

Allergy Testing by Family Physicians in Primary Care

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Abstract: This article focuses on the common tests used in allergy testing in primary care setting. We conducted a search using electronic databases; MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL), up to December, 2017. A number of tests are available in order to help physicians in the diagnosis of allergic disease. These tests function by finding specific IgE antibodies. Skin prick testing is rapid, sensitive, and cost effective. Intradermal testing is typically used in individuals that have had a negative skin prick test when clinical history recommends an allergic reaction. It is favored as first line in insect venom allergies. Performing these tests will allow physicians to help determine the particular allergen associated with a person's allergic illness. From here, the next steps could be taken in helping patients manage their allergic conditions.

Keywords: Allergic diseases, family physicians.

1. INTRODUCTION

Allergic diseases are typically seen in the primary care setting. Asthma affects regarding 20 to 30 million Americans, which in many instances has an allergic part to it [1]. Allergic skin disease are likewise prevalent. Primary care physicians require to be comfy examining and handling patients with these disorders. Allergic illness are typically seen in the primary care office setting; indiscriminate battery of allergic testing is not regularly suggested without existence of clinical symptoms. Understanding and appropriate use allergic reaction testing is a vital part of allergic disorder management. Serum total IgE level measurement is not really useful, yet assays for certain IgE antibodies could be thought about in appropriate situations. In instances of persistent or chronic allergic rhinitis and allergic asthma, particular allergic testing may be practical. Allergy screening could help in the feasible recognition of the specific allergen that is associated with the allergy, which in the long run could assist to decrease the morbidity and death for patients. Box 1 summarizes the indicators of allergy testing.

This article focuses on the common tests used in allergy testing in primary care setting.

2. METHODOLOGY

We conducted a search using electronic databases; MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL), up to December, 2017. Search strategies used following MeSH terms in searching via these databases: "Allergy testing", "primary care", "strategies". Then we also searched the bibliographies of included studies for further relevant references to our review.

3. DISCUSSION

- **SKIN PRICK TESTING:**

The skin prick method is the most effective initial methods for screening people who have possible allergies. The treatment includes cleansing the skin with a 70% alcohol service. Then, a concentration of 1 to 10 or 1 to 20 g/L of the allergen is put on the skin. It is vital to make certain that the proper concentration of allergen, as stated in the package

insert, is made use of. It is additionally crucial to earn sure that each drop has just 1 allergen when trying to determine a hatred a particular compound. In particular circumstances, it is acceptable to make use of several allergens (eg, multiple forms of tree plant pollen). When performing the examination, the drops must be placed a minimum of 2 centimeters apart. Placing the declines closer to each various other increases the capacity for cross-contamination of the allergens resulting in potential false-positive or false-negative reading of the test. After the drops are placed, a commercial tool is made use of to puncture the skin causing the declines of allergen to go beneath the outer layer of the skin. The older method of "scratching" the skin with a needle or other gadget is hardly ever used currently since it brings a greater threat for systemic responses, and is extra likely to cause scars or other damages to the skin [2].Appropriate controls are important. The test must include both a positive and an adverse control to verify that the patient's skin responds appropriately. The positive control is usually a 10 g/L focus of histamine dichloride. The unfavorable control is usually the identical concentration of glycerinated saline. A positive examination outcomes is an elevated wheal on the skin with surrounding erythema. The histamine control usually generates a wheal of at the very least 3 mm in size. If the favorable control does not provide a wheal with a 3 mm diameter, it is feasible to merely count any type of wheal 3 mm or higher as a positive [3].The wheal of a positive test need to be of at the very least the very same size or larger compared to the histamine control. The dimensions for the size take place at 10 minutes for the control, and 15 to 20 minutes for the allergens themselves. A more accurate measurement can be done by determining the fattest and thinnest component of the wheal, and afterwards revealing this as an average [4].In some cases, utilizing ink and placing the size of the wheals on an item of paper is practical for the objectives of keeping documents.

Box 1. Indications for allergy testing

Perennial or seasonal rhinitis
Rhinosinusitis
Rhinoconjunctivitis
Rhinitis with otitis media
Suspected food allergy
Suspected drug allergy
Suspected insect bite or sting
Persistent asthma

