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Comparison of Subject-Reported Allergy Versus Skin Test Results in a Common Cold Trial

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ABSTRACT

Background: *Few studies have examined the relationship between subject-reported allergy and results of allergy skin testing in large unselected or unbiased cohorts. The objective of this study was to compare the results of self-reported allergy via verbal questioning with the results of allergy skin testing by the puncture method in 237 healthy adult subjects enrolled in a common cold study.*

Methods: *On enrollment, all subjects were verbally asked if they had a history of allergy and then underwent puncture skin testing to 19 relevant aeroallergens, as well as appropriate positive and negative controls. A skin test was considered positive if its wheal diameter was at least 3 mm larger than that obtained with the negative control.*

Results: *Forty-eight (20%) subjects reported a history of allergy and 124 (52%) subjects had at least one positive skin test response. A history of allergy was reported in 40 (32%) of the skin test-positive subjects and 8 (7%) of the skin test-negative subjects. At least one positive skin test response was found in 40 (83%) of those subjects reporting a history of allergy and 84 (44%) of those subjects denying a history of allergy.*

Conclusion: *These data indicate that there is a relatively poor correlation between self-reported history of allergy and skin test results in subjects enrolled in a common cold study. These results have implications in both clinical practice and research settings.* (American Journal of Rhinology 17, 159–162, 2003)

Patient perceptions of the presence or absence of allergic disease may be largely inaccurate. Additionally, patients who have allergies may routinely misidentify the cause of their symptoms. For example, they may attribute chronic rhinorrhea, sneezing, and nasal congestion to recurrent viral upper-respiratory infections instead of perennial allergen exposure. Failure to recognize allergy symptoms or misidentification of the cause of the symptoms may result in the failure to obtain appropriate treatment interventions, including environmental controls, pharmacotherapy, and immunotherapy. Furthermore, misidentification of the cause of allergic symptoms may result in the use of costly and ineffective treatment strategies.

The appropriate diagnosis of allergic rhinitis also has implications in the clinical research setting. Many clinical trials of common cold therapies often consider allergy as a confounding factor but formulate the diagnosis solely on subjective reports of medical history. Without objective confirmation of allergic status, subjects may be misclassified. This could have important implications regarding the interpretation of results of clinical trials. The purpose of this study was to examine the relationship between subjective

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(responses to verbal questionnaires) and objective (results of allergy skin testing) reports regarding allergy status among subjects recruited into a common cold study

METHODS

Subjects

The study population consisted of 237 healthy, adult volunteers (aged 18–55 years) who were enrolled in a common cold study.[1] This study was approved by the Institutional Review Board at the University of Pittsburgh School of Medicine and Carnegie Mellon University, and informed consent was obtained from all subjects before enrollment. Subjects were recruited from the University of Pittsburgh and the surrounding community by advertisements, which were designed to target the general population and did not specifically recruit subjects based on allergy history. All subjects had a general physical examination, urinalysis, and blood taken for assay of markers of hepatic and renal function and for assay of serum antibodies to human immunodeficiency virus using standard methods. Subjects were excluded if presenting with findings or a history suggestive of systemic illness or recent upper-respiratory infection, if they had marked elevations in the assayed parameters indicative of hepatic or renal impairment, if they required prescription medication for any condition other than birth control, or if they had antibodies to human immunodeficiency virus.

Allergy Self-Report

During the screening visit for the common cold study, one of the research personnel verbally asked each subject the following question: "Do you have allergies?" If a subject responded "yes," they then were asked "What are your allergies?" If a subject responded "no," no further questions were asked. No other history regarding allergic disease was obtained. Subjects responded to these questions without any prompting from the research personnel. Only reports of respiratory allergy were included in the analysis. Reports of food, venom, or drug allergy were not included.

