

# Allergy Testing and Immunotherapy

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## Practice Gaps

General pediatricians should be aware of currently available options for both allergy testing and treatment of allergic disease, including immunotherapy. These are areas that practitioners may have limited exposure to during pediatric training and beyond, thus there are misconceptions about the evaluation and management of various allergic conditions.

## Objectives After completing this article, readers should be able to:

1. Understand when allergy testing is indicated and the different methods used.
2. Recognize what conditions can be treated with allergy immunotherapy and the different modalities currently available for pediatric patients.

## GLOSSARY OF TERMS

Aeroallergen Organ Provocation Test – An objective measure of clinical allergy symptoms by applying a known concentration of aeroallergen directly to an area such as the nasal mucosa or conjunctiva.

Anaphylaxis – An immunoglobulin E (IgE)–mediated systemic hypersensitivity reaction typically resulting in immediate and severe symptoms secondary to the immunologic release of mast cell and basophil mediators throughout the body.

Allergen Immunotherapy – A form of treatment that can be given as either sublingual tablets or subcutaneous injections, effective in the long-term management of various allergic diseases (asthma, rhinitis, venom hypersensitivity) by desensitizing patients to clinically relevant allergens over time.

Sensitization – Presence of allergen-specific IgE on allergen exposure, regardless of clinical symptoms.

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## ABBREVIATIONS

EoE	eosinophilic esophagitis
FDA	Food and Drug Administration
IDT	intradermal testing
IgE	immunoglobulin E
SCIT	subcutaneous immunotherapy
SLIT	sublingual immunotherapy
SPT	skin prick testing

## INTRODUCTION

Atopic diseases in the pediatric population often become a source of major concern for both patients and their caretakers. These conditions are quite common in children, with 5.6% having reported food allergies, 9% with hay fever, 11% with respiratory allergies, and 12% with skin allergies based on the 2012 National Health Interview Survey of US children. (1) Allergies are generally

chronic and can significantly affect the child's quality of life. For example, food and venom allergies necessitate carrying an epinephrine autoinjector at all times and limiting exposure whenever possible. This can be burdensome, particularly for adolescent patients. In contrast, some allergens cannot be avoided, such as pollens or dust mites. Exposure to these inhalants may exacerbate allergic asthma or cause persistent symptoms that affect daily functioning and sleep. As such, it is important for general pediatricians to be able to identify and treat atopic disease in children as well as direct patients to specialists for further evaluation and treatment when indicated.

## BACKGROUND/HISTORY

Skin testing for allergies was first demonstrated by Charles Harrison Blackley in the late 19th century during experiments regarding the etiology of hay fever. His technique at the time included applying pollen extracts onto abraded skin, with a resulting wheal and surrounding erythema. (2) Percutaneous (or skin prick) testing, currently the most commonly used technique, was first described by Lewis and Grant in 1924. (3) This type of allergy testing became widespread in the 1970s after Pepys modified the technique by using a hypodermic needle. (3) The discovery of immunoglobulin E (IgE) led to the development of the radioallergen sorbent test described by Wide et al (4) in 1967 that used radioactive labels. There have been several technical improvements since, including the use of enzyme labels, in modern serum-specific IgE testing. Serum testing is widely used in conjunction with skin testing to detect sensitization to various allergens. (4)

Allergy immunotherapy in humans was first attempted and described by Leonard Noon and later by his colleague John Freeman in 1911. Patients affected by hay fever were injected with grass pollen allergen extracts, and its effects were assessed with conjunctival provocation tests (placing drops of extract into the patient's eyes). This therapy became widespread beginning in the 1950s after clinical trials were performed. (5)

## ALLERGY TESTING

There are 2 main forms of testing for immediate (IgE-mediated) allergies: skin testing and serum testing. For contact dermatitis, which is a non-IgE-mediated, delayed-type hypersensitivity reaction, patch testing is often performed in an allergy or dermatology office.

Exposure to the suspected allergen in a supervised clinical setting, such as oral food challenges, medication

challenges, and aeroallergen organ provocation challenges, is considered the gold standard for diagnostic allergy testing. (6) However, when considering patient safety and comfort, these options are not always the most practical first step. Allergy skin and serum testing are less time-consuming and more comfortable procedures, with a lower risk of adverse reactions. Challenges can then be performed if appropriate and necessary based on these results.

