INTRODUCTION

Many physicians have the mistaken impression that allergic disease is diagnosed by allergy testing. The diagnosis of allergic disease is primarily dependent on the patient’s history of signs and symptoms typical of allergic disease during or shortly after allergen exposure. A common clinical example is a patient who states that every time he or she visits a home with a pet cat, he or she develops red, itchy eyes and sneezing. The ocular and nasal symptoms are typical of allergic disease, and the onset of symptoms when in homes with pet cats suggests that the symptoms are related to exposure to cat allergen. Two additional factors to consider when evaluating a history are the number of times the patient has noted the association between allergen exposure and symptoms, and whether similar symptoms occur at other times. If the symptoms are exclusively related to cat exposure and have occurred on multiple occasions, the diagnosis is relatively certain. The final step in confirming a diagnosis of cat allergy would be demonstration that the patient has detectable cat-specific IgE antibodies.

To clarify further the role of allergy tests in the diagnosis of allergic disease, it is useful to define a “gold standard” for diagnosis (see Table 1). To be certain that a patient has an allergic disease, it would be necessary to demonstrate that exposure to the putative allergen, under double-blind, placebo-controlled conditions, produces signs and symptoms of the disease process in question. It would also be necessary to demonstrate that the signs and symptoms are the result of chemical mediators released from mast cells and basophils via IgE binding to the allergen. This stringent definition of allergic disease is rarely met, even in research studies, because performing allergen challenge is very difficult.
Table 1
Criteria for Diagnosis of Allergic Disease

1. Absolute criteria for diagnosis of allergic disease (the Gold Standard)
   - Reproducible symptoms occurring during double-blind, placebo-controlled, allergen exposure when the route, dose, and duration of allergen exposure are consistent with estimated or measured natural or occupational exposure, and
   - The observed symptoms must be the direct result of the release of chemical mediators when the release of the mediators is triggered by the binding of IgE antibodies to the allergen
2. Clinical criteria for diagnosis of allergic disease
   - A history of signs and symptoms typical of allergic disease at a time and place when allergen exposure is probably occurring, and
   - The demonstration that the patient has IgE antibodies specific for the allergen associated with the occurrence of symptoms

Because of the difficulty in trying to satisfy the criteria of the gold standard, clinical criteria are usually accepted for diagnosis of allergic disease. Clinical criteria vary to some degree depending on the clinical situation and the relative risks and benefits to the patient, but usually include a history of recurrent symptoms of allergic disease when allergen exposure is occurring and the demonstration of allergen-specific IgE antibodies (Table 1). Thus, allergy tests are only adjuncts to the clinical diagnosis of allergic disease. There is a great temptation to equate the presence of detectable allergen-specific IgE antibodies with the diagnosis of allergic disease, but many individuals with antibodies are asymptomatic. In fact, some studies of large, relatively unselected populations have shown that over 90% of persons with IgE antibodies to stinging insect venom have no history of allergic reactions from insect stings. It is very important to understand that tests for allergen-specific IgE antibody, whether skin tests or in vitro tests, have little clinical value unless they can be interpreted in association with the patient’s clinical history.

SKIN TESTING FOR DETECTION OF ALLERGEN-SPECIFIC IgE

Physiology of Skin Tests

Skin tests are performed by introducing a small quantity of allergen into the epidermis by pricking, puncturing, or scratching the skin or by intradermal injection. The immediate wheal and flare response resulting from a skin test is the result of a complex series of interactions. After the allergen has been introduced into the skin, the allergen diffuses through the skin and interacts with IgE antibody bound to mast cells. Binding of the allergen to IgE antibodies bound to mast cells initiates the release of preformed (histamine, tryptase, chymase, heparin) and newly synthesized (prostaglandins, leukotrienes, cytokines) mediators.

The central wheal of the skin response is the result of histamine-induced vasopermeability and secondary edema. The central erythema results from histamine-induced arteriolar vasodilation, and the circumferential erythema results from the stimulation of nerve receptors and a resulting axon reflex vasodilation. The wheal and flare responses