Allergy Testing

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KEYWORDS

• Allergy testing • Skin prick testing • Intradermal testing • In vitro allergy testing • Patch testing • IgE hypersensitivity • Allergen

KEY POINTS

- Allergic diseases are commonly seen in the primary care office setting; indiscriminate battery of allergic testing is not routinely recommended without presence of clinical symptoms.
- Symptomatic patients can undergo allergen specific immunoglobulin E (IgE) testing to help guide allergen avoidance.
- Skin testing can be performed by percutaneous or intradermal route.
- Serum total IgE level measurement is not very helpful, but assays for specific IgE antibodies can be considered in appropriate situations.
- In cases of persistent or chronic allergic rhinitis and allergic asthma, specific allergic testing may be helpful.

INTRODUCTION

Allergic diseases are commonly seen in the primary care setting. More than 50 million Americans suffer from allergic rhinitis. Asthma affects about 20 to 30 million Americans, which in many instances has an allergic component to it.[1] Allergic skin conditions are also prevalent. Primary care physicians need to be comfortable assessing and managing patients with these disorders. Knowledge and appropriate use of allergy testing is an important component of allergic disorder management. Allergy testing can assist in the possible identification of the individual allergen that is involved in the allergic reaction, which in the long run can help to decrease the morbidity and mortality for patients. **Box 1** summarizes the indications of allergy testing. This article focuses on the common tests used in allergy testing.

SKIN PRICK TESTING

The skin prick method is the best initial means for testing individuals who have potential allergies. The procedure involves cleaning the skin with a 70% alcohol solution.

Disclosure Statement: The authors have nothing to disclose.
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Prim Care Clin Office Pract 43 (2016) 363–374
http://dx.doi.org/10.1016/j.pop.2016.04.001 **primarycare.theclinics.com**
0095-4543/16/$ – see front matter

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

After that, a concentration of 1 to 10 or 1 to 20 g/L of the allergen is placed on the skin. It is important to ensure that the correct concentration of allergen, as stated in the package insert, is used. It is also important to make sure that each drop has only 1 allergen when attempting to identify an allergy to a specific substance. In certain circumstances, it is acceptable to use multiple allergens (eg, multiple forms of tree pollen).

When performing the test, the drops should be placed at least 2 centimeters apart. Placing the drops closer to each other increases the potential 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 device is used to prick the skin causing the drops of allergen to go underneath the outer layer of the skin. The older method of "scratching" the skin with a needle or other device is rarely used now because it carries a greater risk for systemic reactions, and is more likely to lead to scars or other damage to the skin.[2]

Appropriate controls are important. The test should include both a positive and a negative control to verify that the patient's skin responds appropriately. The positive control is generally a 10 g/L concentration of histamine dichloride. The negative control is generally the identical concentration of glycerinated saline.

A positive test results is a raised wheal on the skin with surrounding erythema. The histamine control normally produces a wheal of at least 3 mm in diameter. If the positive control does not provide a wheal with a 3 mm diameter, it is possible to simply count any wheal 3 mm or greater as a positive.[3] The wheal of a positive test must be of at least the same size or larger than the histamine control.

The measurements for the size occur at 10 minutes for the control, and 15 to 20 minutes for the allergens themselves. A more precise measurement can be done by measuring the fattest and thinnest part of the wheal, and then expressing this as an average.[4] Sometimes, using ink and putting the size of the wheals on a piece of paper is helpful for the purposes of keeping records.

CONTRAINDICATIONS

Overall, allergy skin prick testing is a safe procedure. Rarely, it can cause systemic reactions, such as anaphylaxis. It is important to make sure that individuals are not at a risk for anaphylaxis. Individuals with a high risk for anaphylaxis include those who have uncontrolled asthma and those who have reduced lung function.

Individuals who have experienced anaphylaxis within the previous 30 days are not good candidates for skin prick tests because the tests results may have a

false-negative result. Prior anaphylactic shock causes the skin to be unreactive, a condition that lasts approximately 2 to 4 weeks. If the skin test results in a positive test, the results are still accurate and useful for the purposes of diagnosis of an allergy.