### Skin Prick Testing

Skin prick testing (SPT) is the most common method of testing used by allergists and typically is preferred as an initial approach. It can be performed in patients as young as 1 month of age, when deemed appropriate. (6) Although infants typically exhibit appropriate cutaneous reactivity to antigen, several studies have shown the wheal size produced by SPT to be smaller in this population compared with older (preschool-aged) children and adults. (7)(8)

Also called *percutaneous skin testing*, SPT is performed by placing a desired antigen on the skin (usually the forearm or back, given the sensitivity of the skin in these areas, is preferable). Antigen is available commercially in an aqueous form or is created from fresh foods or medications. Once the extract (or allergen/antigen) is applied, the skin is then punctured to introduce the antigen into the epidermis. Several different instruments can be used in SPT, including hypodermic needles, solid-bore needles, single-headed lancet devices, and multiheaded lancet devices. After 15 to 20 minutes, the resulting wheal diameter and surrounding erythema are measured and compared with controls. Histamine is generally used as the positive control, with saline acting as a negative control. A wheal that exceeds the negative control by 3 mm or more is usually considered positive. The specificity of SPT is 70% to 95% for inhalant allergens and 30% to 70% for food allergens. The sensitivity of SPT is 80% to 90% for inhalant allergens and 20% to 60% for food allergens, and it increases to as high as 90% when fresh foods are used. (9)

### Intradermal Testing

Intradermal testing (IDT) involves the injection of an allergen extract intracutaneously. As with SPT, the subsequent wheal and erythema that develop are measured and compared with positive and negative controls. This type of skin testing should be performed only if there is a convincing clinical history with negative SPT results because IDT is more sensitive but less specific. In addition, the risk of a systemic reaction to IDT is higher compared with SPT. Thus, SPT is generally performed first because allergens that are prick positive should not be tested via IDT. (6)(10) It

is particularly useful for drug and stinging insect allergy and should not be performed for foods. (9)

Factors that can affect skin test results include cutaneous reactivity, technician performance, and extract potency. The most common cause of false-negative results in skin testing is the use of medications having antihistaminic properties. These medications include first- and second-generation oral antihistamines (including those used for conditions other than allergy, such as cyproheptadine), topical antihistamines (nasal, ocular), and tricyclic antidepressants. Most oral medications with antihistaminic properties should be held for 5 to 7 days before testing, with topical agents held for at least 2 days. Even H<sub>2</sub> antagonists can have some activity in the skin and ideally should be held for 24 hours prior. Table 1 lists common medications that inhibit cutaneous allergy test results (SPT and IDT). Short courses of oral corticosteroids (such as those used for an asthma exacerbation) do not affect test results, although prolonged use of potent topical corticosteroids is discouraged before testing because these may interfere with results. (6)

### Serum Testing

Radioallergosorbent testing detects serum IgE antibodies for specific allergens. The average sensitivity compared with SPT has been reported to be approximately 70% to 75%, thus SPT is preferred. (6) Serum testing is favored in certain situations, such as for patients who have diffuse skin disease or who are unable to discontinue the use of suppressive medications before testing. Radioallergosorbent testing is often used in conjunction with SPT to monitor the severity of food allergies and to further determine whether an oral food challenge may be indicated.

For the techniques described thus far, it is important to remember that a thorough clinical history is just as, if not more, important than testing. Positive findings on SPT, IDT, or serum-specific IgE testing indicate only the presence of allergen-specific IgE, and these results alone are not enough to diagnose clinical allergy. Both skin and serum test results may be either false-positive or false-negative. Therefore, positive allergy testing represents sensitization only and not clinical allergy. Based on the combination of a suggestive history and (positive) testing, it is the provider's responsibility to determine whether clinical allergy is present.