Allergy Skin Testing

Each subject underwent puncture skin testing to locally relevant inhalant allergens. The panel included 1:20 dilutions of ragweed mix, grass mix, English plantain, tree mix (1:20), cocklebur (common), lamb's quarters, and pigweed; 1:10 dilutions of *Alternaria*, *Aspergillus*, *Helminthosporium*, *Hormodendrum*, *Penicillium*, *Epicoccum*, feathers, and dog hair/dander; 30,000 AU/mL of dust mites (*Dermatophagoides farinae* and *D pteronyssinus*); and 10,000 BAU/mL of cat pelt and cat hair (all obtained from Bayer Corp., Elkhart, IN). Histamine (1:1,000) and glycerinated phenol-saline (both obtained from Center Laboratories, Port Washington, NY) served as positive and negative controls, respectively.

Trained personnel of the Allergy and Asthma Research Center of Children's Hospital of Pittsburgh performed all puncture skin testing using standard methods.[2] In brief, each test solution was applied to the subject's forearm and the skin was punctured using a disposable steel puncture needle (Greer Laboratories, Lenoir, NC). Fifteen minutes later, a fine-point, felt-tip pen was used to trace the outline of the wheal and flare of each reaction. Transparent tape was then used to transfer the tracings to a data-recording sheet. The same person measured the wheal diameter of each reaction at its widest point using a clear millimeter ruler. A positive skin test response was defined as a wheal diameter at least 3 mm greater than the negative (saline) control.[2] For presentation, data were summarized using descriptive techniques.

RESULTS

The distribution of subjects based on reported history of allergy and skin test results is shown in Fig. 1. Forty-eight (20%) subjects reported a history of allergy and 124 (52%) subjects had at least one positive skin test response. A history of allergy was reported in 40 (32%) of the skin test-positive subjects and 8 (7%) of the skin test-negative subjects. At least one positive skin test response was found in 40 (83%) of those subjects reporting a history of allergy and 84 (44%) of those subjects denying a history of allergy.

Figure 2 shows the frequency of subjects manifesting positive skin test responses to different numbers of allergens. All subjects represented in this figure skin tested positive to at least one allergen and are subgrouped according to whether they denied or reported a history of allergy. The frequency of subjects with one, two, or three positive skin tests was higher in the group that denied a history of allergy, as compared with the group that reported a history

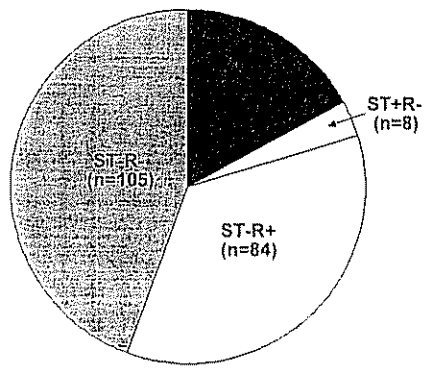

Figure 1. The distribution of subjects based on reported history of allergy and skin test results is shown. Black (ST^+R^+) corresponds to subjects who manifested at least one positive skin test response and reported a history of allergy. white (ST^+R^-) corresponds to subjects who manifested at least one positive skin test response and denied a history of allergy. gray corresponds to subjects who had negative skin test responses and reported a history of allergy (ST^-R^+), and cross-hatch (ST^-R^-) corresponds to subjects who had negative skin tests and denied a history of allergy.

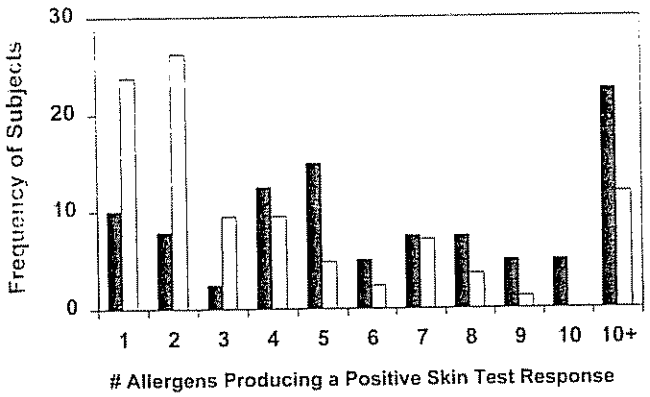

Figure 2. The frequency of subjects manifesting positive skin test responses to different numbers of allergens is shown. Black bars correspond to subjects who manifested at least one positive skin test response and reported a history of allergy. White bars correspond to subjects who manifested at least one positive skin test response and denied a history of allergy.

of allergy. Conversely, the frequency of subjects with other numbers of positive skin tests was higher in the group that reported allergy, as compared with the group that denied allergy. In subjects denying or reporting a history of allergy, the highest frequencies were observed for 2 and >10 positive skin test responses, respectively.

