



Abstract

RATIONALE: Atopy, the genetic propensity to develop immunoglobulin E (IgE) antibodies in response to exposure to allergen, is often assessed by allergy skin testing.

METHODS: Allergy skin testing was conducted and total and specific IgE concentrations were measured in the Asthma Control Evaluation Study, a clinical trial involving 546 inner-city asthmatics aged 12-20 years. Correlations between wheal diameters and concentrations of total and specific IgE (log transformed) were evaluated for 5 allergens with Pearson correlation coefficients. Prevalences of a positive test were compared between allergy skin testing and IgE testing. The overall ability of the allergen-specific skin test to discriminate between individuals with and without elevated specific IgE (≥ 0.35 kU/L) was evaluated by calculating areas under the receiver operating characteristic (ROC) curves. A perfect test has an area of 1.0, a useless test 0.5.

RESULTS: Correlation coefficients for associations between allergen-specific wheal sizes and specific IgE were 0.70 and 0.65 for the dust mites *D. pteronyssinus* and *D. farinae*, respectively, 0.70 for cat, 0.67 for German cockroach, and 0.57 for *Alternaria tenius*. Correlations between allergen-specific wheal sizes and total IgE were much weaker: from 0.18 to 0.37. Compared to IgE testing, allergy skin testing underestimated the prevalence of a positive test for *A. tenius*, *D. farinae*, and *D. pteronyssinus* and overestimated the prevalence for cat. However, both tests gave the same prevalence of atopy (81%, defined as at least 1 positive test). Areas under the ROC curves were 0.92 for cat, 0.82 for German cockroach, 0.82 for *D. pteronyssinus*, 0.78 for *D. farinae*, and 0.77 for *A. tenius*. The wheal size that provided the optimal tradeoff between sensitivity and specificity varied by allergen from 0.5 mm to 5 mm.

CONCLUSION: Among this study population of inner-city asthmatics, the ability of allergen-specific skin tests to discriminate between persons with and without elevated specific IgE varied from fair to excellent depending on the allergen; however, both tests gave the same estimate of atopy.

Objectives

- To estimate correlations between allergy skin test wheal sizes and specific and total IgE
- To compare positive and negative results between allergy skin testing and IgE testing
- To compare the prevalence of atopy estimated by allergy skin testing and by IgE testing
- To determine the overall ability of allergy skin testing to discriminate between persons with and without elevated specific IgE

Introduction

- Atopy is the genetic propensity to develop IgE antibodies in response to allergen¹
- Atopy can be assessed by allergy skin testing or serum IgE
- Allergy skin testing is the most widely used method
- Several factors may affect skin test results: medications, area of the body tested, type of device used, experience of the tester, and quality of the allergen extract^{2,3}
- Variations in skin sensitivity to histamine between subjects may affect skin test results^{2,4}
- In contrast to in vitro IgE testing, results of allergy skin testing can be determined immediately and less expensively²
- Few studies have investigated the ability of allergy skin testing to predict serum IgE levels

Methods

- Data were obtained from the Asthma Control Evaluation Study (ACE), a randomized controlled trial that tested the use of exhaled nitric oxide in asthma therapy
- 546 asthmatics aged 12 to 20 years were enrolled at 10 centers
- Skin testing was performed by the prick puncture method on the volar surface of the forearm using a Multi-Test II device (Lincoln Diagnostics; Decatur, IL)
- Specific and total IgE were measured with the UniCap System (Phadia; Uppsala, Sweden)
- Wheal size was calculated as the difference between the mean diameter of the allergen wheal and the negative control, resulting in a negative wheal size for some tests
- Positive allergy skin test: ≥ 3 mm wheal size
- Positive specific IgE test: ≥ 0.35 kU/L
- ROC curves were plotted to determine the overall ability of the skin test to discriminate between persons with and with a positive IgE test

Allergen	Specific IgE		Total IgE	
	Spearman	Pearson	Spearman	Pearson
<i>Alternaria tenius</i>	0.52	0.57	0.14	0.18
Cat	0.73	0.70	0.38	0.37
<i>D. farinae</i>	0.62	0.65	0.22	0.20
<i>D. pteronyssinus</i>	0.67	0.70	0.31	0.28
German cockroach	0.67	0.67	0.36	0.35

Table 1. Spearman and Pearson correlation coefficients for the associations between allergen-specific skin test wheal sizes (mm) and specific and total IgE (kU/L). IgE values were log transformed. All correlations have a p-value < 0.0001.