• **CONTRAINDICATIONS:**

In general, allergy skin prick testing is a secure procedure. Rarely, it can cause systemic reactions, such as anaphylaxis. It is necessary to earn certain that people are not at a threat for anaphylaxis. Individuals with a high threat for anaphylaxis consist of those who have unrestrained asthma and those that have reduced lung function. People who have experienced anaphylaxis within the previous 30 days are bad candidates for skin prick tests because the examinations outcomes could have a false-negative result. Prior anaphylactic shock triggers the skin to be unreactive, a condition that lasts approximately 2 to 4 weeks. If the skin test leads to a positive examination, the outcomes are still precise and useful for the functions of medical diagnosis of an allergy. If the person has had anaphylaxis within the past month, it is still feasible to execute in vitro testing. This alternative does not have a risk of having false negatives due to the fact that the free immunoglobulins are usually much less impacted by recent anaphylaxis. Individuals with certain skin problem need to not have skin prick tests since these conditions make it more probable to have incorrect positive results. Some of these problems include dermatographism, urticaria (whether acute or chronic), cutaneous mastocytosis, and atopic dermatitis. For individuals that have atopic dermatitis, it is feasible to efficiently do the skin examination on locations of the skin that are not influenced by the problem. Other factors not to do skin tests (relative contraindications) consist of energetic angina and cardiac arrhythmias, older grownups who are in poor wellness, and ladies who are expecting. These teams are not necessarily at any type of higher risk for anaphylaxis, however are a lot extra vulnerable to the negative results of its treatment. Therefore, it is not suggested to carry out allergy skin tests on those individuals. Box 2 lays out some contraindications and care for skin prick screening.

Box 2 .Contraindications for skin prick testing

Individuals at high risk for anaphylaxis <ul style="list-style-type: none"> ○ History of severe allergic reaction to small amounts of allergen ○ Poorly controlled asthma and reduced lung function
Anaphylaxis within the last 30 days
Certain skin condition <ul style="list-style-type: none"> ○ Dermographism ○ Urticaria ○ Cutaneous mastocytosis
Relative contraindications <ul style="list-style-type: none"> ○ Significant cardiovascular disease ○ Frail elderly adults ○ Pregnancy

• **FACTORS THAT AFFECT RESULTS:**

Beyond the variables that impact whether an individual needs to undergo the allergy screening procedure, there are likewise a variety of elements that influence the real outcomes of the test. General aspects that influence the accuracy of outcomes include the resource of the allergen, or the sorts of skin examination devices that the screening individual makes a decision to use [5], [6], [7], [8].For instance, pollutants in the allergens could trigger false-positive test results. The purity and quality of the sample may not be high enough to cause a positive test result. Therefore, these variables have to be thought about when analyzing/interpreting test results.

• **FACTORS THAT AFFECT RESULTS: MEDICATIONS:**

Individuals going through allergy testing ought to stop taking specific medications. Particular medicines are taken into consideration perfectly risk-free and have no result on allergy testing. The medications that do not hinder skin test results consist of: leukotriene receptor agonists, many decongestants, beta agonists, breathed in or intranasal glucocorticoids, oral theophylline and cyclosporine [9], [10].Among the most common drugs that people should quit taking prior to an allergy test include all types of antihistamine drugs. This is because antihistamines are developed to assist decrease the allergic feedback and can cause the private to have a false-negative test. All sorts of antihistamines should be stopped including eye declines, nasal sprays, and oral drugs. Quitting all antihistamines 1 week or more prior to administering the skin prick test should suffice to avoid any interference [11].When individuals have particular kinds of problems that need the usage of glucocorticoids, it is vital to make sure that the screening happens on parts of the skin that has not been treated with those topical agents [12].Furthermore, specific types of antiimmunoglobulin therapies for asthma, including omalizumab, can lower skin reactivity for as much as 6 months, and it might be far better to cease making use of these drugs for 6 months prior to performing the skin prick test [13].H2 receptor blockers are various other medicines that people ought to discontinue 48 hours before administering a skin test [14].One more class of medications that can have an impact on skin sensitivity are tricyclic antidepressants, which could interfere with skin sensitivity for as much as 2 weeks [15].Antidepressants may be difficult to discontinue for that time period, so keeping in mind that people are on the medicines when executing the skin test is necessary. If the skin examination either has a weak result or has a negative result, it could be far better to do an in vitro allergy test versus a skin prick test. Physicians should bear in mind that careful serotonin reuptake inhibitors do not affect skin testing, and making use of these medicines as a choice might be a practical. The information on topical calcineurin inhibitors show mixed results, yet a whole lot of studies suggest that stopping the use of these drugs 1 week prior to doing the skin prick test must be fine. Generally, whenever there are medicines that could disrupt the results of a skin prick examination (Box 3), it is possible to execute artificial insemination testing.