Figure 3 shows the frequency of subjects manifesting positive skin test responses to each specific allergen. All subjects represented in this figure skin tested positive to at least one allergen and are subgrouped according to whether they denied or reported a history of allergy. The most prevalent positive responses in subjects who denied a history of allergy were to dust mites. Those subjects also had a high frequency of positive responses to cat and some of the seasonal allergens. The most prevalent positive responses in subjects who reported a history of allergy were to seasonal allergens such as ragweed and grass.

DISCUSSION

The results of this study indicate a poor concordance between self-reported allergy and the results of puncture skin testing in a large number of subjects screened for a clinical trial. The unique aspect of this study is that subjects were recruited from the general population and not specifically targeted based on their allergic status. Consequently, the population is not expected to be biased toward selective enrollment of those with personal and/or family histories of allergy. This is in contrast to many studies that enrolled subjects based on personal and family history of allergy.[3–7] The value of classification based on personal and/or family history is disputed within the literature.[4,8,9] Results from studies using more detailed queries about personal and family history may yield increased concordance between subjective reports and objective assessments of allergy.

The inability of subjects to recognize allergies is evidenced by the fact that 80% of the study population denied a history of allergy while 52% had at least one positive skin test response. Although not investigated in this study, the failure to recognize allergy symptoms may be attributed to a variety of factors. For example, some subjects may have been asymptomatic, unaware of or acclimated to their symp-

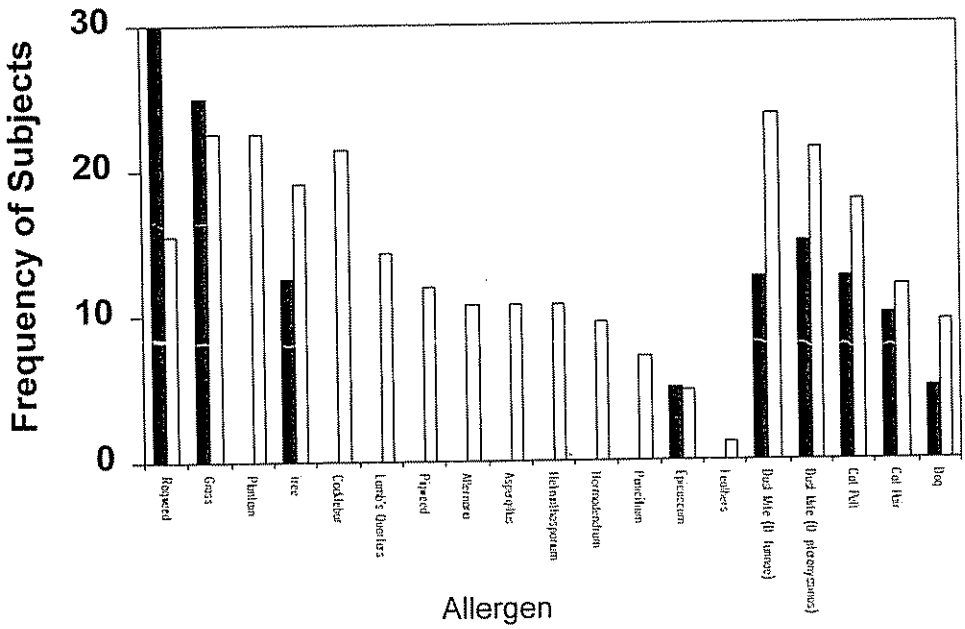

Figure 3. The frequency of subjects manifesting positive skin test responses to each specific allergen is shown. Black bars correspond to subjects who manifested at least one positive skin test response and reported a history of allergy. White bars correspond to subjects who manifested at least one positive skin test response and denied a history of allergy.

toms or misidentifying the causal factors. Alternatively, it is conceivable that a positive skin test is irrelevant in terms of symptom production.[10] Indeed, it is not uncommon for individuals to have positive reactions to skin tests and not experience any noticeable symptoms such as rhinitis, sneezing, coughing, or watery eyes.