If the individual has had anaphylaxis within the past month, it is still possible to perform in vitro testing. This alternative does not have a risk of having false negatives because the free immunoglobulins are generally less affected by recent anaphylaxis.

Individuals with certain skin conditions should not have skin prick tests because these conditions make it more likely to have false positive results. Some of these conditions include dermographism, urticaria (whether acute or chronic), cutaneous mastocytosis, and atopic dermatitis. For individuals who have atopic dermatitis, it is possible to successfully perform the skin test on areas of the skin that are not affected by the condition.

Other reasons not to perform skin tests (relative contraindications) include active angina and cardiac arrhythmias, older adults who are in poor health, and women who are pregnant. These groups are not necessarily at any greater risk for anaphylaxis, but are much more susceptible to the adverse effects of its treatment. Thus, it is not recommended to perform allergy skin tests on those individuals. **Box 2** outlines some contraindications and caution for skin prick testing.

FACTORS THAT AFFECT RESULTS

Beyond the factors that affect whether or not an individual should undergo the allergy testing procedure, there are also a number of factors that affect the actual results of the test. General factors that affect the accuracy of results include the source of the allergen, or the types of skin test devices that the testing individual decides to use.[5–8] For example, contaminants in the allergens may cause false-positive test results. The purity and quality of the sample may not be high enough to cause a positive test result. Thus, these factors need to be considered when analyzing/interpreting test results.

FACTORS THAT AFFECT RESULTS: MEDICATIONS

Individuals undergoing allergy testing should stop taking certain medications. Certain medications are considered perfectly safe and have no effect on allergy testing. The

Box 2
Contraindications for skin prick testing

- Individuals at high risk for anaphylaxis
  - 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
  - Dermographism
  - Urticaria
  - Cutaneous mastocytosis
- Relative contraindications
  - Significant cardiovascular disease
  - Frail elderly adults
  - Pregnancy

medications that do not impair skin test results include: leukotriene receptor agonists, many decongestants, beta agonists, inhaled or intranasal glucocorticoids, oral theophylline and cyclosporine.[9–15]

Among the most common medications that people should stop taking before an allergy test include all types of antihistamine medications. This is because antihistamines are designed to help decrease the allergic response and can cause the individual to have a false-negative test. All types of antihistamines should be discontinued including eye drops, nasal sprays, and oral medications. Stopping all antihistamines 1 week or more before administering the skin prick test should be sufficient to prevent any interference.[16–18]

When individuals have certain types of conditions that require the use of glucocorticoids, it is important to make sure that the testing occurs on parts of the skin that has not been treated with those topical agents.[19–21] In addition, certain types of antiimmunoglobulin treatments for asthma, including omalizumab, can decrease skin reactivity for up to 6 months, and it may be better to discontinue the use of these medications for 6 months before performing the skin prick test.[22,23] H_2 receptor blockers are other medications that people should discontinue 48 hours before administering a skin test.[24]

Another class of medications that can have an effect on skin reactivity are tricyclic antidepressants, which may interfere with skin reactivity for up to 2 weeks.[25] Antidepressants may be difficult to discontinue for that period of time, so noting that individuals are on the medications when performing the skin test is important. If the skin test either has a weak result or has a negative result, it may be better to perform an in vitro allergy test versus a skin prick test. Physicians should remember that selective serotonin reuptake inhibitors do not affect skin testing, and using these medications as an alternative may be a reasonable.

The data on topical calcineurin inhibitors show mixed results, but a lot of studies suggest that discontinuing the use of these medications 1 week before performing the skin prick test should be fine. In general, whenever there are medications that may interfere with the results of a skin prick test (**Box 3**), it is possible to perform in vitro 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
- H_2 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

RISKS

For the most part, skin prick testing results in a localized reaction and is a safe procedure that has little to no risk of complications. However, some individuals may have systemic reactions, such as breathing issues. For this reason, the recommendation is to have emergency equipment available, including epinephrine, to handle these possible systemic reactions.

