut (12.4%, n 5 230), with prevalence higher in children compared to adults ($p<0.001$ for both). The most common sensitizing aeroallergens were dust mites (30.5%, n5566) and cockroach (24.9%, n5461), with prevalence higher in males ($p<0.01$ for both).

CONCLUSIONS: Sensitization to foods and aeroallergens was common in this rural Chinese population, particularly to shellfish, peanut, dust mites, and cockroach. The prevalence of atopy varied by age and gender.
Funding: This study is supported in part by grant R01 HD049059 from the National Institute of Child Health and Human Development and by the Food Allergy Project

2.1.10. 368 Indicators Of IgE-Mediated Clinical Reactivity To Peanut In Children

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RATIONALE: Diagnosis of peanut allergy is primarily based upon history. Prick skin tests (PST) and allergen specific IgE (sIgE) are sometimes obtained without a clear history of clinical reactivity (CR). This study evaluates the relationship between PST, sIgE, atopic dermatitis (AD), multiple food allergies (MFA) and parental atopy (PA) with CR to peanut.

METHODS: Children enrolled in a family-based food allergy study underwent standard questionnaire interview, PST (Multi-Test II, Lincoln Diagnostics) and sIgE analysis (ImmunoCAP, Phadia). CR was defined as typical symptoms of IgE-mediated reactions affecting _2 organ systems within 30 minutes of peanut ingestion. Multiple logistic regression models were utilized to examine the associations with adjustment for age, gender, and intrafamilial correlation. Odds ratios (OR) for continuous wheal size were for a 5 mm increase over 3 mm and for continuous log10IgE, an increase to log10 of 15 kIU/L from log10 of detectable.

RESULTS: Among 499 study children, 33 (7%) had CR to peanut. Including both PST and log10sIgE resulted in the best model for CR (PST: OR 5 1.8; 95%CI: 1.1-2.8, p 5 0.01; log10sIgE: OR 5 5.5; 95%CI: 2.1- 14.5, p 5 0.0006). AD and MFA were associated with CR in separate models (AD: OR 5 5.3; 95%CI: 2.1-13.0, p 5 0.001; MFA: OR 5 6.3; 95%CI: 3.0-13.7, p < 0.0001) but became insignificant when including PST and log10sIgE in the models. PA was not associated with CR.

CONCLUSIONS: Both PST and log10sIgE were independently associated with CR to peanut but other variables did not add predictive value. Our findings suggest that using both tests may better indicate CR to peanut than using either one alone.
Funding: The Food Allergy Project and Children's Memorial Hospital's General Clinical Research Center supported by the National Center for Research Resources, National Institutes of Health (M01 RR-00048)

2.1.11. 911 Associations and Temporal Relationship between Food Allergy and Asthma

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RATIONALE: Food allergy (FA) is a potential risk factor for asthma. Further investigation is important because of the potential to understand the etiologic pathway, anticipate evelopment of asthma, and consider early intervention.

METHODS: This analysis included 379 children, 6 years and older, from a family-based FA cohort in Chicago, IL. Asthma was defined by physician diagnosis and symptoms beyond age six. FA status was determined using criteria based on prick skin tests, allergen specific IgE (Phadia ImmunoCap) and type and timing of symptoms. Analyses were carried out using logistic regression adjusting for age, gender, ethnicity and intrafamilial correlation. Kaplan-Meier curves compared the time to onset of asthma by FA status.

RESULTS: Associations were seen between both symptomatic FA (OR: 5.1, 95% CI: 3.1-8.4, $p < 0.0001$) and asthma and asymptomatic food sensitization (OR: 1.9, 95% CI: 1.0-3.6, p 5 0.04) and asthma. As compared to children without FA, the association was stronger as the number of food allergies in children increased from 1-2 (OR: 4.4, 95% CI: 2.6-7.4, $p < 0.0001$) to 3 or more food allergies (OR: 11.2, 95% CI: 3.5-36.1, $p < 0.0001$). There was a median 1.25-year lag from the development of FA to the development of asthma. Children with FA developed asthma significantly earlier than children without FA (25th percentile: 2 years versus 6 years, log-rank test, $p < 0.0001$).