Box 3.Medications affecting skin prick testing results

H1a antihistamines – stop 1 week before testing
Antihistamine nasal sprays – stop 3 days before testing
Antihistamine eye drops – stop 3 days before testing
Antihistamines used for nonallergic states (ie, promethazine, prochlorperazine) – stop 2 weeks before testing
Medications used for vertigo/motion sickness or insomnia (ie, meclizine, doxylamine) – stop 2 weeks before testing
H2 receptor blockers – stop at least 48 hours before testing
Topical corticosteroids – testing should be performed on skin that has not been treated

Tricyclic antidepressants – may need to stop 2 weeks before testing
Calcineurin inhibitors – stop at least 1 week before testing
Omalizumab – may need to 6 months before testing

Generally, skin prick testing causes a localized response and is a secure treatment that has little to no threat of complications. However, some people may have systemic responses, such as taking a breath issues. Consequently, the suggestion is to have emergency situation tools available, including epinephrine, to manage these possible systemic responses. Specific food allergens or latex might provide a much greater danger of having systemic reactions as compared with other allergens. Intradermal testing (rather than skin prick testing) is more most likely to lead to systemic reactions; nonetheless, the threat stays reduced. Therefore, skin prick testing is a far better option to intradermal testing. It is suggested to examine with skin prick testing prior to testing with intradermal screening to minimize the chance of anaphylaxis or undesirable results. A potential research study by Bagg and coworkers [16] entailing regarding 1500 participants reported the total rate of systemic responses secondary to skin tests to be 3.6%, none of which were severe. Aeroallergens were liable for the best number of systemic reactions, mostly from intradermal screening as opposed to simple skin prick screening. Anaphylaxis existed in a really small percent of individuals who underwent prick or puncture testing, although all of these individuals had a background of asthma. Other risk aspects for serious reactions consist of youngsters less compared to 1 year old and children who have energetic eczema. Additionally, youngsters who had asthma were more probable to experience anaphylaxis as compared to kids who did not have asthma [17]. Anaphylaxis in grownups that have asthma is likewise exceptionally unusual. Normally, with appropriate preparation it is very unlikely that anaphylaxis will lead to death [18].

• **INTRADERMAL TEST:**

Owing to the issues with the precision of the skin prick testing, an option is to do an intradermal test. These tests bring a much higher threat of systemic responses, including anaphylactic shock; nonetheless, the threat remains low [19]. Intradermal testing is a lot more delicate, and identifies immune feedbacks to irritants with much higher precision. Nevertheless, false-positive results are also much extra common, which means that these examinations are much less important to people who provide with no clinical signs and symptoms.

Table 1. Interpretation of skin prick test results[23].

Grade	Wheal
0	<Negative control
1	1 mm > control
2	2–4 mm > control
3	5 mm > control
4	Wheal with pseudopods

The strategy for providing the test is the exact like a tuberculin skin examination. Thus, a needle is made use of to inject of 0.02 to 0.05 mL of a 1:500 to 1:1000 weight per quantity irritant remove into the skin [20]. It is not necessary to have a favorable control if the skin prick test has already shown sensitivity to histamine. If this is not present, nevertheless, it could be needed to inject histamine to demonstrate the same feedback as the positive control. Intradermal testing is executed generally after an unfavorable skin prick test [21]. This lessens the risk of a private experiencing any systemic responses. The only exception to this is allergies associated with insect venom. Venom allergies are a lot more most likely to trigger fatality so intradermal tests are preferred, due to the fact that they are much more sensitive [22]. Better, it is not a good idea to make use of intradermal skin prick tests for food allergens because greater rates of systemic responses that have been reported.

The high danger of anaphylaxis in addition to the sensitivity of the test implies that it is feasible to use more dilute concentrations when performing this test. A lower focus not only decreases the chance of systemic responses, it additionally reduces the probability of a false-positive feedback [1]. A positive reaction is defined as either a wheal that is at the very least 5 mm in size; however, a survey done in 2008 showed that 85% of American board-certified allergists were defining at favorable result as any kind of wheal 3 mm or higher in diameter compared to the unfavorable control wheal. In enhancement, the 2008 technique parameter of the American Academy of Allergy, Asthma and Immunology states that "Any response larger than the negative control might indicate the visibility of specific IgE antibody." Table 2 shows the grading scale utilized for interpretation of intradermal test results [22].

False-positive results are more common with intradermal testing, particularly for inhalant allergens. Intracutaneous bleeding triggered by needle trauma throughout the administration of the test could be analyzed wrongly as a positive outcome.

Table 2. Interpretation of intradermal test results [23].

Grade	Wheal (mm)	Erythema (mm)
0	<5	<5
±	5-10	5-10
1	5-10	11-20
2	5-10	21-30
3	5-10 or with pseudopods	31-4
4	>15 or with many pseudopods	>400

4. CONCLUSION

A number of tests are available in order to help physicians in the diagnosis of allergic disease. These tests function by finding specific IgE antibodies. Skin prick testing is rapid, sensitive, and cost effective. Intradermal testing is typically used in individuals that have had a negative skin prick test when clinical history recommends an allergic reaction. It is favored as first line in insect venom allergies. Performing these tests will allow physicians to help determine the particular allergen associated with a person's allergic illness. From here, the next steps could be taken in helping patients manage their allergic conditions.

