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ORIGINAL RESEARCH—ALLERGY

Prospective analysis of epicutaneous testing for inhalant allergy: Comparison of arm and back subsites with mRAST

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OBJECTIVES: 1) To compare epicutaneous testing (ET) from four skin subsites (forearm, upper arm, upper back, lower back) and 2) to compare ET to modified RAST (mRAST) for inhalant allergens.

STUDY DESIGN: Prospective clinical trial.

SUBJECTS AND METHODS: Fifty one patients underwent ET at four skin subsites and mRAST to six antigens and positive and negative controls.

RESULTS: The forearm and upper back showed best sensitivity to positive controls and all subsites demonstrated similar specificity to negative controls. The forearm and upper back demonstrated best sensitivity and specificity for most antigens. No statistically significant differences were noted for antigen sensitivity and specificity for the four subsites. ET and mRAST agreed best on *D. farinae* and timothy grass and least on short ragweed and dog epithelium.

CONCLUSION: This study confirms that forearm and upper back demonstrate very good sensitivity and specificity for positive and negative controls and most tested antigens. This has important diagnostic implications for clinical practice of inhalant allergy.

Since its initial description by Lewis and Grant in 1926,[1] skin prick, or epicutaneous testing (ET), has become a common diagnostic modality for defining the allergic profile. ET has been found to be reliable and convenient; it is more sensitive and reproducible than scratch testing and correlates better with intradermal testing.[2] The US Council of Allergy, Asthma, and Immunology[3] and the European Academy of Allergology and Clinical Immunology[4] have recommended ET as the preferred method for diagnosis of IgE-mediated allergic disease.

Multi-test II (MTII) (Lincoln Diagnostics, Inc., Decatur, IL) is a disposable, sterile, epicutaneous test applicator that allows for simultaneous application of eight antigens.[5] MTII has gained popularity secondary to convenience, reproducibility, safety, and patient acceptance.[6] Despite its advantages, MTII is a semi-quantitative test compared to modified radioallergosorbent testing (mRAST) or intradermal testing (IDT). A recent study by Levine et al evaluated the correlation between RAST and MTII.[7] They demonstrated poor positive correlation between results with overall average agreement of 67.86%, although agreement for negative tests was 95.15%.

Data available on the variation in regional skin responses and optimal site for skin testing is sparse at best.[8,9] Alexander and McConnell initially demonstrated the superior reactivity of the back compared to the forearm in 1930.[8] Nelson et al also have reported on the more notable skin response on the back compared to the forearm for histamine and cat allergen.[9] One must also account for the regional skin differences in mast cell distribution.[10] Since sensitized mast cells release histamine in response to skin testing, regional variations in mast cell concentration could potentially impact the results seen with skin testing at various sites. Despite this data, some clinicians test for multiple allergens at varied skin subsites simultaneously and report results as equivalent measures of allergy.

The goal of this study was twofold: 1) to compare ET responses from four skin subsites (forearm, upper arm, upper back, lower back) and 2) to compare ET responses to mRAST for inhalant allergens. The study hopes to define the optimal site for placement of ET utilizing the MTII, while taking into consideration its correlation to mRAST.

METHODS

Fifty-one adult subjects with history of inhalant allergies were prospectively recruited for inclusion in the study from March 2005 to August 2006. The study setting was an academic center–affiliated regional rhinology practice

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Table 1
MTII wheal size and grade and the corresponding mRAST class

MTII wheal size	MTII grade	mRAST class
<5 mm	0	0
5-6 mm	2+	I, II
7-10 mm	3+	III
>10 mm ± pseudopod formation	4+	IV

(Cleveland Clinic Beachwood). All subjects were recruited from the clinical practices of Pete S. Batra, MD, and Martin J. Citardi, MD, of the Section of Nasal and Sinus Disorders at the Cleveland Clinic Head and Neck Institute. Institutional Review Board (IRB) approval was obtained prior to commencing with the study; all subjects signed an IRB-approved consent form prior to enrollment.