The results of this study agree with some but not all of those from other studies examining the concordance between subjective reports and objective assessments of allergy. In this study, 83% of subjects reporting and 44% of those denying a history of allergy manifested at least one positive skin test response. One previous study reported at least one positive skin test response in 90% of subjects reporting a history of allergy, and others reported an elevated total or allergen-specific immunoglobulin E level and/or a positive allergy skin test response in 9–23% of subjects who denied a history of allergy.

In this study, subjects who reported a history of allergy and showed at least one positive skin test response were most likely to manifest a positive response to one of the seasonal allergens, including ragweed and grass. In contrast, subjects who denied a history of allergy but manifested at least one positive skin test response were most likely to manifest a positive response to dust mites, a perennial allergen. These findings are not surprising given the fact that there may be a greater level of awareness and association with seasonal as compared with perennial allergens. This heightened awareness is partially because of the explosive onset of seasonal allergic symptoms and may be influenced by the broad media exposure given to pollen counts during allergy seasons. In this study, the most prevalent skin test response among all subjects was to ragweed. This is consistent with findings reported in a previous study.[4]

The results of this study have important implications for certain clinical trials. Reliance solely on self-report of allergies may result in the misclassification of subjects and could confound the results of clinical trials. This is particularly true for trials investigating the physiological or pharmacologic aspects of diseases with similar symptoms such as allergy and respiratory infection. To avoid these unwanted outcomes, it is essential that allergy skin testing be done to confirm the selection criteria of a desired population. If appropriate screening measures are not taken, clinical investigators cannot be certain that the population under study is suitable for the evaluation of study-specific outcomes.

REFERENCES

1. Cohen S, Doyle WJ, Skoner DP, et al. Social ties and susceptibility to the common cold. JAMA 277:1940–1944, 1997
2. Demoly P, Michel F-B, and Bousquet J. In vivo methods for study of allergy: skin tests, techniques, and interpretation. In Allergy: Principles and Practice. Middleton E, Ellis EF, Yunginger JW, et al (Eds.). Vol. I. St. Louis, MO: Mosby Year Book, Inc., p. 32, 1998
3. Pecoud A, Bonstein HS, and Frei PC. Value of the case history in the diagnosis of allergic state and the detection of allergens. Clin Allergy 13:141–147, 1989
4. Eriksson NE. Diagnosis of reaginic allergy with house dust, animal dander, and pollen allergens in adult patients. III. Case histories and combinations of case histories, skin tests and the radio-allergosorbent test, RAST, compared with provocation tests. Int Arch Allergy Appl Immunol 53:441, 1997
5. Eriksson NE. Diagnosis of reaginic allergy with house dust, animal dander, and pollen allergens in adult patients. IV. An evaluation of the clinical value of skin tests, radioallergosorbent test, case history and combinations of these methods. Int Arch Allergy Appl Immunol 53:450, 1997
6. Mariotta S, Mannino F, Masullo M, et al. Allergic skin tests and respiratory allergy in 1612 subjects. Allergol Immunopathol 21: 30–34, 1993
7. Barbee RA, Lebowitz MD, Thompson HC, and Burrows B. Immediate skin-test reactivity in a general population sample. Ann Intern Med 84:129–133, 1976.
8. Brown HM. Taking a history. Practitioner 231:463–468, 1987
9. Nielson NH, Dirksen A, and Madsen F. Can subjects with a positive allergen skin test be selected by a short questionnaire? Allergy 48:319–326, 1993
10. Curran WS, and Goldman G. The incidence of immediately reacting allergy skin tests in a "normal" adult population. Ann Intern Med 55:777–783, 1961 □