Skin Testing for Food Allergy

The most clinically useful statistical descriptors of skin prick tests (SPTs) are the positive predictive accuracy (PPA) and the negative predictive accuracy (NPA). These measures describe, respectively, the probability of a positive double-blind, placebo-controlled oral food challenge (DBPCFC) in a patient with a positive test and the probability of a negative DBPCFC in a patient with a negative test. These measures are, however, dependent on the sensitivity and specificity of the tests and on the prevalence of the disorder in the population studied, as the formulas below indicate:

\[ PPA = \frac{sP}{sP + (1-f)(1-P)} \]

\[ NPA = \frac{f(1-P)}{f(1-P) + (1-s)P} \]

where \( f \) equals specificity, \( P \) equals prevalence (number of confirmed positive cases divided by the number of cases studied), and \( s \) equals sensitivity.

Skin testing by prick technique has an excellent safety record in the evaluation of food hypersensitivity. Skin prick tests for the common food allergens are excellent tools for identifying those at very low risk of reaction on eating the food but are of variable value in identifying patients who will be positive on challenge. Intradermal skin tests to foods are less safe and appear to add no predictive information. Skin tests to less common food allergens, especially fruits, are less well characterized and may require use of the food item itself as the source of allergen rather than a commercial extract. For a few foods, the CAP system fluorescent enzyme immunoassay (Pharmacia, Peapack, NJ) recently has been shown to have good ability to identify patients at very high probability of reaction on oral challenge. Oral challenge remains the definitive method of demonstrating sensitivity or tolerance to a food. The double-blind, placebo-controlled food challenge is the gold standard of diagnosis, but in many situations, simpler open or single-blind challenge procedures may be substituted. With careful, incremental dosing and a low starting dose, oral challenges for food hypersensitivity have an excellent safety record. Skin prick tests are of little value in the evaluation of adverse food reactions not mediated by IgE. Oral challenge is relied upon in this situation for definitive diagnosis, but challenges may be cumbersome if the time course of the presumed reaction is not rapid.
Importantly, PPA and NPA vary with prevalence in the population studied. Thus, values determined in a group of severe atopic dermatitis patients will not reflect accurately the PPA and NPA in a group of patients with a lower prevalence. However, if the prevalence is roughly known for a different group, and the sensitivity and specificity do not vary between the groups, the values may be estimated for the group with a differing prevalence (Table 1) [2–4].

In a population with a high prevalence of food allergy, the NPA for the common food allergens (egg, peanut, milk, wheat, soy, and fish) is high (usually greater than 95%). In a low-prevalence population, the NPA is even higher because it varies with the inverse of the prevalence. This observation is valuable in clinical practice because the patient population in a routine allergy practice is likely to have a relatively low prevalence of food allergy. In a routine office setting, a negative SPT to a food is a very strong evidence that the food may be consumed without systemic symptoms.

On the other hand, a positive skin test to a food is not a very strong evidence for the existence of food allergy (with the possible exception of confirmation of sensitivity after anaphylaxis to an isolated ingestion of a food). The PPA, even in a high-prevalence population, is seldom more than approximately 70% for the most predictive skin test (egg) and is lower for other foods. Because PPA varies directly with the prevalence, it is lower if a population with a lower prevalence is studied. Therefore, in a typical office practice, no positive skin test to a food is likely to have a high PPA, unless the patient is a member of a high-prevalence group (eg, severe atopic dermatitis patients) (Table 1). This observation is overlooked frequently by practitioners who use the skin test result as justification for food elimination without regard for the likely prevalence in similar patients. Unfortunately, most of such food eliminations are unnecessary and inappropriate.

The studies that defined these statistical parameters employed SPT techniques. Presently, there is no role for intradermal skin testing in evaluation of food allergy because it has been well demonstrated that only false-positives (clinically irrelevant IgE) are found by performing intradermal skin tests to foods for which SPTs are negative [1]. In addition, the risk of anaphylaxis is much increased compared with a SPT. Also important is the definition of a positive SPT to a food. Studies in the 1970s demonstrated that a SPT inducing a wheal less than 3 mm larger than the negative control was not predictive of reaction on DBPCFC [1]. Thus, skin test wheals less than 3 mm greater than the negative control are considered negative. This appears to be independent of the testing device as long as a prick technique (as opposed to puncture techniques requiring pressure to be exerted on the skin) is used.

Obviously, for skin tests, as for all tests, some judgement is required in selecting those who should be tested. Several groups of patients can be selected rationally as candidates for skin food testing. A fuller discussion of patient selection and the test algorithm is available [5•]. Children with atopic dermatitis who require daily medications for more than a few months may be tested because they have an approximately 30% prevalence of food sensitivity proved by DBPCFC [6, 7•]. Children with very severe atopic dermatitis have an even higher probability of food sensitivity (as high as 65%) [1]. The number of tests required in such children is probably fairly low because more than 80% of reactions to foods are due to five common foods: milk, egg, peanut, wheat, and soy. There is also evidence that SPTs with seven foods (milk, egg, peanut, wheat, soy, cod/catfish, and cashew) will detect 99% of children with a food allergy [7•]. Thus, when no specific food is implicated by history, testing to a broad panel of foods in hopes of finding a cause for symptoms is seldom helpful, except possibly in very severe atopic dermatitis.

Testing may also be useful for the patient when there is concern about food allergy in the absence of a very supportive history. In this case, there is an expectation that a negative test will speed reintroduction of avoided foods to the diet. However, the physician should be aware that an atopic patient may have clinically irrelevant positive (so-called false-positive) skin tests that may foster further patient anxiety.

A subset of food hypersensitivity reactions has been given the label “oral allergy syndrome” [8,9]. Patients with this variety of reaction typically describe oral itching or discomfort, and sometimes oral and lip swelling, related to consumption of foods that rarely are implicated in the food allergy studies described above. Fruits and vegetables are common inciting foods. The literature on oral allergy syndrome is problematic because of over-