CONCLUSIONS: There was a strong association between FA and asthma in our population, especially in the subset with multiple food allergies. There was also evidence of a temporal relationship, with FA preceding the development of asthma by approximately 1.25 years in this selected cohort.
Funding: Food Allergy Project

2.1.12. 1040 Protective Effect of Early Fresh Fruit Ingestion on the Development of Food Allergy

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RATIONALE: Food allergy (FA) is increasing in prevalence in Westernized countries but knowledge regarding early life factors remains limited. We sought to evaluate the role of diet on FA development.

METHODS: This is part of a family-based study in Chicago, including 286 children with FA and 276 without FA (controls). FA was determined by objective symptoms developing within 2 hours of ingestion to one of 9 foods (cow milk, soybean, egg, wheat, peanut, walnut, codfish, shrimp, sesame), corroborated by positive skin prick test (Multi-Test II, [Decatur,
IL]) or ImmunoCAP >0.1 kUA/L (Phadia [Sweden]). Information on introduction of solid food in early childhood was obtained by parental questionnaire interview. Multivariate logistic regressions were performed with adjustment for child's age, gender, C-section delivery, and breastfeeding for _4 months along with maternal education, family income, parental atopy, and correlations between siblings.

RESULTS: The mean age of this sample was 3.6 years (range 0.5-7.0). When examined collectively, solid food introduction before 6 months [OR 0.90 (0.64, 1.29)] was not significantly associated with FA. However, when specific types of food were examined, introduction of fresh fruit before 6 months was highly protective [OR 0.28 (0.11, 0.72)] against
FA development. Introduction of jarred fruits [OR 0.92 (0.55, 1.52)] or green/orange vegetables [OR 0.84 (0.42, 1.68)] before 6 months was not protective.

CONCLUSIONS: Introduction of fresh fruit prior to 6 months appears to have an independent, protective effect against FA development. Further studies are needed on baby food processing and early food intake, including antioxidant micronutrients, in the development of FA.

2.1.13. 972 A Comparison of Fresh vs Commercial Extracts for Food Testing

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RATIONALE
The purpose of this study was to determine the presence of sensitization by using commercial vs fresh food extracts in the diagnosis of food allergy.

METHODS
Paired skin prick testing (SPT) was done using commercial (C) (ALK) and fresh foods (FF) (prick-prick method). Thirty seven patients were selected based on disease and history. Oral allergy syndrome was excluded. Testing was done using a Duotip-test II bifurcated needle (Lincoln Diagnostics).

RESULTS
Mean age: 5.5 years **Range:** 10 months-22 years.
Disease states: Acute allergic reactions (AAR): 22; Atopic dermatitis (AD): 17; Eosinophilic esophagitis (EE**):**12.
SPT Results: (number tested), measurements expressed as mm wheal/flare
Food
Egg white: (24) (C) 6/8; (FF) 18/30
Milk: (10) (C) 4/8(FF) 8/17
Corn: (3) (C) 0/0 (FF) 17/24
Potato: (1) (C) 0/0 (FF) 6/26
Shrimp: (3) (C) 8/18 (FF) 18/32
Peanut: (3) (C) 11/25 (FF) 11/31
Negative SPT with (C): egg: 5; corn: 3; milk: 2; potato: 1; shrimp: 1.

CONCLUSIONS
A SPT >3 mm is considered positive. However small wheal sizes can provide equivocal data making clinical decisions on restricting diet difficult… The use of fresh foods, especially for egg, milk, corn and potato provided significantly clearer positive responses. In addition 20% of egg and milk SPT were negative and 100% of potato and corn SPT were negative with commercial extracts. All corn negative patients had EE. Allergists are seeing more complex food allergic patients. The use of fresh foods for SPT provides greater sensitivity than commercial extracts. It is recommended that fresh extracts be used for SPT especially for egg, milk and corn.