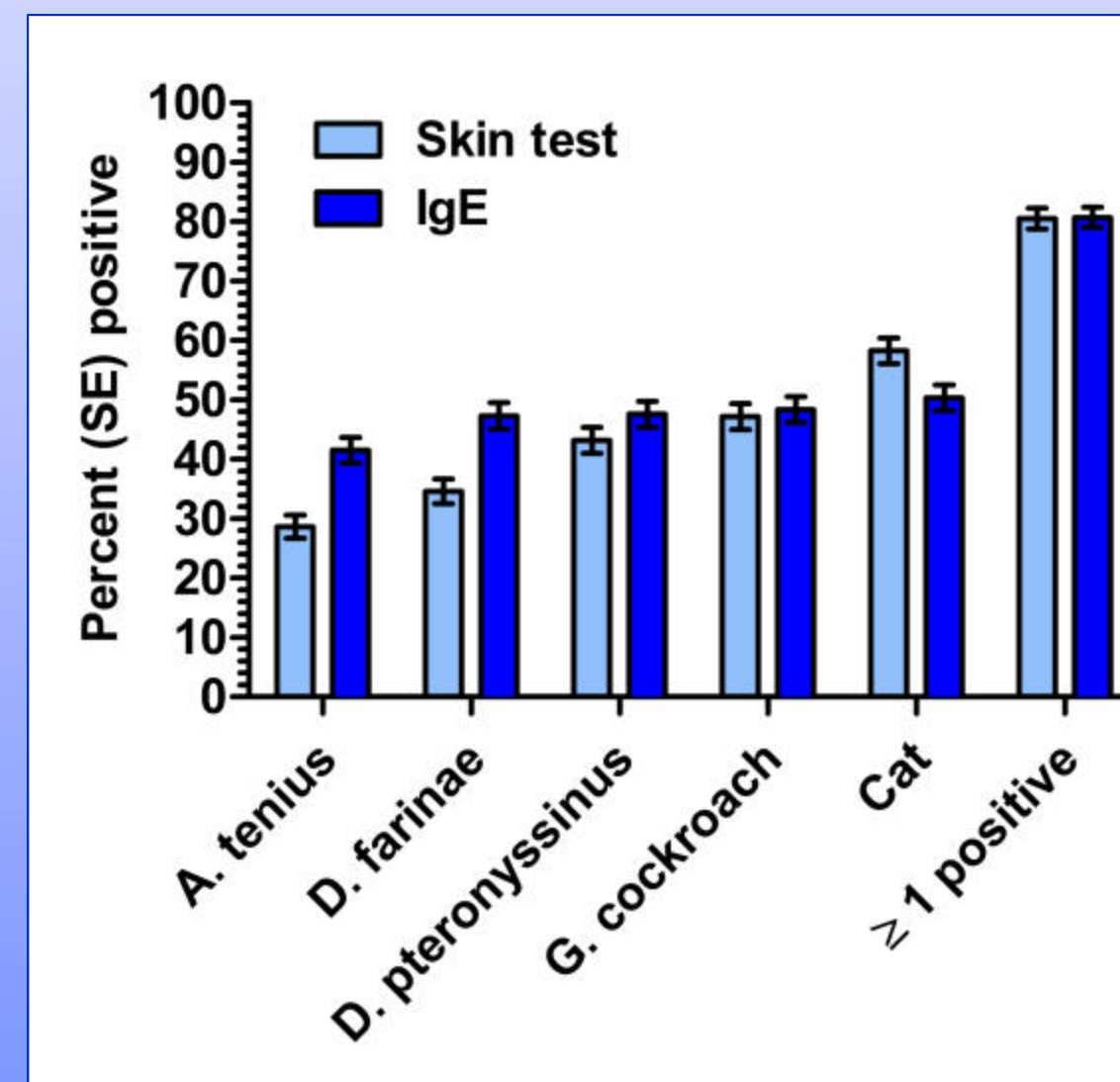


Figure 1. Prevalences of positive tests comparing skin testing to IgE testing

Allergen	Percent Agreement	Sensitivity	Specificity	PPV	NPV
<i>Alternaria tenius</i>	78.2	58.3	92.4	84.6	75.7
Cat	83.3	91.2	75.2	78.9	89.4
<i>D. farinae</i>	74.6	59.8	88.0	81.7	70.9
<i>D. pteronyssinus</i>	77.2	71.4	82.4	78.7	76.0
German cockroach	76.6	74.6	78.4	76.4	76.7

Table 2. Percent agreement, sensitivity, specificity, and positive and negative predictive values for each allergen-specific skin test (positive test defined as ≥ 3 mm) with specific IgE as the gold standard (positive test defined as ≥ 0.35 kU/L).

