

Nasal mucosal brush biopsy for cat allergy

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We present preliminary data estimating the sensitivity, specificity, and predictive value of nasal mucosal brush biopsy (MBB) for the measurement of specific immunoglobulin E (sIgE) against cat dander.

Allergic rhinitis (AR) affects 10% to 30% of adults.¹ In 2016, 1.4% of U.S. physician visits resulted in the diagnosis.² The most common tests for AR, serum IgE detection and skin-prick testing (SPT), have significant false-positive rates. In addition, sIgE can be detected in locally symptomatic regions of the aerodigestive tract despite negative SPT and in vitro testing. MBB has detected local sIgE in people with AR, nonallergic rhinitis, food allergy, and eosinophilic esophagitis.³ Sensitivity and specificity estimates for MBB using respiratory allergens, however, has not been performed. Determining optimal testing cutoff levels is important for accurate environmental control counseling and immunotherapy decisions. Cat dander was chosen because of its high prevalence (12.1% in the United States) and self-identifiable nature.⁴

Patients and methods

Institutional Review Board approval was obtained (Protocol #1909020768). Those aged ≥ 18 years who had undergone nasal MBB were included. Clinical symptoms when around cats, age, gender, tobacco use, history of smoking, and results of serum sIgE and or SPT were collected from electronic health records and by telephone survey.

Nasal MBB was obtained and processed for IgE as previously described.⁵ Optimal cutoff levels were based on the highest level of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and test efficiency.

Data was evaluated with the nonparametric Mann-Whitney *U* test and Fisher's Exact Probability Test. Two-tailed *p* values were calculated and $p < 0.05$ was considered statistically significant. Receiver operating characteristic (ROC) curves were created in R Version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria; <https://www.r-project.org/>). For 10 individuals with cat allergy and 30 without, a 2-sample *t* test with a 0.05 2-sided significance level has 80% power to detect an effect size of 1.05.

Results

Of the 40 individuals identified with adequate information for inclusion, 10 were cat reactive. Table 1 displays demographic information.

The sensitivity, specificity, and predictive values at various cutoff levels are presented in Table 2. There was a significant association between cat sIgE from nasal MBB and clinical reactivity ($p = 0.007$). Six of 10 (60%) reactive participants had sIgE to cat dander on nasal MBB (mean $\pm$ standard deviation [SD] 0.52 ± 0.16 kU/L; range, 0.17 to 3.19 kU/L) vs 4 of 30 (13%) nonreactive participants (0.06 ± 0.01 kU/L; range, 0.10 to 1.53 kU/L) ($p = 0.002$).

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TABLE 1. Study population demographics for the cat-reactive and cat-nonreactive groups*

Characteristic	Reactive	Nonreactive	<i>p</i>
N	10	30	
Age (years), mean (range)	41.5 (30–58)	36.6 (19–67)	>0.05
Female: male, n	1:1	2.8:1	>0.05
History of tobacco use, n (%)	1 (10)	4 (13.3)	1.0
History of asthma, n (%)	5 (50)	2 (6.7)	0.006

*Values of *p* are based on Fisher's exact test; statistically significant values are in bold.

TABLE 2. Sensitivity, specificity, PPV, NPV, and correct classification rate using several cutoff levels for cat sIgE from nasal MBB testing in cat-reactive and cat-nonreactive individuals*

Cutoff level (kU/L)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Correctly classified (%)	<i>p</i>
0.05	60	87	60	87	80	0.007
0.1	67	87	60	90	82.5	0.003
0.11	75	88	60	93	85	0.001
0.12	75	88	60	93	85	0.001
0.14	75	88	60	93	85	0.001
0.17	71	85	50	93	82.5	0.006
0.2	80	83	40	97	82.5	0.01
0.26	80	83	40	97	82.5	0.01
1.6	100	77	10	100	77.5	0.25
3.18	100	77	10	100	77.5	0.25

*Values of *p* are based on Fisher's exact testing; statistically significant values are in bold. Optimal cutoff levels are highlighted in yellow. MBB = mucosal brush biopsy; NPV = negative predictive value; PPV = positive predictive value; sIgE = specific immunoglobulin E.

Mean total IgE in the reactive group was 12.90 ± 4.08 kU/L (range, 3 to 40 kU/L), whereas in the nonreactive group, the mean was 4.56 ± 0.83 kU/L (range, 2.6 to 14.6 kU/L) ($p = 0.003$). The median total IgE for all participants was 4.0 kU/L, and total IgE ≥ 4.0 kU/L was associated with clinical reactivity ($p = 0.02$). The optimal nasal MBB total IgE cutoff level was 10 kU/L, which had a sensitivity of 83%, specificity of 85%, PPV of 50%, NPV of 97%, and efficiency of 85%.

The ROC curve for cat sIgE from nasal MBB had an area under the curve (AUC) of 0.75 (95% confidence interval [CI], 0.57 to 0.93; $p < 0.05$), whereas total IgE from MBB had an AUC of 0.82 (95% CI, 0.64 to 0.99; $p < 0.05$), both of which are categorized as “good.”

Applying dual cutoff criteria (≥ 0.12 kU/L for sIgE and ≥ 10 kU/L for total IgE), there was a strong association between cat reactivity and positive testing ($p = 0.00005$). The sensitivity for nasal MBB using these criteria was 70%, the specificity was 97%, the PPV was 88%, the NPV was 91%, and efficiency was 90%.

SPT had been performed on 8 of 10 (80%) of the reactive group and 3 of 27 (11%) of the nonreactive group and was not associated ($p = 0.55$). Serum testing had been per-

formed in 4 of 10 (40%) of the reactive group and 27 of 30 (90%) of the nonreactive group, also revealing no association ($p = 0.35$).

Discussion

This preliminary study demonstrates for the first time that sensitivity, specificity, and predictive value of local sIgE testing for cat dander allergy is similar to serum and skin testing. Previously, peanut-specific IgE using oral MBB demonstrated a similar efficiency and optimal cutoff level of 0.12 kU/L.⁶

Wood et al.⁷ found SPT and serum sIgE had sensitivities of 97% and 87%, specificities of 80% and 90%, PPVs of 90% and 91%, NPVs of 87% and 86%, and efficiencies of 89% and 89%, respectively. In our study, both MBB sIgE and total IgE correctly classified 85% of those with cat reactivity, whereas applying dual cutoff criteria increased efficiency to 90%.

We found no association between cat allergy and SPT or serum sIgE. In a recent study, 95% of participants had nasal sIgE above a 0.10 kU/L cutoff, but only 40% had serum levels above this cutoff.⁸ Similarly, Zhang et al.⁹ found that in

children with adenotonsillar hypertrophy who tested negative for serum sIgE, local sIgE was detected in 44% of tonsils and 36% of adenoids.

Ono et al.¹⁰ found conjunctival levels of Japanese Cedar sIgE were a better predictor of symptoms than serum sIgE, which remained high in the asymptomatic offseason. Therefore, seasonally adjusted cutoff levels should be considered in future studies.

Nasal MBB predicts clinical reactivity to cats, with a sensitivity, predictive value, and efficiency similar to skin and serum testing. Because local sensitization can be present in the absence of systemic sensitization, mucosal sIgE levels may provide unique diagnostic information. Future studies in larger populations will help clarify the role of local sIgE testing as either a supplemental or stand-alone test.

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