2.2 ARTIGOS COMPLETOS

2.2.1. Comparative performance of five commercial prick skin test devices

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ABSTRACT: Five commercially available devices for performing prick skin testing were compared for reproducibility, patient acceptance, occurrence of false-negative skin test results, and size distribution of reactions at the negative control sites. Reproducibility of skin testing with 10 mg/ml histamine base, as expressed by coefficient of variation, was similar. However, a clear range of trauma to the skin was produced by the devices. This trauma was least with the Hollister-Stier and ALK Laboratories lancets, intermediate for the bifurcated needle by either prick or puncture, and greatest for the Multi-Test and DermaPIK devices. The more traumatic devices produced larger mean wheats and more frequent and large reactions at saline control sites, and were less acceptable to subjects. However, except for the Multi-Test device, they less often yielded false-negative responses. It is proposed that for each device a different size of wheal must be produced at the allergen site to have confidence that it exceeds the control site. The wheal size necessary for 99% specificity were as follows: Hollister-Stier lancet, 2 mm; ALK lancet, 3.0 mm; bifurcated needle prick, 4.0 mm; bifurcated needle puncture, 4.5 mm; Multi-Test device, 5.0 mm; and DermaPIK device, 5.5 mm. An additional observation was the presence of a significant gradient of reaction size on the back to both histamine and allergen ($p < 0.0001$), with the smallest reactions in the upper third and the largest in the lower third of the back.

2.2.2. Evaluation of Duotip-test

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Abbreviations:
CV (Coefficient of variation)

Duotip-Test (Lincoln Diagnostics) is a recently developed skin testing device used in detecting immediate hypersensitivity. It is a plastic disposable cylinder that measures 3 mm in diameter and 41 mm in length. At one end of the device there is a notched finish for grasping, and at the other end are two fine tapered points.

Duotip-Test is used with either a modified prick method or a rotation technique. We studied this new device, by using the rotation technique, to determine its reproducibility, sensitivity, and specificity with histamine and glycerosaline.

METHODS
This study was conducted in the outpatient Allergy and Immunology Clinic at St. Louis University Health Sciences Center. Subjects were recruited from patients seen in the clinic and from employees of St. Louis University Health Sciences Center. Institutional Review Board approval for the study was obtained, and each test subject gave written consent. Twenty subjects ranging in age from 26 to 65 years (mean age, 39.6 years) were tested. The subjects were nonatopic or atopic, were in good health, and had not used antihistamines or other inhibiting medications. Skin testing was performed on the volar surface of the arm, the right arm for 10 subjects and the left arm for 10 subjects.

The points of the device are loaded by capillary action after immersion in the test solution.

When the rotation technique is used, the shaft of the device is placed at a 90-degree angle to the skin, and just enough pressure is applied from the points to cause a small dimple in the test subject's skin. When rapidly rotated, the device makes a small circular abrasion in the epidermis and deposits the test solution.

In a blinded fashion, using the new device, one investigator administered a row of five epicutaneous tests spaced approximately 2.5 cm apart, four of which were 27 mg/ml histamine phosphate (10 mg/ml histamine base) in 50% glycerosaline and one of which was the negative control (50% glycerosaline). Another investigator, also in blinded fashion, read and recorded the wheal sizes at 15 minutes. A circular caliper disk, marked in 1 mm increments from 0 mm to 45 mm, was used to measure the wheals. Test solutions were obtained from Center Laboratories (Port Washington, N.Y.). Test devices were obtained from Lincoln Diagnostics (Decatur, Ill.).

RESULTS
A total of 80 histamine and 20 glycerosaline test sites were graded in the 20 subjects. Mean histamine wheal size was 7.5 mm (range, 4.0 to 10.5 mm) with a standard deviation of 1.5 mm. The mean coefficient of variation (CV) was 8.8% (range, 0% to 21%). Ninety-five percent of wheals at the negative control site ranged in size from 1.5 to 3.5 mm, with a mean size of 2.6 mm. One of the 20 test subjects had a negative control site with a wheal size of 4.0 mm. When 4.0 mm was used as the minimum wheal size regarded as positive, Duotip-Test had a sensitivity of 100%, a specificity of 95%, and a low mean CV (8.8%).