Certain food allergens or latex may present a much higher risk of having systemic reactions as compared with other allergens. Intradermal testing (rather than skin prick testing) is more likely to result in systemic reactions; however, the risk remains low. Thus, skin prick testing is a much better alternative to intradermal testing. It is advisable to test with skin prick testing before testing with intradermal testing to minimize the chance of anaphylaxis or undesirable outcomes.

A prospective study by Bagg and colleagues[26] involving about 1500 participants reported the overall rate of systemic reactions secondary to skin tests to be 3.6%, none of which were severe. Aeroallergens were responsible for the greatest number of systemic reactions, mostly from intradermal testing rather than simple skin prick testing. Anaphylaxis was present in a very small percentage of individuals who underwent prick or puncture testing, although all of these individuals had a history of asthma. Other risk factors for severe reactions include children less than 1 year of age and children who have active eczema. Additionally, children who had asthma were more likely to experience anaphylaxis as compared with children who did not have asthma.[27,28]

Anaphylaxis in adults who have asthma is also exceedingly rare. Generally, with proper preparation it is highly unlikely that anaphylaxis will result in death.[29]

SKIN PRICK: INTERPRETATION OF RESULTS

A positive result of a skin prick test only demonstrates that there is an immunoglobulin (Ig)E-specific antibody present, but it does not necessarily mean that the individual will have symptoms when exposed to that particular allergen. It is important to ensure that the clinical history coincides with the result. If an individual has no clinical history and a positive result, then this could be indicative of subclinical sensitization or it could be a false-positive result. Individuals who are sensitized subclinically can develop symptoms at any point in time.

By contrast, a negative result is much more informative. A negative result means that the individual does not have an immunoglobulin for a particular allergen, which effectively means that the individual will not display symptoms when they are exposed to the particular allergen.[30]

Table 1 shows the grading scale from 0 to 4 that can be used for assisting in the interpretation of skin prick test results; however, a higher grade does not always indicate worse clinical symptoms.

INTRADERMAL TEST

Owing to the issues with the accuracy of the skin prick testing, an alternative is to perform an intradermal test. These tests carry a much greater risk of systemic reactions, including anaphylactic shock; however, the risk remains low.[31] Intradermal testing is more sensitive, and detects immune responses to allergens with much greater accuracy. However, false-positive results are also much more common, which means that these tests are much less valuable to individuals who present without any clinical symptoms.

Table 1
Interpretation of skin prick test results

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

Adapted from Bush RK. Diagnostic tests in allergy. In: Slavin RG, Reisman RE, editors. Expert guide to allergy and immunology. Philadelphia: American College of Physicians; 1999. p. 8.

The technique for administering the test is the exact same as a tuberculin skin test. Thus, a needle is used to inject of 0.02 to 0.05 mL of a 1:500 to 1:1000 weight per volume allergen extract into the skin.[32] It is not necessary to have a positive control if the skin prick test has already shown sensitivity to histamine. If this is not present, however, it may be necessary to inject histamine to demonstrate the same response as the positive control.

Intradermal testing is performed generally after a negative skin prick test.[33–35] This minimizes the risk of an individual experiencing any systemic reactions. The only exception to this is allergies related to insect venom. Venom allergies are more likely to cause death so intradermal tests are preferred, because they are more sensitive.[36,37] Further, it is not advisable to use intradermal skin prick tests for food allergens because higher rates of systemic reactions that have been reported.

The high risk of anaphylaxis as well as the sensitivity of the test means that it is possible to use more dilute concentrations when performing this test. A lower concentration not only decreases the likelihood of systemic reactions, it also decreases the likelihood of a false-positive response.[1] A positive response is defined as either a wheal that is at least 5 mm in diameter; however, a survey done in 2008 showed that 85% of American board-certified allergists were defining at positive result as any wheal 3 mm or greater in diameter than the negative control wheal. In addition, the 2008 practice parameter of the American Academy of Allergy, Asthma and Immunology states that "Any reaction larger than the negative control may indicate the presence of specific IgE antibody." **Table 2** shows the grading scale used for interpretation of intradermal test results.[38]

Table 2
Interpretation of intradermal test results

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	31–40
4	>15 or with many pseudopods	>40

Adapted from Bush RK. Diagnostic tests in allergy. In: Slavin RG, Reisman RE, editors. Expert guide to allergy and immunology. Philadelphia: American College of Physicians; 1999. p. 8.