Inclusion criteria were as follows: 1) age between 18 and 65 years, 2) good general health, and 3) two or more symptoms (sneezing fits, itchy eyes, watery eyes, itchy nose, runny nose, itchy palate) suggestive of inhalant allergy, or one symptom suggestive of inhalant allergy with positive family history for inhalant allergy.

Exclusion criteria were as follows: 1) age less than 18 or greater than 65 years, 2) poorly controlled asthma, 3) pregnancy, 4) beta-blocker usage, 5) history of dermatographism, 6) history of latex sensitivity, 7) history of immunotherapy, 8) history of systemic reactions to skin testing, and/or 9) recent viral upper respiratory infection.

Complete history and head and neck examination were performed on all patients. Demographic data, clinical symptomatology, past medical history, concomitant sinonasal diagnoses (chronic rhinosinusitis, sinonasal polyposis, septal deviation, inferior turbinate hypertrophy, and history of previous sinus surgery), and family history of allergies were recorded in all patients.

MTII was initially performed on the forearm to six antigens and positive and negative controls. All reactions were recorded at 20 minutes. If no significant local or systemic reaction was noted after the initial testing, upper arm, upper back, and lower back were sequentially tested in all subjects.

Six inhalant allergens were tested, along with positive and negative controls: timothy grass (100,000 BAU/mL), short ragweed (1:20 w/v), *Dermatophagoides farinae* (10,000 AU/mL), cat dander (10,000 BAU/mL), dog epithelium (1:20 w/v), *Alternaria tenius* (1:10 w/v), positive control (histamine phosphate 2.75 mg/mL), and negative control (buffered saline in 50% glycerin). The antigens were standardized as per international standards set forth through the International Union of Immunological Societies' Committee for Allergen Standardization. The antigens and the controls were purchased from ALK-Abelló (Round Rock, TX).

Subsequent to ET, all patients were sent to the lab for blood testing. The mRAST utilized for testing in this study was ImmunoCap (Phadia AB, Portage, MI).

The reactions for MTII for the four subsites were recorded by wheal size in mm for the antigens and the controls. The wheals were converted to a scale of 0, 2+, 3+, and 4+ (Table 1). The responses for the mRAST were recorded as Class 0, I, II, III, and IV. The correlation between MTII and mRAST was determined as demonstrated in Table 1.

Statistical Analysis

Summaries of the demographic values were constructed using means and standard deviations for continuous measures. For each site, the sensitivity (using positive controls) and specificity (using negative controls) were calculated along with 95% confidence intervals. Pairwise comparisons of the sensitivities and specificities were performed using McNemar's test. Sensitivity and specificity for the six antigens by ET was determined by presuming mRAST to be the gold standard for the purposes of statistical analysis.

Weighted kappa statistics were used to evaluate agreement between skin subsites and between mRAST and each site for all allergens. Confidence intervals for each kappa statistic were calculated. As a reference, a kappa of 0.4 to 0.6 indicated moderate agreement, 0.6 to 0.8 indicated good agreement, and greater than 0.8 indicated near-perfect agreement. All tests assumed use of a 0.05 significance level.

RESULTS

The mean age of the 51 patients was 38 years with a male:female ratio of 0.8:1. Table 2 summarizes the distri-

Table 2
Demographic and clinical factors for the 51 patients

Measure	Level	N	Percentage
Gender	Male	23	45.1%
	Female	28	54.9%
CRS	No	28	54.9%
	Yes	23	45.1%
SNP	No	46	90.2%
	Yes	5	9.8%
Septal deviation	No	10	19.6%
	Yes	41	80.4%
ITH	No	31	60.8%
	Yes	20	39.2%
Previous FESS	No	40	78.4%
	Yes	11	21.6%
FH allergy	No	22	43.1%
	Yes	29	56.9%

CRS, chronic rhinosinusitis; *SNP*, sinonasal polyposis; *ITH*, inferior turbinate hypertrophy; *FESS*, functional endoscopic sinus surgery; *FH*, family history.