DISCUSSION

In recent years there has been a proliferation of skin testing devices, each requiring evaluation for sensitivity, specificity, and reproducibility of test results. Establishing wheal size confidence limits for each device, as suggested by Nelson et al.,1 appears to be practical. At the 4 mm wheal size for Duotip-Test, the sensitivity was 100% and the specificity was 95%. The low CV (8.8%) from this device reflects high reproducibility of results.

When comparing our findings from Duotip-Test with those obtained by other techniques, we note that Nelson et al.1 reported sensitivity and specificity at a 3 mm wheal positivity level from several one-at-a-time devices with histamine (10 mg/ml) and glycerosaline: HS lancet (Hollister Stier Miles Inc.), 98% and 100%; ALK lancet (ALK Laboratories), 100% and 95%; BN bifurcated needle (ALO Laboratories) prick, 100% and 87%; BN bifurcated needle puncture, 100% and 81%; DermaPIK (Greer Laboratories), 100% and 20%. The sensitivity and specificity results from Duotip-Test are comparable to those from HS lancet and ALK lancet but superior to results from the bifurcated needle and DermaPIK.

The 8.8% mean CV from Duotip-Test is substantially lower than the CV from any of the devices evaluated by Nelson et al.1 In the study by Nelson et al.,1 the CV ranged from 15% for the HS lancet to 19% for the bifurcated needle.

The Duotip-Test procedure was well accepted by all 20 adult subjects, and its administration was rapid and convenient.

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2.2.3. Clinical aspects of allergic disease - Evaluation of devices for skin prick testing

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The Journal of Allergy and Clinical Immunology
Volume 101, Issue 2, Pages 153–156, February 1998

BACKGROUND:
Previous comparisons of devices for percutaneous skin testing have revealed statistically and clinically significant differences, from one device to another, in the size of reactions to histamine and allergen extracts and at negative control sites.

OBJECTIVE:
The objective of this study was to compare the performance of several skin test devices which are either new, modified, or used with a modified technique.

METHODS:
Twenty subjects were tested five to eight times with each of the devices both to glycerol-saline and to 10 mg/ml histamine base. The devices tested were the MultiTest II, Duo Tip-Test (prick and scarification), Quintest, DermaPik (prick and scarification), and small pox needle.

RESULTS:
There were highly significant differences among the devices for the size of the reaction to histamine (mean wheal diameter 4.28 to 8.59 mm, $p < 0.0001$), the standard errors of the wheals to histamine (0.82 to 1.45 mm, $p < 0.05$) and in the mean wheal size with glycerol-saline (0.00 to 2.48 mm, $p < 0.0001$).

CONCLUSIONS:
Devices for performing skin prick testing vary greatly in several characteristics, including the size of reactions at both positive and negative test sites. Each skin test technician should be tested with the device used in that skin testing laboratory to establish criteria for positive and negative tests.

2.2.4. Letters to the editor: A comparison of multiheaded devices for allergy skin testing

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The Journal of Allergy and Clinical Immunology
Volume 113, Issue 6, Pages 1218–1219, June 2004

Previous studies comparing devices for percutaneous (ie, prick and puncture) skin testing have revealed significant differences in the size of wheal reactions to both the positive (allergen extract or histamine) and negative (saline) challenge sites. The tendency has been for devices that produce larger reactions with histamine to also be more likely to produce reactions at the negative control sites. The size of the reaction at both positive and negative control sites appears to reflect the degree of trauma imparted to the skin by the device, an interpretation that was reinforced by the fact that those devices producing larger wheals also caused greater patient discomfort. To some extent, the tendency to cause false-negative reactions to histamine corresponds to the tendency to produce smaller wheals. However, an exception is that for any size reaction to histamine, those devices with multiple heads appear to produce more false-negative reactions than single-headed devices.

