

Allergy Testing

James T. Li

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Percutaneous and intradermal skin tests and laboratory assays of specific IgE antibodies may be useful in selected cases of allergy management. Percutaneous testing kits are available from various manufacturers. A number of common allergens are available in standardized preparations. Positive and negative skin controls are important in establishing reliable results. Antihistamine medications can interfere with skin testing and should be stopped beforehand. Serious reactions to skin testing are rare. Establishing the sensitivity and specificity of percutaneous testing is difficult because there is no widely accepted gold standard for defining a true allergic reaction. Intradermal testing is more sensitive than percutaneous methods but much less specific. Its use is restricted to testing for allergy to insect stings or penicillin. In cases where skin testing is not available or desirable, laboratory assays for IgE antibodies to specific allergens may be used. These assays are generally less sensitive than skin testing methods. Selected patients with allergic rhinitis or asthma that is not controlled with standard therapy may benefit from allergy testing, especially when it can target allergen avoidance measures or guide immunotherapy.

Table 1. Major Indications for Allergy Testing

Condition

Major indication

Rhinitis

Symptoms not controlled by medications and allergen avoidance

Asthma

Persistent asthma in patients exposed to perennial indoor allergens

Suspected food allergy

Previous suspected systemic reaction to food

Suspected drug allergy

Previous suspected systemic reaction to drug, and clinical indication for suspected drug

Suspected insect sting

Previous suspected systemic reaction to insect sting.

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.

Table 2. Management Principles of Allergic Conditions

Condition

Management modalities

Allergic rhinitis

Environmental interventions to reduce allergen exposure, medications, immunotherapy

Allergic asthma

Environmental interventions to reduce allergen exposure, medications, immunotherapy

Food allergy

Dietary modification, self-administered epinephrine for reaction

Drug allergy

Avoidance of suspected drug, drug desensitization

Insect-sting allergy

Precautions to reduce insect exposure, immunotherapy, self-administered epinephrine for reactions.

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, 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. Medications with antihistamine properties, such as anticholinergic agents, phenothiazine, and tricyclic antidepressants, also should be discontinued before skin testing. Histamine H₂-receptor antagonists (eg, cimetidine (Tagamet), ranitidine (Zantac)), have a limited inhibitory effect; these medications may be stopped on the day of skin testing. 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 study 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.

Allergy to airborne substances (ie, 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.

Table 3. Standardized Extracts for Allergy Skin Testing

| | |
|---|---------------------|
| Cat hair | June grass |
| Cat pelt | Perennial rye grass |
| Dust mite (<i>Dermatophagoides farinae</i>) | Orchard grass |
| Dust mite (<i>Dermatophagoides pteronyssinus</i>) | Timothy grass |
| Bermuda grass | Sweet vernal grass |
| Red top grass | Short ragweed. |

Note: Many other nonstandardized allergens are available for skin testing.

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. Experimental trials where allergy exposure is carefully controlled provide better data about percutaneous testing.

In a recently published trial, 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 study where the gold standard for allergy was a double-blind food challenge to the suspected allergen (eg, egg, milk, peanut, soy, wheat, or fish), the sensitivity of percutaneous tests was 76 to 98 percent, with specificity ranging from 29 to 57 percent, depending on the food extract used for testing.

The specificity for food allergen tests is generally low, partly because of cross reactions between some food groups (eg, legumes). Negative reactions to suggested food allergens on percutaneous tests make a diagnosis of true food allergy unlikely in most cases; however, the poor specificity of these tests precludes a definitive diagnosis of food allergy based on positive test results alone. A double-blind food challenge should be considered when more clinical certainty is needed in diagnosing a serious food allergy.

Intradermal Testing

Intradermal tests are much more sensitive than percutaneous methods (the tested allergen is 10- to 100-fold more diluted), but they have a lower specificity. Intradermal testing is usually reserved for venom and penicillin allergy testing when percutaneous tests are negative but here is high clinical suspicion of allergy.

Stinging-Insect Hypersensitivity. Adults who present with a history of a systemic reaction to insects (eg, bee, yellow jacket, hornet, wasp, fire ant) should be evaluated with allergy skin tests. Children who present with only dermatologic manifestations of a systemic reaction are not at substantially increased risk for future anaphylaxis and do not need allergy skin tests. Management of sensitive patients may include education, avoidance measures, self-administered epinephrine, and allergen immunotherapy.

Drug Allergy. Reliable allergy tests for drugs are available only for penicillin and local anesthetics. In many patients with a history of penicillin allergy, the simplest course is to prescribe an antimicrobial agent that does not contain a beta-lactam ring. In patients with a history of penicillin allergy who have a strong indication for use of a beta-lactam antibiotic, penicillin skin tests can be helpful.

A large study of patients with penicillin allergy showed that 1.220 of 1.227 patients (99 percent) with intradermal skin tests negative to penicillin did not experience a drug reaction when given penicillin. Of the nine patients with positive penicillin skin tests who received penicillin, two (22 percent) developed a drug reaction. In a similar but smaller study, 96 percent of patients with negative penicillin skin tests had no reaction when given penicillin, and 50 percent of

patients with positive penicillin skin tests developed a drug reaction when given penicillin.

These results suggest that penicillin can be given safely to patients with negative intradermal skin tests to penicillin. Patients with positive penicillin skin tests may be at increased risk for drug reaction, but the specificity of intradermal testing is low.

Assays for Specific IgE Antibodies

Although widely used in the past, serum measurement of the total IgE level is unhelpful in the diagnosis of allergy. Of more clinical use are assays for specific IgE antibodies to suspected allergens.

Assays for IgE antibodies specific to common airborne and food allergens are readily available. IgE antibody tests for venom and drugs have less clinical utility and are not routinely used. RAST was the first widely employed method of detecting IgE antibodies in blood that are specific for a given allergen. Several closely related variants are marketed (eg, modified RAST, Quidel QuickVue One-Step Allergen screen, Pharmacia Immuncap). Quantitative assays that include a reference curve calibrated against standardized IgE are preferred. It is important to select a reliable laboratory to perform RAST testing.

In general, RAST and other laboratory methods for IgE testing are highly specific but somewhat less sensitive than percutaneous tests. Results of laboratory testing for food-specific IgE are generally poor, even less helpful than those for percutaneous skin testing.

RAST or other laboratory testing is typically considered when skin testing is inconvenient or difficult to perform. Most primary care physicians do not have immediate access to a clinical skin testing laboratory, so RAST may be easier to obtain. Some patients cannot undergo skin testing because of skin disease that would obscure wheal and flare results (eg, extensive atopic dermatitis) or because they cannot stop taking medications that suppress the skin test response. In cases of life-threatening allergy (eg, 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 (eg, with regard to pets).