### INDICATIONS FOR TESTING

As a general principle, allergy testing should be performed only if the results would affect management. If a diagnosis is strongly suspected, confirmatory testing may also be

TABLE 1. Common Medications that Inhibit Cutaneous Allergy Testing (Skin Prick and Intradermal Testing)

MEDICATION	SUPPRESSION OF SKIN TEST RESULTS, D
First-generation H <sub>1</sub> antihistamines	
Chlorpheniramine	1–3
Cyproheptadine	1–8
Diphenhydramine	1–3
Hydroxyzine	1–10
Promethazine	1–3
Second-generation H <sub>1</sub> antihistamines	
Cetirizine	3–10
Fexofenadine	3–7
Loratadine	3–10
Levocetirizine	3–7
Tricyclic antidepressants	
Doxepin	6
Doxepin, topical	11
Imipramine	>10
H <sub>2</sub> antihistamines	
Ranitidine	<1
Leukotriene antagonists	
Montelukast	0
Nasal sprays	
Fluticasone	0
Mometasone	0
Budesonide	0
Azelastine	3–10

Derived from Bernstein IL, Li JT, Bernstein DI, et al; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol.* 2008;100(3)(suppl 3):S1–S148 (6) and Chiriac AM, Bousquet J, Demoly P. In vivo methods for the study and diagnosis of allergy. In: Adkinson NF, Yunginger JW, Bochner BS, et al, eds. *Middleton's Allergy.* 8th ed. Philadelphia, PA: Elsevier; 2014:1119–1132. (9)

important so that the appropriate counseling and treatment would be offered. For example, if a child has environmental allergies causing severe allergic rhinoconjunctivitis despite multiple medications, and skin or serum testing identifies sensitization to a relevant allergen, avoidance may be advised

(such as to animals or dust mites) and allergy immunotherapy could be offered. Alternatively, if the diagnosis is uncertain, testing may be helpful to avoid unnecessary treatment or the possible overlooking of additional etiologies. For example, if a child does not have evidence of an IgE-mediated hypersensitivity to a food, then this food could potentially be reintroduced into the diet and an epinephrine autoinjector may not be indicated.

### Environmental Allergens

Skin testing (SPT and occasionally IDT when appropriate) for environmental allergens is useful in patients with chronic seasonal or perennial symptoms of allergic rhinitis or rhinoconjunctivitis, recurrent sinusitis (especially with seasonality), or if there is concern for allergic asthma. However, negative environmental allergy skin testing at a single point in time does not exclude the chance for sensitization in the future because skin test positivity can lag in the pediatric population (especially for children <2 years old), with clinical symptoms preceding positive skin test results. (6)

### Food Allergens

Regarding food allergens, skin testing is clearly indicated when an anaphylactic reaction has occurred or symptoms suspicious of an IgE-mediated allergy (hives, intractable vomiting, etc) are demonstrated with ingestion of a specific food. Negative SPT results can be particularly helpful because the tests are highly sensitive, with negative predictive accuracy generally 85% to 95%. (11) Currently, strict dietary avoidance is the mainstay of treatment, in addition to having an epinephrine autoinjector accessible at all times in case of accidental exposure. This is especially important because previous reactions do not predict future symptoms with subsequent ingestions, as many cofactors can play a role during a reaction.

### Medication Allergy (Penicillin)

Skin testing for penicillin allergy is well validated and reliable. (6) Penicillin hypersensitivity is the most common self-reported drug allergy and is reported in approximately 10% to 20% of the general population. However, maculopapular and urticarial rashes seen with  $\beta$ -lactam antibiotics given during childhood are more likely due to concurrent viral infection or exanthems and do not necessarily represent an IgE-mediated drug allergy. When the results of both SPT and IDT to penicillin and its major (penicilloyl) and minor (penicilloate) determinants (if available) are negative, tolerance is typically confirmed with an oral medication challenge in the allergist's office. In 2011, one trial specifically looked into pediatric patients with a history of

maculopapular or urticarial rash while taking a  $\beta$ -lactam antibiotic. Only 6.8% of the children in that study who were labeled as allergic experienced a reproducible reaction after oral medication challenge with the suspected antibiotic agent within 2 months after initial presentation. Further studies continue to demonstrate this finding, indicating that penicillin allergy is overdiagnosed in this population. (12)(13) In addition, more recent evidence suggests that skin testing may not be necessary in these very-low-risk patients and that a confirmatory graded oral provocation challenge alone is safe and appropriate for many children with a history of mild cutaneous reaction to aminopenicillins. (14) There is a relative lack of evidence regarding validated testing for other agents, and, thus, skin testing is performed with less frequency for classes other than penicillin and is based on the specific situation. Serum IgE testing to penicillin is available but is neither sensitive nor specific and offers little utility in clinical practice. (6) Allergy testing for drugs is exclusively performed for suspected immediate, IgE-mediated hypersensitivity and does not diagnose or exclude the presence of delayed-type hypersensitivity.