2.2.5. Rhinitis, sinusitis, and ocular diseases - Comparison of test devices for skin prick testing

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The Journal of Allergy and Clinical Immunology
Volume 116, Issue 2, Pages 341–346, August 2005

BACKGROUND
Allergy skin testing guides developing avoidance plans and writing an immunotherapy prescription. The goal for the allergist is to apply allergen skin testing to the appropriate patient population by using a device that minimizes both false-negative and false-positive findings while minimizing patient discomfort. New skin testing devices continue to be developed with a trend toward production of multiheaded devices. Data on the performance of these devices in a head-to-head prospective fashion are limited.

OBJECTIVE
Our goal was to study 8 commonly used devices to compare their performance in a head-to-head fashion.

METHODS
In a prospective, double-blind fashion, the performance of 8 skin test devices was evaluated. Devices were tested with histamine and saline on both the arms and back of each subject. Devices were rotated over 4 testing sessions, at least a week apart, so each device was tested in each anatomic testing location. Performance elements examined included wheal, flare, pain, sensitivity, specificity, and intradevice variability.

RESULTS
We found significant differences in all areas of device performance among all devices examined. Multiheaded devices also demonstrated significant intradevice variability and were more painful than single devices. Furthermore, multiheaded devices had larger reactions on the back, whereas single devices had larger reactions on the arms.

CONCLUSION
Statistically significant differences exist among all devices tested. Providers should consider this data when choosing a device that suits their practice setting and ensure that technicians are sufficiently trained on the correct use of that device.

2.2.6. 1081 Comparison of Multi-Test II and Skintestor Omni Allergy Skin Test Devices

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The Journal of Allergy and Clinical Immunology
Volume 117, Issue 2, Supplement, Page S280, February 2006

RATIONALE: Because different devices for percutaneous allergy skin testing have demonstrated statistically and clinically significant differences in performance characteristics, we compared two FDA-approved multi-head allergy skin testing devices, Multi-Test II (MT2) (Lincoln Diagnostics) and Skintestor Omni (STO) (Greer).

METHODS: Skin tests with glycerinated histamine (6 mg/ml base) and glycerinated saline were applied to 31 adults using MT2 on the volar surface of one forearm, and STO on the opposite forearm. Diameters of wheals were measured at 20 minutes.

RESULTS: Collectively, the trial accumulated data from 155 histamine sites and 93 negative control sites for each device. Using wheal size cutoff levels of 3mm vs. 5 mm inclusive to define a positive result, MT2 sensitivity remained at 100%, but specificity increased from 74 to 97%, whereas STO sensitivity decreased from 94% to 87%, and specificity increased from 58% to 88%. For MT2 and STO respectively, histamine mean wheal sizes were 9.23 mm vs. 7.74 mm ($p < 0.001$), SD 1.37 vs. 2.83, mean coefficient of variance 14.8% vs. 36.6%, and pooled estimate of variance 0.642 vs. 6.974. MT2 produced similar histamine wheal sizes regardless of test head position used, whereas STO produced statistically smaller histamine wheals at certain test head positions (Games-Howell test).

CONCLUSIONS: Compared to STO, MT2 had higher sensitivity and specificity, and produced reproducible wheal sizes from all test head positions. In contrast, some STO test head positions produced significantly smaller histamine wheal sizes. In clinical testing with allergen extracts, this might lead to underdiagnosis of allergy.

2.2.7. 676 Stability of Allergenic Extracts in Multi-Test II_and Duotip-Test_ Skin Testing Wells

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The Journal of Allergy and Clinical Immunology
Volume 121, Issue 2, Supplement 1, Page S176, February 2008

RATIONALE: Skin testing routinely uses prick devices that fit into plastic well trays that contain the testing allergen extract. The allergen solution in the wells can be used several times with new devices for various lengths of time and practice conditions. The purpose of this study was to determine the stability of several allergenic proteins that contribute to the activity of the extracts in these wells.

