
What does a positive intradermal skin test result really mean?

Credit for the first skin testing device goes to Charles H. Blackley, a homeopathic physician from Manchester, England, who had allergic rhinitis. In 1865 he abraded a quarter-inch area of his skin with a lancet, applied grass pollen grains that had been placed on a piece of wet lint, and covered the scarified area with an occlusive bandage.¹ This resulted in intense itching and a large cutaneous response. Even today in the allergist's office, allergy skin testing (AST) remains the central test to confirm an allergic response to validated allergen extracts. This is not surprising because it is minimally invasive and, when performed correctly, has good reproducibility. Unfortunately, AST is not a perfect test because both false-positive and false-negative results may be seen. In theory, one could apply allergen directly to a mucous membrane, such as the eyes, nose, or bronchi, but this is much more time-consuming and has greater inherent risk to the patient.

Significant variations occur in AST methods in the US allergist's office. One of the more significant issues involves the practice of performing intradermal skin tests (IDSTs) in skin prick test (SPT)-negative patients despite the lack of data demonstrating utility of IDSTs²⁻⁸ in confirming allergic sensitivity in these patients. In a recent survey of US allergists, Oppenheimer and Nelson⁹ found that approximately 85% of allergists relied on the use of IDSTs in patients with negative SPT results. This finding is despite several prospective studies that have demonstrated that IDSTs add little to diagnostic accuracy in SPT-negative patients.²⁻⁸ Calabria and Hagan¹⁰ have provided an excellent review in their recent *Annals* publication examining the data regarding this issue. They review 7 studies that relied on challenge as the gold standard of allergy diagnosis in which patients demonstrated negative SPT results with positive IDST results and found that these results "correlate with history and provocation testing in only a few instances."

Allergists have been searching for a perfect tool to confirm allergic sensitivity. In most allergists' offices, the patient's history guides the choice of specific AST. Most allergists begin by performing SPTs, and if a negative result is produced, they next perform IDSTs with clinically suspicious allergens.⁹ Their rationale for this protocol is the belief that added sensitivity is seen with the IDST method. This seems reasonable because studies demonstrate that the IDST is at least 1,000 times more sensitive than the SPT.¹¹ The question

we are left with, however, is what is the cost of this added sensitivity? Is there a way for the allergist to differentiate a true-positive from false-positive IDST result? Some might argue that history is the discriminator. If that is true, why is there a need for the IDST? Others might argue that a negative IDST result allows the physician to know that the patient is not allergic to a historically suspicious allergen.

With regard to these issues, it is important to consider that a possible mechanism for a negative IDST result despite a strong history of allergen sensitivity could include the local production of IgE or the fact that the patient is allergic to a related allergen (such as a minor mold species) not tested for by the allergist. With regard to local IgE production, several authors have highlighted that one may not detect systemic elevation in specific IgE through skin testing or in vitro tests, yet when local mucosa is analyzed (both nasally and in the gut) one may detect elevated allergen specific IgE levels consistent with patient history.¹²⁻¹⁵ Regarding the issue of minor mold allergy, it is well known that there are millions of antigenically distinct molds, with only a hand-full well validated for allergy evaluation. Another important question allergists are left to grapple with is, in the case of an IDST-positive response with a negative SPT result, what added information is gleaned beyond history because there have been no controlled studies reported that examine the use of allergen immunotherapy based on a negative SPT result and a positive IDST result.

As pointed out by Calabria and Hagan in their review, the use of IDSTs adds little if any to SPTs when testing to potent allergens, such as cat and grass. In the case of less potent or unstandardized allergens, such as molds or trees, the addition of an IDST may provide further utility. It remains, however, for this issue to be confirmed with well-designed clinical studies. In the mean time, allergists are left to grapple with what a positive IDST result really means in the face of a negative SPT result.

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