### Venom Hypersensitivity

Life-threatening systemic reactions secondary to insect stings are estimated to occur in 0.4% to 0.8% of the pediatric population. Children with symptoms limited to the skin (local swelling, flushing, pruritus, urticaria) are considered to be at low risk for a more severe reaction. In particular, for children with large local reactions there is a less than 10% chance of a systemic reaction (usually milder than the index event) and a less than 5% chance of anaphylaxis. Thus, venom testing is not indicated in children with isolated cutaneous symptoms. In contrast, a patient of any age who has experienced a life-threatening systemic reaction after an insect sting should have testing performed because the risk of anaphylaxis with subsequent stings is 30% to 40% in children and immunotherapy to identified insects can dramatically reduce the risk of future systemic reactions. Systemic reactions may present with variable symptoms, ranging from mild to severe with anaphylaxis, including hypotension or the involvement of at least 2 organ systems. Given the high frequency of asymptomatic sensitization, venom testing should not be used for screening purposes. (15)(16)

In children with chronic idiopathic urticaria (>6 weeks of symptoms) with an otherwise unremarkable clinical history, allergy testing is not indicated. Skin or serum IgE testing to search for an etiology rarely yields any answers, and the high rate of false-positives with allergy skin testing can be confusing and of little assistance. (17)

## Other Allergic Disease

Allergy testing is sometimes performed for patients with other conditions, such as eosinophilic esophagitis (EoE) or atopic dermatitis (eczema). The former involves tissue infiltration of eosinophils causing chronic inflammation in the esophagus and is thought to be, at least in some patients, a gastrointestinal manifestation of food allergy. Although skin testing may be used in an attempt to identify possible food triggers, EoE is not solely IgE-mediated, and, thus, skin testing to foods is not entirely an accurate test in this setting. (18)(19) There is evidence that food impactions in some patients with EoE occur seasonally and that treatment for environmental allergens (with subcutaneous immunotherapy) reduces the pollen burden, which might also contribute to chronic inflammation, and, in turn, aid in the long-term management of EoE as well as the patient's allergic rhinitis. (20)(21)

Patients with moderate to severe atopic dermatitis that remains uncontrolled despite optimal skin care may also benefit from allergy testing (to both environmental and food allergens) to identify potential triggers. (22) However, caution should be taken in the case of both EoE and atopic dermatitis regarding dietary recommendations made solely based on positive testing. As discussed, false-positives in allergy testing are not rare events, and positive testing to a food in the absence of immediate symptoms indicates sensitization only; it does not confirm clinical allergy. In the case that a food is tolerated regularly in a person's diet without identifiable symptoms, the risk of avoidance in a growing child's diet should be weighed with any potential benefit that elimination from the diet may offer for the underlying atopic disease. It is helpful in these situations to offer a limited trial of dietary avoidance under the care of a registered dietitian to offer alternatives to the foods (or food groups) that are to be avoided.

## CONTRAINDICATIONS TO TESTING

Contraindications to allergy skin testing include uncontrolled asthma, diffuse skin rash, current use of antihistaminic medication, pregnancy, and generalized edema. Concurrent use of  $\beta$ -blockers is also a relative contraindication because the symptoms of anaphylaxis may be amplified and the response to epinephrine may be blunted. (6)(23)(24)

## ALLERGY IMMUNOTHERAPY

Allergy immunotherapy is indicated for the treatment of patients with allergic rhinitis, allergic conjunctivitis, allergic

asthma, or stinging insect hypersensitivity who have clinical symptoms with exposure and also exhibit evidence of specific IgE antibodies on testing. At present, this is the only disease-modifying treatment available for these conditions. Repeated doses of specific allergens are administered with a resulting decrease in the sensitivity of end organs (skin, conjunctiva, nasal mucosa, bronchi). Changes are also noted in the cellular and humoral responses to these allergens. Interestingly, IgE levels for specific allergens actually increase at the start of immunotherapy before steadily decreasing. Thus far, this observed change in IgE has not been shown to strongly correlate with a patient's clinical response to immunotherapy. Thus, repeated skin or serum testing during or after completion of a course of immunotherapy is generally not recommended. There is no lower age limit for allergy immunotherapy, and children as young as 3 years old have been initiated on treatment. (25)