False-positive results are more common with intradermal testing, especially for inhalant allergens. Intracutaneous bleeding caused by needle trauma during the administration of the test can be interpreted falsely as a positive result.

IN VITRO TESTING

There are several other possible ways of testing for allergies. One of these ways is testing in vitro for specific IgE antibodies in the blood, such as the radioallergosorbent test and the enzyme-linked immunosorbent assay. This is generally an acceptable way of testing for allergies when an individual cannot undergo intradermal testing or skin prick testing, owing to contraindications or not being able to stop medications. The sensitivity (60%–95%) and specificity (30%–95%) for these tests are much broader than the skin prick tests.[38,39]

This test detects the presence of allergen-specific IgE antibodies in the bloodstream. The presence of these antibodies is sufficient to predict that a person will have an allergic reaction when exposed to the allergen. However, even if there is a high level of antibodies in the blood, this does not always correlate with severity of the allergic response, if any.

The results of the in vitro testing are classified into multiple classes (**Table 3**) to help increase the predictive value of the test. The higher the allergen class in **Table 3**, the greater the level of allergen-specific IgE antibody present. These categories are helpful in predicting whether or not an individual will display symptoms. Asymptomatic sensitization can be seen in some individuals having less than class III and levels greater than or equal to class III are more consistently related to symptoms upon exposure.[40–42] Therefore, the clinical history of the individual, the level of positivity in the result, and the allergen in question, influence the clinical relevance of the results.

Highly positive results (class VI result) and a history of typical allergic symptoms indicate an allergic reaction to that particular allergen. When there is a slightly positive result (class I result), and no past history of symptoms, this generally requires additional testing. A negative test in the presence of symptoms does not rule out an allergy, and it may be best to perform a skin prick test. In cases where individuals have experienced some symptoms, and the potential allergy is life threatening, in vitro testing may be helpful to confirm a negative skin test.[37]

PATCH TESTING

Patch testing is a very specific form of testing used to determine if an individual has suspected allergic contact dermatitis. The general theory behind patch testing is that individuals who are sensitized to a particular antigen will be able to produce an allergic reaction even when a low concentration of the antigen is placed on normal

Table 3
Phadia Immunoglobulin E immunoassay classes

Class (By Phadia)	Concentration (kIU/L)	Interpretation
0	<0.35	Levels less than class III is generally associated with asymptomatic sensitization. Levels ≥ class III are more consistently related to symptoms upon exposure. The clinical history of the individual, the level of positivity in the result, and the allergen in question, influence the clinical relevance of the results.
1	0.35–0.7	
2	0.7–3.5	
3	3.5–17.5	
4	17.5–50	
5	50–100	
6	>100	

skin. Patch testing is useful in individuals who have dermatitis for unknown reasons, individuals who work in a field that have high occurrences of dermatitis, and/or worsening of a previous stable dermatitis.[43]

To perform the patch test, a physician places a test allergen on the upper back for 2 days (48 hours). After patch removal, the skin is analyzed to determine whether or not there has been an allergic reaction. This initial reading occurs 15 to 60 minutes after taking off the patch, so that the transient erythema caused by patch placement can resolve. It is important to perform a second read; read the patch over the course of days, so that one can distinguish between irritant reactions (reactions that fade) versus true allergic reactions (reactions that persist) versus delayed allergic reactions (reactions that do not appear at the time of patch removal; **Table 4**).[42] Certain reactions fade quickly, like those related to fragrances. Allergies to nickel and corticosteroids occur over the course of days, and having an additional reading after 6 to seven days ensures that these allergies are not missed. Performing the readings at the appropriate intervals helps minimize the risk of false negatives. Day 4 readings seem to be associated with a low number of false-negative reactions.[44]