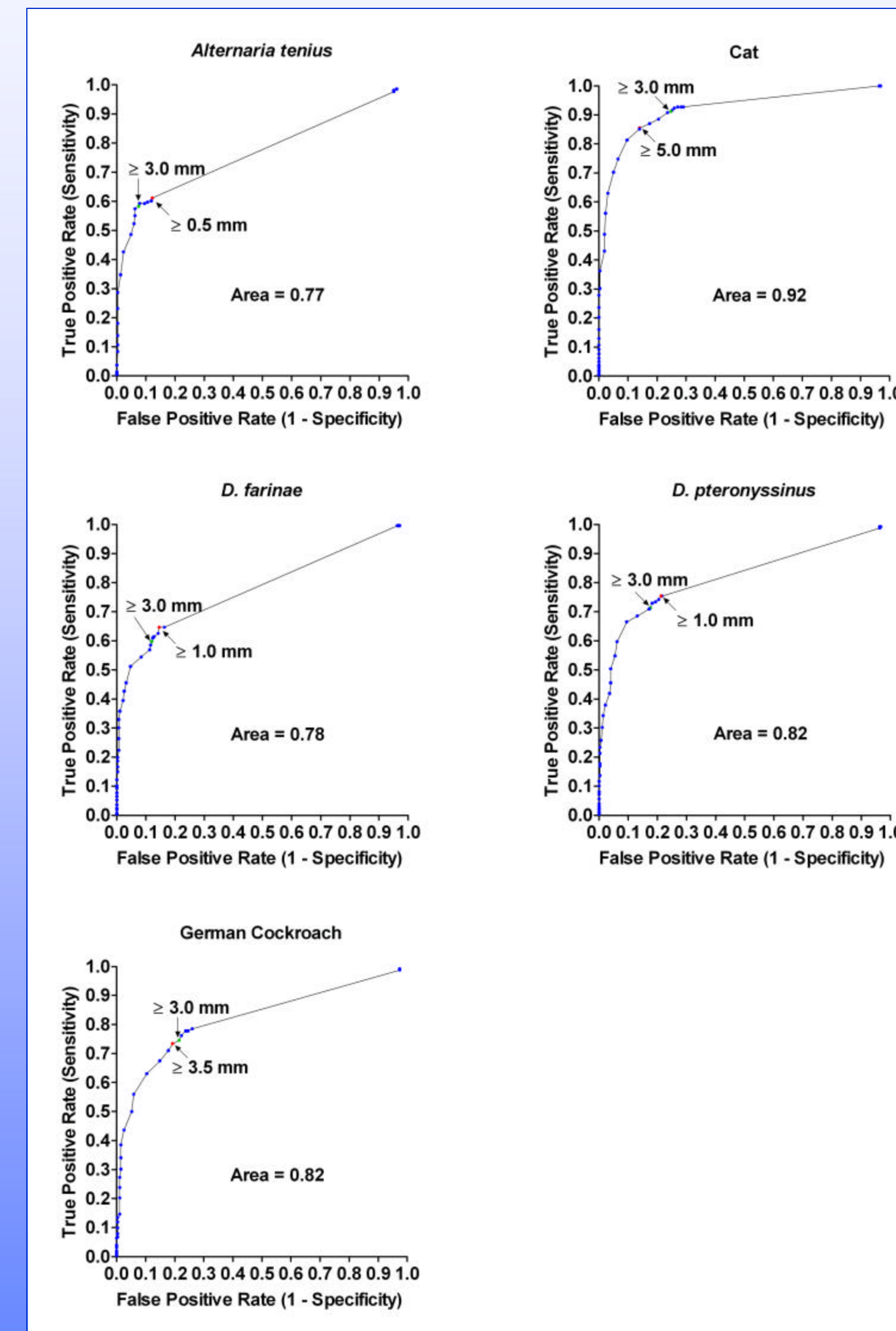


Figure 2. ROC curves for each of the allergen-specific skin tests. The gold standard test was specific IgE, with a positive test defined as ≥ 0.35 kU/L. Allergy skin test wheal sizes in 0.5 mm increments (result of taking the mean length and width of a wheal) are represented by dots on the curve. Across the allergens, wheal sizes, adjusted for the size of the negative wheal, varied from -3.0 to 24.0 mm. The red dot represents the wheal size that optimizes the tradeoff between sensitivity and specificity whereas the green dot represents a wheal size of ≥ 3 mm.

Results

- Allergen-specific wheal sizes were much more strongly correlated with specific IgE than with total IgE (**Table 1**)
- Allergy skin testing underestimated the prevalence of a positive test for *Alternaria tenius*, *D. farinae*, and *D. pteronyssinus* and overestimated the prevalence for cat (**Fig 1**)
- Both tests gave a prevalence of atopy of 81% (**Fig 1**)
- Percent agreements between allergen-specific skin test results and IgE test results varied from 74.6% to 83.3% (**Table 2**)
- Of the 5 allergy skin tests, cat was the most sensitive (91.2%) and *Alternaria tenius* was the most specific (92.4%) (**Table 2**)
- Areas under the ROC curves indicate that the ability of the allergen-specific skin tests to discriminate between positive and negative IgE tests varied from fair to excellent, with cat being excellent (**Fig 2**)
- The wheal size that optimized sensitivity and specificity varied from 0.5 mm for *Alternaria tenius* to 5.0 mm for cat (**Fig 2**)

Conclusions

- Correlations with allergen-specific wheal sizes were much stronger for specific IgE than for total IgE
- Compared to IgE testing, allergy skin testing underestimated the prevalence of a positive test for some allergens and overestimated the prevalence for one allergen
- Both IgE and skin testing gave the same prevalence of atopy
- The ability of allergen-specific skin tests to discriminate between persons with and without elevated specific IgE ranged from fair to excellent depending on the allergen
- A 3 mm threshold for a positive test did not provide the optimal tradeoff between sensitivity and specificity for any of the allergens; however, differences in sensitivity and specificity between the optimal wheal size and a wheal of 3 mm were likely too small to be clinically important

References

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