Immunotherapy is currently the only way to build tolerance to an allergen, leading to lasting relief of allergy symptoms in most individuals who complete a 3- to 5-year course. (26) Several studies have demonstrated clinical improvement with this recommended length of therapy even after cessation. One study in particular showed sustained relief 12 years after a 3-year course, although lasting relief varies from patient to patient. (25)(26)(27) There are currently no specific tests or markers that can predict whether a patient will achieve prolonged clinical remission versus relapse after stopping immunotherapy. Thus, clinical evaluation of the patient every 6 to 12 months is recommended to assess for efficacy and tolerance. Duration is tailored to the individual patient, with lack of clinical effect and intolerable adverse effects being the most significant reasons to discontinue therapy.

Although immunotherapy is certainly a time commitment for the patient and the caretaker, the alternative is pharmacotherapy for symptomatic relief that would be continued indefinitely. Some studies have even shown that the cost of a course of immunotherapy is significantly less than the cost of years of medications used to treat the allergic conditions. (26) There are also situations in which the patient continues to have bothersome and persistent symptoms despite proper adherence to medications. In addition, in children, it has been well-established that allergy immunotherapy can have long-term benefits for prevention and treatment of allergic asthma as well. (28)(29) Allergy immunotherapy is generally covered (at least in part) by the patient's health insurance, although prior authorization may need to be obtained for the newer sublingual therapies.

### Subcutaneous Immunotherapy

Subcutaneous immunotherapy (SCIT) is the most prevalent and longstanding form of allergy immunotherapy. Gradually increasing doses of allergen extracts are given over time (buildup phase) until the monthly target maintenance dose is achieved. The maintenance dose refers to the therapeutic effective dose. Extracts are derived from allergen source materials and are prepared individually for each patient based on testing results. Technique is important as subcutaneous administration is depended on for proper absorption. An accidental intramuscular injection would result in rapid absorption, with increased risk of a systemic reaction. Injections should be administered in a location under the direct supervision of appropriate medical personnel. The necessary medications and equipment should also be immediately available for the treatment of anaphylaxis, including intramuscular epinephrine. There are various dosing schedules that may be used. Injections are typically initiated at weekly intervals during a conventional buildup phase, eventually reaching a target dose at which maintenance injections can be spaced at monthly intervals. Alternatively, for conditions such as venom hypersensitivity, rush and cluster protocols can shorten the buildup phase, although these carry a significantly greater risk of systemic reactions and have not been well studied in children. (25) (26)

Premedication with an oral antihistamine is advised before each injection to mitigate adverse reactions. Common adverse effects of SCIT include local injection site reactions with large swelling, pruritus, erythema, or pain. These can be treated with supportive measures, including ice, topical corticosteroids, additional oral antihistamines, and nonsteroidal anti-inflammatory drugs or acetaminophen as needed. In previous studies, the frequency of local reactions varies from 26% to 82% of patients treated with SCIT. Due to the possibility of anaphylaxis (<1% of patients receiving conventional SCIT), all patients are asked to remain in the medical office for at least 30 minutes after the injection. Although delayed-onset systemic reactions can occur, life-threatening anaphylaxis outside of the observation time is exceedingly rare. Dosing adjustments are often necessary for reactions and missed doses, especially during the buildup phase given the frequency of injections. Contraindications to SCIT include uncontrolled asthma, inability to communicate clearly to the physician should a reaction occur, concurrent use of  $\beta$ -blockers, and other comorbidities that weaken a patient's ability to survive a systemic allergic reaction. (25) For venom immunotherapy in particular, concurrent use of angiotensin-

converting enzyme inhibitors leads to a greater risk of more serious anaphylaxis to a sting. (15)

### Sublingual Immunotherapy

Sublingual immunotherapy (SLIT) is a relatively recent therapeutic development that may be more convenient for patients with environmental allergies. Administration of the specific allergen to the oral mucosa is done via fast-dissolving tablets placed underneath the tongue. The medication is taken daily, with the first dose given in the clinic under the direct supervision of appropriate medical personnel. The patient can then continue the remainder of therapy at home, with an epinephrine autoinjector available at all times. Currently in the United States, there are only 4 Food and Drug Administration (FDA)-approved SLIT products available, one of which is approved for ages 5 years and older (Table 2). (25)(34)(35)