If a patch test is negative, despite suggestive clinical history of acute contact dermatitis, then a repeated open application test or usage test can be performed.[43] The repeated open application test is performed by applying 0.1 mL of the allergen in question to an area of skin twice daily for up to 28 days or until an eczematous skin reaction develops.[43,45,46] The usage test is performed by having the individual use the allergen in question in his or her everyday real-world conditions. This test tries to reproduce all the factors (ie, sweating, friction, etc) associated with the original dermatitis. The 1 drawback of this test is that it may fail to differentiate irritant from allergic dermatitis.[43]

SUMMARY

A number of tests are available to help physicians in the diagnosis of allergic disease. These tests work by detecting specific IgE antibodies. Skin prick testing is rapid, sensitive, and cost effective. Intradermal testing is generally used in individuals who have had a negative skin prick test when clinical history suggests an allergic reaction. It is preferred as first line in insect venom allergies. In vitro testing should be used in individuals who cannot undergo skin prick testing, or if skin prick testing is unavailable. Patch testing is useful in individuals with allergic contact dermatitis. Performing these tests will allow physicians to help identify the specific allergen involved in an individual's allergic disease. From here, the next steps can be taken in helping patients manage their allergic conditions. **Table 5** summarizes commonly used allergy tests.

Table 4
Interpretation of patch test results

Reaction Severity	Result Interpretation
–	No skin changes – negative reaction
? or +/–	Mild erythema – questionable reaction
+	Erythema, slight infiltration – mild reaction
++	Erythema, infiltration and vesicles – strong reaction
+++	Bullous, ulcerative lesions – extreme reaction

Table 5
Summary of commonly used allergy tests

Types of Skin Testing	Indications	Contraindications	Risks	Key Points
Skin prick testing	Perennial or seasonal rhinitis Rhinosinusitis Rhinoconjunctivitis Rhinitis with otitis media Suspected food allergy Suspected drug allergy Suspected insect venom allergy Persistent asthma	Individuals at high risk for anaphylaxis Anaphylaxis within the last 30 d Individuals with dermographism, urticarial or cutaneous mastocytosis	Low risk for systemic reactions	Rapid Sensitive Cost effective
Intradermal testing	Same as skin prick testing; however, should generally only be done after a negative skin prick test	Same as skin prick testing	Higher rates of systemic reactions; however, this is still very low	Preferred as first line for insect venom allergies Generally performed after a negative skin prick test, if suspicion still high More reproducible and more sensitive
In vitro testing	Used in individuals who cannot undergo skin prick or intradermal testing, owing to contraindications or not being able to stop medications	None	No risk of systemic reactions	Not affected by the medications patient is taking Not affected by skin disease or reliant on skin integrity Wide sensitivity (60%–95%) and specificity (30%–95%)
Patch testing	Used to identify specific allergens in allergic contact dermatitis Individuals with eczematous dermatitis or chronic dermatitis	Do not place patch on nonintact skin or skin with a dermatitis	An irritant or allergic skin reaction may occur at the site of patch testing, including a rash and a burnlike reaction Low risk for anaphylaxis	Performing a second read is important, so that one can distinguish between irritant reactions vs true allergic reactions vs delayed allergic reactions If patch testing is negative, however, history is suggestive of allergic contact dermatitis, then the repeated open application test or usage test can be performed

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. Ruëff 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 [in German].
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. Cuhadaroglu C, Erelel M, Kiyan E, et al. Role of Zafirlukast on skin prick test. Allergol Immunopathol (Madr) 2001;29:66–8.
12. Roches Des A, Paradis L, Bougeard YH, et al. Long-term oral corticosteroid therapy does not alter the results of immediate-type allergy skin prick tests. J Allergy Clin Immunol 1996;98:522–7.
13. Olson R, Karpink MH, Shelanski S, et al. Skin reactivity to codeine and histamine during prolonged corticosteroid therapy. J Allergy Clin Immunol 1990;86:153–9.
14. Spector SL. Effect of a selective beta 2 adrenergic agonist and theophylline on skin test reactivity and cardiovascular parameters. J Allergy Clin Immunol 1979;64:23–8.
15. Munro CS, Higgins EM, Marks JM, et al. Cyclosporin A in atopic dermatitis: therapeutic response is dissociated from effects on allergic reactions. Br J Dermatol 1991;124:43–8.
16. dos Santos RV, Magerl M, Mlynek A, et al. Suppression of histamine- and allergen-induced skin reactions: comparison of first- and second-generation antihistamines. Ann Allergy Asthma Immunol 2009;102:495–9.
17. Devillier P, Bousquet J. Inhibition of the histamine-induced weal and flare response: a valid surrogate measure for antihistamine clinical efficacy? Clin Exp Allergy 2007;37:400–14.
18. Dreborg S. The skin prick test in the diagnosis of atopic allergy. J Am Acad Dermatol 1989;21:820–1.
19. 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.

