Allergy Testing

JAMES T. LI, M.D., PH.D., Mayo Clinic and Foundation, Rochester, Minnesota

Allergic diseases are among the most common medical problems encountered in ambulatory practice. However, some patients with suspected allergic disease turn out, on further evaluation, to have a medical problem that cannot be attributed to an allergy. Allergy testing can help the physician determine if a patient's problem is caused by an allergy and identify the specific problem allergens (Table 1). Having established a correct allergy diagnosis, the physician is better equipped to select appropriate therapeutic interventions for that patient, such as allergen avoidance, medications, and, sometimes, immunotherapy (Table 2). For example, a patient with a specific pollen allergy may be instructed to increase medication use during the pollen season. Patients with an animal allergy may be instructed to use allergy or asthma medication before exposure.

There are several types of specific allergy tests. Immediate-type hypersensitivity (IgE) skin tests are typically used to test for airborne allergens, foods, insect stings, and penicillin. Immediate-type hypersensitivity also can be evaluated through serum IgE antibody testing called radioallergosorbent testing (RAST). Delayed-type hypersensitivity skin tests (patch-type skin tests) are commonly used in patients with suspected contact dermatitis. Some common allergens for patch testing are rubber, medications, fragrances, vehicles or preservatives, hair dyes, metals, and resins. This review focuses on immediate-type hypersensitivity skin testing and serum IgE antibody testing.

Immediate-Type Hypersensitivity Skin Testing

Immediate-type hypersensitivity skin testing is most commonly used in the diagnosis of allergic rhinitis, allergic asthma, food allergy, penicillin allergy, and stinging-
insect hypersensitivity. Skin testing can be performed by the percutaneous route (diluted allergen is pricked or scratched into the skin surface) and by the intradermal route (injection of allergen within the dermal layer).

**PERCUTANEOUS TESTING**

Several types of skin testing instruments are available for percutaneous skin testing. Each brand of instrument has its own sensitivities and specificities. Positive-control skin tests (histamine) and negative-control skin tests (diluent) are essential for correct interpretation of skin test reactions. About 15 minutes after the application of allergen to skin, the test site is examined for a wheal and flare reaction. A positive skin test reaction (typically, a wheal 3 mm greater in diameter than the negative control reaction, accompanied by surrounding erythema) reflects the presence of mast cell–bound IgE specific to the tested allergen.

Antihistamines interfere with the development of the wheal and flare reaction and should be stopped before immediate-type skin testing. First-generation antihistamines may be stopped two to three days before testing, but the newer, second-generation antihistamines can affect skin testing results for three to 10 days or longer.1 Medications with antihistamine properties, such as anticholinergic agents, phenothiazine, and tricyclic antidepressants, also should be discontinued before skin testing. Histamine H2-receptor antagonists (e.g., cimetidine [Tagamet], ranitidine [Zantac]) have a limited inhibitory effect; these medications may be stopped on the day of skin testing.1 Inhaled and short-term systemic corticosteroids generally do not significantly suppress the wheal and flare reaction of immediate-type skin tests.

Immediate-type skin testing is a safe procedure with a very small risk of systemic reaction. A retrospective study2 involving 18,311 patients found six mild systemic reactions over a five-year period. A nationwide survey of allergy specialists reported six fatal reactions to skin tests from 1945 to 1986.3

Allergy to airborne substances (i.e., allergic rhinitis and asthma) is typically evaluated using a panel of percutaneous skin tests for about 40 allergens. A number of the most commonly used allergenic extracts for skin tests are now standardized (Table 3). Percutaneous skin testing has been used to test for food allergy; however, it is less reliable for evaluating food allergy than for evaluating reaction to airborne allergens.

Analysis of the clinical performance of percutaneous testing for establishing an allergy diagnosis is limited by the lack of a universal gold standard to confirm a specific allergy. Clinical studies suggest that the medical history is generally inadequate to serve as a gold standard.4,5 Experimental trials where allergy exposure is carefully controlled provide better data about percutaneous testing.

In a recently published trial,6 patients with suspected cat allergy were tested through enclosure in a small room containing two cats. During a one-hour exposure, the study subjects were monitored for upper respiratory symptoms, lower respiratory symptoms, and spirometry changes. Each patient also underwent percutaneous testing. The sensitivity and specificity of percutaneous testing were 94 and 80 percent for upper respiratory symptoms, respectively; 84 and 87 percent for lower respiratory symptoms; and 97 and 81 percent for decreased forced expiratory volume in one second (a 15 percent fall or greater). A negative result for percutaneous testing indicated that a true cat allergy was unlikely.

The performance of percutaneous tests in the diagnosis of food allergy also has been widely investigated. In a study7 where the gold standard for allergy was a double-blind food challenge to the suspected allergen (e.g., egg, milk, peanut, soy, wheat, or fish), the sensitivity of percutaneous tests was 76 to 98 percent, with specificity ranging...
The low specificity of percutaneous testing for food allergens precludes a diagnosis of food allergy based on a positive skin test alone. A double-blind food challenge should be considered.
Allergy Testing

easier to obtain. Some patients cannot undergo skin testing because of skin disease that would obscure wheal and flare results (e.g., extensive atopic dermatitis) or because they cannot stop taking medications that suppress the skin test response. In cases of life-threatening allergy (e.g., anaphylaxis), laboratory testing is sometimes used as a proxy result, keeping in mind its limited sensitivity.

Allergic Rhinitis

The most common allergy-mediated clinical problem where specific testing may be needed is chronic rhinitis. The differential diagnosis of chronic rhinitis (nasal congestion, rhinorrhea, sneezing) includes allergic rhinitis, nonallergic inflammatory rhinitis, and rhinitis from a noninflammatory process, such as vasomotor rhinitis.

Many physicians make a presumptive diagnosis of allergic rhinitis based on the medical history. Management of these patients may include use of antihistamines, decongestants, or intranasal steroids. This is a reasonable and effective approach in many patients. In patients with significantly discomforting or disabling symptoms that are not controlled with standard measures, specific allergy testing may be warranted.

Percutaneous testing can help establish the correct diagnosis and identify the offending allergens (pollen, mold spores, dust mites, cockroaches, or household pets). Allergen avoidance measures often are difficult to implement and costly. After specific testing, avoidance measures can be targeted to allergens to which the patient is known to be allergic.

Allergen immunotherapy is another option in refractory cases of allergic rhinitis not amenable to the usual control measures. Like allergen avoidance, it can involve a lot of labor and expense. Specific allergy testing can identify patients likely to benefit from immunotherapy and provide guidance about which allergens to include in the therapy regimen. Allergen immunotherapy may be especially beneficial when avoidance and medications no longer control the patient’s symptoms.

Asthma

Allergic asthma often shares the same allergic triggers as allergic rhinitis. Allergen exposure in sensitive persons is an important cause of asthma symptoms and exacerbations. When standard control and avoidance measures are not effective, specific allergy testing may be helpful.

The second National Heart, Lung, and Blood Institute (NHLBI) guideline on asthma management recommends that all asthma patients who require daily therapy be evaluated for allergens as possible contributing factors. They also note that, in selected patients with asthma at any level of severity, specific allergy testing may be indicated as a basis for allergen avoidance or immunotherapy. These recommendations would lead to a limited number of allergy tests in about one half of asthma patients, according to guideline predictions. As mentioned previously, the NHLBI notes that specific allergy testing may be particularly helpful in justifying the expense and effort involved in avoidance measures. In addition, it could help promote patient compliance in maintaining environmental controls (e.g., with regard to pets).

The author indicates that he does not have any conflicts of interest. Sources of funding: none reported.

REFERENCES