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# Correspondence

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## THE USE OF INTRADERMAL SKIN TESTING IN ALLERGY DIAGNOSIS

**To the Editor:** As Calabria and Hagan<sup>1</sup> observed in their recent review, 85.2% of allergists perform intradermal skin tests (IDSTs),<sup>2</sup> a practice discordant with their conclusion, “Most of the literature suggests that with a negative skin prick test (SPT) result, a positive IDST result adds little to the diagnostic evaluation of inhalant allergy.” This inconsistency seems to be at least partly explained by frequently used methods of interpretation of IDST results. Virtually all research studies are based on classification of IDST results as either positive or negative.

Unlike cytologic test results that diagnose a patient as either having cancer or not having cancer, in vivo studies, such as skin tests, measure complex physiologic phenomenon along a continuum. Only at the extremes would one divide IQ test results into normal or abnormal. IQ test results correlate with performance, but a number of factors contribute to a student’s outcome. Spirometry is an imperfect but essential test for asthma, with its reliability improved because a large body of data allows correction of measured values for age, height, race, and sex.

Quantitative evaluations of IDST results, interpreting a 7-mm wheal differently than a 14-mm wheal (both positive by common criteria), are rarely reported, although, as with other tests, a more strongly positive result may be more significant. Others have noted better reproducibility of interpretation of SPT results with more strongly positive results.<sup>3</sup>

Hagy and Settiple<sup>4</sup> demonstrated that SPT-positive asymptomatic students had a higher incidence of developing subsequent allergic disease than asymptomatic but SPT-negative classmates, suggesting that even current symptoms are not absolutely reliable markers of allergy. Inhalational challenge would seem to be an ideal “gold standard,” but that too is debatable. Frenz<sup>5</sup> reviewed the complex relationship between pollen counts and symptoms, including days of demonstrated delay in the onset of symptoms after pollen counts increase and the effect of prior exposures in heightening hypersensitivity. A reactive IDST result, after a nonreactive or equivocal SPT result, correlates with atopy<sup>6</sup> rather than just being a random phenomenon that reflects cutaneous irritation. The role of an equivocal SPT result is also often ignored. It may be difficult to interpret an SPT result with heightened or reduced cutaneous reactivity.

Allergy diagnosis requires a combination of history, physical examination, and appropriately used diagnostic studies.<sup>7</sup> Properly interpreted by a skilled allergist, an IDST result can provide a useful means of excluding allergy and help identify significant hypersensitivity not detected by other studies.

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**Authors Response:** We thank the authors for their comments. Although most allergists reported in a survey<sup>1</sup> that they routinely use intradermal skin testing (IDST) when evaluating inhalant allergy, most evidence<sup>2–5</sup> suggests that with a negative skin prick test (SPT) result, a positive IDST result is generally clinically irrelevant. It is hoped that the evidence presented in the review<sup>6</sup> will enable physicians to objectively evaluate their approach to inhalant IDST. Although one may obtain a positive IDST result, in most cases, this represents sensitization rather than clinical allergy. In particular, with well-designed challenge models having been performed for cat,<sup>2</sup> timothy grass,<sup>3</sup> and mouse,<sup>4</sup> a positive IDST result for these allergens is unlikely to be helpful. In addition, a recent evidence-based review demonstrated that IDSTs generally have likelihood ratios near 1.0, meaning that they do not shift disease probability and are just as likely to be positive in patients without disease.<sup>7,8</sup>

Despite this, we believe that there is a limited role for IDST when evaluating inhalant allergy, particularly for allergens that are weaker, nonstandardized, or not previously studied using a challenge model. For example, IDST performed well in an evaluation of *Alternaria* hypersensitivity.<sup>9</sup> Our paradigm is to use the clinical history to guide a more selective approach to inhalant IDST, rather than routinely performing many IDSTs. This is consistent with the recommendations of the recent Joint Task Force report,<sup>10</sup> which recommends selecting diagnostic tests based on the patient’s exposure history. For example, in patients with rhinoconjunctivitis symptoms when exposed to dogs but with a negative dog SPT result, a dog IDST may be helpful. In addition, for patients with suspected allergic fungal sinusitis who have negative mold SPT results, mold IDST seems reasonable.