REFERENCES

- [1] Schidlow DV, Smith DS. A practical guide to pediatric respiratory diseases. Philadelphia: Hanley & Belfus; 1994.
- [2] Oppenheimer J, Nelson HS. Skin testing: a survey of allergists. *Ann Allergy Asthma Immunol* 2006; 96:19-23.
- [3] Adinoff AD, Rosloniec DM, McCall LL, et al. Immediate skin test reactivity to Food and Drug Administration-approved standardized extracts. *J Allergy Clin Immunol* 1990; 86:766-74.
- [4] Rueff F, Bergmann KC, Brockow K, et al. Skin tests for diagnostics of allergic immediate-type reactions. Guideline of the German Society for Allergology and Clinical Immunology. *Pneumologie* 2011;65:484-95
- [5] Carr WW, Martin B, Howard RS, et al. Comparison of test devices for skin prick testing. *J Allergy Clin Immunol* 2005; 116:341-6.
- [6] Nelson HS, Kolehmainen C, Lahr J, et al. A comparison of multiheaded devices for allergy skin testing. *J Allergy Clin Immunol* 2004; 113:1218-9.
- [7] Nelson HS, Lahr J, Buchmeier A, et al. Evaluation of devices for skin prick testing. *J Allergy Clin Immunol* 1998; 101:153-6.
- [8] Dykewicz MS, Lemmon JK, Keaney DL. Comparison of the Multi-Test II and Skintestor Omni allergy skin test devices. *Ann Allergy Asthma Immunol* 2007; 98: 559-62.
- [9] Simons FE, Johnston L, Gu X, et al. Suppression of the early and late cutaneous allergic responses using fexofenadine and montelukast. *Ann Allergy Asthma Immunol* 2001; 86:44-50.
- [10] Hill SL, Krouse JH. The effects of montelukast on intradermal wheal and flare. *Otolaryngol Head Neck Surg* 2003; 129:199-203.
- [11] Dreborg S. The skin prick test in the diagnosis of atopic allergy. *J Am Acad Dermatol* 1989; 21:820-1.
- [12] Andersson M, Pipkorn U. Inhibition of the dermal immediate allergic reaction through prolonged treatment with topical glucocorticosteroids. *J Allergy Clin Immunol* 1987; 79:345-9.
- [13] Corren J, Shapiro G, Reimann J, et al. Allergen skin tests and free IgE levels during reduction and cessation of omalizumab therapy. *J Allergy Clin Immunol* 2008; 121:506-11.

- [14] Kupczyk M, Kuprys I, Bochenska-Marciniak M, et al. Ranitidine (150 mg daily) inhibits wheal, flare, and itching reactions in skin-prick tests. *Allergy Asthma Proc* 2007; 28:711–5.
- [15] Rao KS, Menon PK, Hilman BC, et al. Duration of the suppressive effect of tricyclic antidepressants on histamine-induced wheal-and-flare reactions in human skin. *J Allergy Clin Immunol* 1988; 82:752–7.
- [16] Bagg A, Chacko T, Lockey R. Reactions to prick and intradermal skin tests. *Ann Allergy Asthma Immunol* 2009; 102:400–2.
- [17] Norrman G, Fa'lh-Magnusson K. Adverse reactions to skin prick testing in children - prevalence and possible risk factors. *Pediatr Allergy Immunol* 2009; 20: 273–8.
- [18] Bernstein DI, Wanner M, Borish L, et al. Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990-2001. *J Allergy Clin Immunol* 2004; 113:1129–36.
- [19] Lockey RF, Nicoara-Kasti GL, Theodoropoulos DS, et al. Systemic reactions and fatalities associated with allergen immunotherapy. *Ann Allergy Asthma Immunol* 2001; 87:47–55.
- [20] Dolen WK. Skin testing and immunoassays for allergen-specific IgE. *Clin Rev Allergy Immunol* 2001; 21:229–39. 33. Lieberman P, Anderson JA. *Allergic diseases*. New York: Humana press; 2007.
- [21] Strohmeier B, Aberer W, Bokanovic D, et al. Simultaneous intradermal testing with hymenoptera venoms is safe and more efficient than sequential testing. *Allergy* 2013; 68:542–4.
- [22] Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol* 2008; 100:S1–148.
- [23] Slavin RG, Reisman RE, editors. *Expert guide to allergy and immunology*. Philadelphia: American College of Physicians; 1999. p. 8.