METHODS: Multi-Test II_ and Duotip-Test_ devices from Lincoln Diagnostics were placed in their corresponding allergen Dipwell trays loaded with 9 allergen diagnostic strength extracts (50% glycerin concentrates, ALK-Abello, Inc.). The amount of major allergen protein was determined using monoclonal ELISA methods from ALK-Abello or in the case of short ragweed, FDA polyclonal Amb a 1 serum. The wells were tested1 month after storing at room emperature or 3 months after storing refrigerated.

RESULTS: Timothy, Bermuda, English plantain, short ragweed, cat hair, olive tree pollen, mugwort, white birch, and mixed mite all showed very good stability even at room temperature for 1 month. Slight evaporation from the Multi-Test II wells were detected resulting in <10% increases in major allergen concentration. Non-glycerinated birch extract completely evaporated after 1 month at room temperature confirming the manufacturer's recommendation for using 50% glycerinated extracts with their devices.

CONCLUSION: Important allergens related to the potency of diagnostic extracts are stable in Multi Test and Duotip trays for up to 3 months. Occasional room temperature exposure during this time would not affect the activity of these allergens.
Funding: ALK-Abello

2.2.8. A comparison of skin prick tests, intradermal skin tests, and specific IgE in the diagnosis of mouse allergy

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The Journal of Allergy and Clinical Immunology
Volume 121, Issue 4, Pages 933–939, April 2008

BACKGROUND
Mouse sensitization is assessed by using skin testing and serum levels of mouse allergen-specific IgE (m-IgE). However, it is unknown whether a positive skin test response or m-IgE result accurately identifies those with clinically relevant mouse sensitization.

OBJECTIVE
We sought to compare skin testing and m-IgE measurement in the diagnosis of mouse allergy.

METHODS
Sixty-nine mouse laboratory workers underwent skin prick tests (SPTs), intradermal tests (IDTs), and serum IgE measurements to mouse allergen, followed by nasal challenge to increasing concentrations of mouse allergen. Challenge response was assessed by nasal symptom score.

RESULTS
Thirty-eight women and 31 men with a mean age of 30 years were studied. Forty-nine workers reported mouse-related symptoms, of whom 10 had positive m-IgE results and 12 had positive SPT responses. Fifteen had negative SPT responses but positive IDT responses. Positive nasal challenges were observed in 70% of workers with positive m-IgE results, 83% of workers with positive SPT responses, 33% of workers with negative SPT responses/positive IDT responses, and 0% of workers with negative IDT responses. SPTs performed best, having the highest positive and negative predictive values. Among participants with a positive challenge result, those with a positive SPT response or m-IgE result had a significantly lower challenge threshold than those with a positive IDT response (P = .01). Workers with a positive challenge result were more likely to have an increase in nasal eosinophilia after the challenge compared with those with a negative challenge result (P = .03).

CONCLUSIONS
SPTs perform best in discriminating patients with and without mouse allergy. Mouse-specific IgE and IDTs appear to be less useful than SPTs in the diagnosis of mouse allergy.

2.2.9. 783 Comparison of the Multi-Test II and ComforTen Allergy Skin Test Devices

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The Journal of Allergy and Clinical Immunology
Volume 123, Issue 2, Supplement, Page S204, February 2009

RATIONALE: Different devices for percutaneous allergy skin testing have demonstrated statistically and clinically significant differences in performance characteristics. We compared two FDA-approved multi-head allergy skin testing devices: Multi-Test II (Lincoln Diagnostics) and ComforTen (Hollister-Stier Laboratories).

METHODS: Skin tests with glycerinated histamine (6 mg/mL base) and glycerinated saline were applied to 30 adults using Multi-Test II on the volar surface of one forearm and ComforTen on the opposite forearm.