Although it is conceptually appealing that a larger positive IDST wheal (14 mm) would better predict clinical allergy, there is currently limited evidence supporting this. The definition of a positive IDST result in most studies using challenge models was a 5- or 6-mm wheal with surrounding erythema,<sup>2–4</sup> which is comparable with what many allergists call a positive IDST result,<sup>1</sup> making the results applicable to most patients. Presumably, some study patients had 14-mm wheals, yet consistently positive IDST results had low agreement with allergen challenges. Future challenge studies inves-

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tigating a longer duration of allergen exposure,<sup>11</sup> weaker nonstandardized allergens, and positive IDST results along a continuum would clarify the role of inhalant IDST further. Therefore, although in 1 abstract<sup>12</sup> a positive IDST result correlated with atopy, most studies<sup>2-5</sup> demonstrated that with a negative SPT result, a positive IDST result has low agreement with in vitro results, clinical history, and allergen challenges. Thus, we recommend more judicious utilization of IDST for inhalant allergy based on the patient's history and reserved for weaker, nonstandardized allergens.

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## IS MORE INTRADERMAL SKIN TESTING APPROPRIATE FOR OLDER PATIENTS?

**To the Editor:** Shortly after I mentioned the review of indications for intradermal skin tests by Calabria and Hagan<sup>1</sup> to my nonphysician wife, she showed me an article on allergies in the elderly from the *Wall Street Journal*. The consultant for that article, whose name I do not recall, stated that because of reduced skin test sensitivity with advancing age, she depends more on intradermal skin tests for the diagnosis of inhalant allergies in older adults. Could Drs Calabria and Hagan comment on the extent to which available evidence supports, refutes, or fails to definitively evaluate this practice and whether it supports age-based modification of the conclusions and recommendations contained in their review.

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**Authors Response:** We thank Coifman et al for their comments regarding intradermal skin testing (IDST) and elderly individuals, an important question relevant to a group expected to double by 2020 and eventually outnumber children.<sup>1</sup> In elderly individuals, the prevalence of allergic rhinitis (AR) appears to decrease, whereas nonallergic origins increase.<sup>2</sup> In addition, skin test reactivity to aeroallergens in the general population increases through childhood, peaks in young adulthood, and decreases after the age of 50 years.<sup>3,4</sup> The reasons for this are incompletely understood but seem to be partially explained by decreasing total IgE levels with advancing age,<sup>5,6</sup> whereas histamine responsiveness is better preserved.<sup>7,8</sup>

Among atopic patients, however, skin test studies have demonstrated that the allergic response is more persistent into old age. Jackola et al<sup>9</sup> showed that the mean number of positive skin prick test results was similar among all age groups, and among ragweed allergic individuals they reported no change with age in specific IgE levels (skin prick or serum tests) or binding affinity to Amb a 1. Similarly, Stoy et al<sup>10</sup> performed IDST on ragweed allergic asthmatic patients and reported that, although there was decreased wheal and flare to *Alternaria* and house dust with age, there was no decrease in skin test reactivity to ragweed or other allergens. Furthermore, Huss et al<sup>11</sup> found 74.7% of elderly asthmatic patients were atopic, and King et al<sup>12</sup> noted elderly asthmatic patients to have higher total IgE and serum specific IgE levels to *Dermatophagoides pteronyssinus* than elderly, nonasthmatic patients.

Therefore, although in the general population atopy decreases in elderly patients, sensitization persists in many atopic patients into old age. Because new-onset inhalant allergy appears uncommon in advanced age, most elderly atopic patients presumably have a history of AR from younger adulthood. However, the natural history of rhinitis or skin test reactivity in older populations has not been extensively studied. In 1 of a few longitudinal studies of rhinitis in adults, Simola et al<sup>13</sup> noted a decrease in rhinitis severity and a trend for decreased skin test reactivity with aging, but there was no direct correlation between the 2.

In conclusion, evidence is insufficient to definitively support or refute the practice of using IDST more in elderly patients. IDST studies using allergen challenges typically did not include patients older than 65 years, so the clinical relevance of a positive result of IDST in this population has not been investigated. With lower skin test reactivity in elderly individuals, one could argue that IDST would provide enhanced sensitivity. However, with less AR one would be performing more testing in a population with lower disease prevalence, potentially leading to more false-positive results. Therefore, we recommend using the patient's clinical history to guide the decision to perform IDST, regardless of age. As the elderly population increases exponentially, prospective studies focusing on rhinitis and skin test reactivity in this age group seem urgently needed.

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