

# Rational Approach to Allergy Testing



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## KEYWORDS

- Allergy testing • In vitro testing • Skin testing • Skin prick • Intradermal
- Allergic sensitization

## KEY POINTS

- Identification of allergens for patients with allergic rhinitis is useful for confirmation of diagnosis, institution of avoidance measures, and formulation of immunotherapy plans.
- The clinical history is essential in the decision for allergy testing, method of testing, and interpretation of the results.
- Allergy testing can be performed by in vivo or in vitro methods. There are benefits and limitations to both methods, and the clinical scenario should determine the appropriate test for each patient.

## INTRODUCTION

There is an increasing incidence of allergic diseases with up to 1 in 6 people affected by allergic rhinitis in the United States.<sup>1</sup> For patients with refractory symptoms of allergic rhinitis, allergy testing for identification of sensitizations is clinically useful for confirming the diagnosis, institution of avoidance measures, and formation of a desensitization protocol for immunotherapy. The decision to pursue allergy testing is based on clinical factors that include symptom severity, response to medical treatments, and potential usefulness of the positive test results. When deciding to pursue testing, there should be an identified benefit to understanding a patient's sensitizations. If the causative allergen is clear by history and there is no option of changing the environment or lack of interest in pursuing desensitization, testing may not be indicated. The clinical scenario is essential in determining the appropriateness of testing and type of test performed.

The diagnosis of allergic rhinitis remains a clinical entity in which history and physical examination with positive testing in appropriate circumstances are used for diagnosis. The history is essential in making the diagnosis of allergic rhinitis, deciding the

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appropriate allergy tests, and interpreting the significance of positive test results. The information provided by the history regarding symptom quality and timing of symptoms in relation to season, exposures, and environments can often guide the physician to the classes of possible allergens. Because no allergy testing method is 100% sensitive or 100% specific, the clinical information is needed to apply the result of any allergy test to the clinical treatment plan.

A wide range of antigens can cause allergic reactions resulting in testing panels that can be unfeasibly large. Screening tests were created as a more effective means to determine the likelihood of someone having a particular allergic sensitization.<sup>2</sup> Screening tests often consist of antigens that the individual has previously encountered and are common in the geographic region. A representative of each allergen class with consideration of cross-reactivities within classes are used to formulate a screening panel. Screening tests typically contain 8 to 12 common environmental allergens that are typical for a particular geographic location or specific environmental exposure.<sup>2</sup>

Once the decision for testing has been made, the method of testing is dictated by factors in the clinical history and an informed decision by the patient. Because there is no perfect testing method, understanding what each test is measuring is important. Allergic rhinitis is an IgE-mediated disease in which IgE on mast cells leads to activation by binding of allergens and subsequent release of mediators such as histamine.<sup>3</sup> Commonly used tests for allergic rhinitis rely on either measurement of in vitro–specific binding of allergens to circulating IgE in the serum or the in vivo release of histamine by mast cells, which react with antigens placed in the skin.

In vitro testing measures circulating IgE, which comprises only a small percentage of the total IgE in the body. Most IgE is bound to mast cells within tissue; thus, testing of sera may fail to identify an existing sensitization (false-negative, lower sensitivity). Conversely, in vivo testing measures a skin reaction to an applied allergen, which may react positively because of a non-IgE-mediated trigger or alternate mechanism than by the intended antigen (false-positive, lower specificity). The presence of circulating IgE or skin reaction to allergens can only confirm the diagnosis of allergic rhinitis if the history and physical examination findings correlate with the test results. Direct nasal responses with nasal challenge tests are not typically used in clinical practice because of logistics, side effects, and risks of severe reactions.

Both in vivo and in vitro methods have benefits and limitations that are important to consider in clinical practice. When allergy tests results are positive despite lack of clinical symptoms, false-positive results must be considered. Alternately, negative results in the scenario of clinically reproducible symptoms at the time of exposure suggest possible false-negative results. The decision for method of testing and interpretation of results continues to be a clinical entity that relies on the history, physical examination, and interpretation of allergy testing results to determine the optimal treatment regimens for patients.

## SKIN TESTING

In vivo skin testing evaluates the body's natural response to direct contact with an allergen. Skin testing was first described in 1872 when Dr Charles Blackley applied grass pollen to an abraded area of skin, causing an allergic response.<sup>2</sup> von Pirquet later performed skin testing for tuberculosis, prompting further development of skin testing. The scratch test was the first type of allergy skin test used, which consisted of applying the allergen into a scratched area on the forearm. Scratch testing is no

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