RESULTS: Data were accumulated from 150 histamine sites and 90 negative control sites for each device. Using cutoff wheal sizes of 5 vs 3 mm inclusive to define a positive result, Multi-Test II sensitivity increased from 97% to 100%, and specificity decreased from 100% to 97%, whereas ComforTen sensitivity increased from 27% to 82%, and specificity decreased from 100% to 99%. For Multi-Test II vs ComforTen, histamine mean (SD) wheal sizes were 7.47 (1.72) vs 3.93 (1.59) mm (p 5 0.000), mean coefficients of variation were 23.0% vs 40.5%, and pooled estimates of variance were 1.42 vs 1.29. At different test head positions, there was no statistically significant variation in histamine wheal sizes with either Multi-Test II or omforTen.

CONCLUSIONS: Multi-Test II had notably greater wheal size and higher sensitivity, but similar specificity to ComforTen. Multi-Test II had superior performance at both 3 mm and 5 mm wheal cutoffs. Because ComforTen had a low sensitivity at the 3 mm and particularly the 5 mm wheal cutoff, skin testing with this device might result in underdiagnosis of allergy using either cutoff.

2.2.10. Effect of pretreatment with omalizumab on the tolerability of specific immunotherapy in allergic asthma

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The Journal of Allergy and Clinical Immunology
Volume 125, Issue 2, Pages 383–389, February 2010.

BACKGROUND
Although specific immunotherapy is a valuable treatment option for patients with allergic asthma, the potential for systemic allergic reactions has limited its use, especially for patients with symptomatic disease.

OBJECTIVE
To evaluate omalizumab's effect on the tolerability of specific immunotherapy in patients with symptomatic persistent asthma not adequately controlled with inhaled corticosteroids.

METHODS
This multicenter, double-blind, parallel-group study randomized patients to treatment with omalizumab or placebo, after which they received specific immunotherapy to at least 1 of 3 perennial aeroallergens (cat, dog, and house dust mite) according to a 4-week, 18-injection cluster regimen, followed by 7 weeks of maintenance therapy. The primary efficacy variable, a systemic allergic reaction after immunotherapy, was analyzed by using the Cochrane-Mantel-Haenszel test.

RESULTS
A total of 248 randomized patients (126 omalizumab, 122 placebo) received at least 1 dose of immunotherapy and were evaluated for efficacy. Patients receiving omalizumab experienced significantly fewer systemic allergic reactions to immunotherapy than those receiving placebo (17/126 [13.5%] vs 32/122 [26.2%]; *P* = .017; 95% CI, 2.91% to 22.56%) and had fewer respiratory-related (grade 3) systemic allergic reactions (6 vs 24, respectively). Grade 4 reactions were reported in 2 patients in each group. More omalizumab patients were able to reach the target maintenance immunotherapy dose (110 [87.3%] vs 88 [72.1%], respectively; *P* = .004).

CONCLUSION
Use of omalizumab in patients whose asthma was symptomatic despite use of inhaled corticosteroids was associated with fewer systemic allergic reactions to specific immunotherapy and enabled more patients to achieve the target immunotherapy maintenance dose.

2.2.11. Amish children living in northern Indiana have a very low prevalence of allergic sensitization

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The Journal of Allergy and Clinical Immunology
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The prevalence of allergic sensitization has increased in most developed counties over the past century. In the United States, the third National Health and Nutrition Examination Survey found 54.3% of the study population to have evidence of allergic sensitization. European studies have shown similar findings. In contrast to these studies of increasing prevalence, there are now a number of studies demonstrating that certain populations have a significantly lower prevalence of allergic sensitization and a lower prevalence of asthma.

2.2.12. Evaluation of a skin test device designed to be less painful

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The Journal of Allergy and Clinical Immunology
Volume 130, Issue 6, Pages 1422–1423, December 2012.

In 1965, Melzack and Wall proposed the “gate control theory of pain. ”The basic proposition of this theory is that signals from the periphery that are perceived in the brain as pain can be modulated and suppressed in the spinal cord by central influences, such as attention and emotions, and by peripheral input through large, rapidly conducting nerve fibers termed A-beta. Among the stimuli that activate these pain-suppressing nerve fibers, the authors listed vibration, scratching, and application of gentle pressure to the skin.