20. Pipkorn U, Hammarlund A, Enerbäck L. Prolonged treatment with topical glucocorticoids results in an inhibition of the allergen-induced weal-and-flare response and a reduction in skin mast cell numbers and histamine content. Clin Exp Allergy 1989;19:19–25.
21. Gradman J, Wolthers OD. Suppressive effects of topical mometasone furoate and tacrolimus on skin prick testing in children. Pediatr Dermatol 2008;25:269–70.
22. Noga O, Hanf G, Kunkel G. Immunological and clinical changes in allergic asthmatics following treatment with omalizumab. Int Arch Allergy Immunol 2003;131:46–52.
23. 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.
24. Kupczyk M, Kupryś I, Bocheńska-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.
25. 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.
26. Bagg A, Chacko T, Lockey R. Reactions to prick and intradermal skin tests. Ann Allergy Asthma Immunol 2009;102:400–2.
27. Norrman G, Fälth-Magnusson K. Adverse reactions to skin prick testing in children - prevalence and possible risk factors. Pediatr Allergy Immunol 2009;20:273–8.
28. Pitsios C, Dimitriou A, Stefanaki EC, et al. Anaphylaxis during skin testing with food allergens in children. Eur J Pediatr 2010;169:613–5.
29. 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.
30. Sampson HA. Update on food allergy. J Allergy Clin Immunol 2004;113:805–19 [quiz: 820].
31. 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.
32. 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.
34. Franklin Adkinson N, Bochner BS, Burks AW, et al. Middleton's allergy: principles and practice e-dition. Philadelphia: Saunders; 2003.
35. Proceedings of the task force on guidelines for standardizing old and new technologies used for the diagnosis and treatment of allergic diseases. Washington, DC. June 18-19, 1987. J Allergy Clin Immunol 1988;82:487–526.
36. Georgitis JW, Reisman RE. Venom skin tests in insect-allergic and insect-nonallergic populations. J Allergy Clin Immunol 1985;76:803–7.
37. 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.
38. Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter. Ann Allergy Asthma Immunol 2008;100:S1–148.

39. Williams PB, Dolen WK, Koepke JW, et al. Comparison of skin testing and three in vitro assays for specific IgE in the clinical evaluation of immediate hypersensitivity. Ann Allergy 1992;68:35–45.
40. Sampson H, Ho DG. Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. J Allergy Clin Immunol 1997;100:444–51.
41. Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. J Allergy Clin Immunol 2001;107:891–6.
42. Uter WJ, Geier J, Schnuch A. Good clinical practice in patch testing: readings beyond day 2 are necessary: a confirmatory analysis. Members of the Information Network of Departments of Dermatology. Am J Contact Dermatitis 1996;7:231–7.
43. Bourke J, Coulson I, English J, et al. Guidelines for the management of contact dermatitis: an update. Br J Dermatol 2009;160:946–54.
44. Todd DJ, Handley J, Metwali M, et al. Day 4 is better than day 3 for a single patch test reading. Contact Derm 1996;34:402–4.
45. Hannuksela M, Salo H. The repeated open application test (ROAT). Contact Derm 1986;14:221–7.
46. Villarama CD, Maibach HI. Correlations of patch test reactivity and the repeated open application test (ROAT)/provocative use test (PUT). Food Chem Toxicol 2004;42:1719–25.