Local adverse effects of SLIT include pruritus or swelling of the mouth, tongue, or lip; throat irritation; nausea/vomiting; diarrhea; abdominal discomfort; heartburn; and uvular edema. Most local reactions improve or resolve with repeated use of SLIT, typically in a few weeks or less. Systemic reactions with SLIT are extremely rare. Contraindications include uncontrolled asthma, a history of a severe local reaction to SLIT, a history of a severe systemic reaction to SCIT, as well as known EoE. (34)(35)

Table 3 provides a summary of allergy testing and immunotherapy.

### FUTURE DEVELOPMENTS/CONSIDERATIONS

Allergy testing and immunotherapy continue to be fluid areas with ongoing research leading to new developments and improvements in treatment and prevention, especially in the management of food allergy.

One recent development in our understanding of peanut allergy has resulted in a major shift in practice guidelines for general pediatricians. Where previous feeding

TABLE 2. Food and Drug Administration–Approved Sublingual Immunotherapy (30)(31)(32)(33)

MEDICATION	APPROVED AGES (Y)
Grastek (Timothy grass)	≥5
Oralair (5-grass mix)	≥10
Ragwitek (ragweed)	≥18
Odactra (house dust mite)	≥18

TABLE 3. Summary of Allergy Testing and Immunotherapy

ALLERGY	ALLERGY TESTING GENERALLY RECOMMENDED	IMMUNOTHERAPY AVAILABLE
Food (IgE-mediated)	SPT, serum-specific IgE	No
Environmental (rhinitis, conjunctivitis, asthma)	SPT, IDT, serum-specific IgE	Yes (SCIT, SLIT)
Medication (penicillin, amoxicillin)	SPT, IDT	No
Venom/stinging insect (systemic reaction)	SPT, IDT, serum-specific IgE	Yes (SCIT)

IDT=intradermal testing, SCIT=subcutaneous immunotherapy, SLIT=sublingual immunotherapy, SPT=skin prick testing.

recommendations had been to delay introduction of highly allergenic foods from the infant/toddler diet with the goal to prevent development of food allergy, the LEAP (Learning Early About Peanut Allergy) trial published in 2015 demonstrated the opposite effect regarding peanut. High-risk infants (defined as those with moderate to severe eczema, previously diagnosed egg allergy, or both) randomized to consistent peanut consumption starting within the first 11 months of life (most at approximately 4–6 months of age) had a significantly decreased risk of peanut allergy compared with those who withheld peanut from the diet. Additional studies, including the EAT (Enquiring About Tolerance) trial, have since shown similar effects for early introduction of other highly allergenic foods, although further studies are needed to provide more specific recommendations regarding foods other than peanut. (36) As such, current feeding guidelines have changed to reflect this evidence. Most infants should be fed highly allergenic foods whenever developmentally and culturally appropriate, with emphasis placed on high-risk infants. Infants with severe eczema, already identified or suspected food allergies, or a strong family history of food allergy should be referred to an allergist for further evaluation. They may be candidates for skin or serum IgE testing to foods at 4 to 6 months of age to evaluate appropriateness of early peanut introduction to prevent peanut allergy development. Even when testing is slightly positive, an oral food challenge can be performed in the allergist's office to confirm tolerance. If peanut is introduced successfully without adverse reaction, recommendations are to continue 6 to 7 g per week

over at least 3 feedings. Whole peanut should be avoided secondary to risk of choking, but alternate forms to give include thinned peanut butter, Bamba peanut snack, peanut flour, and peanut butter powder. (37)(38)

Oral immunotherapy and epicutaneous immunotherapy for foods is presently being extensively studied in several ongoing clinical trials. This is encouraging because the current treatment for food hypersensitivity is strict avoidance and treatment of accidental ingestions. The results for peanut allergy have been particularly promising, with milk, egg, and fish also being studied. (25)(39)(40)

Regarding environmental allergens, extending the age range for sublingual immunotherapy tablets to include younger patients would certainly be beneficial and is currently being pursued. Applying this modality to other allergens, such as for foods, would also be of interest. Having this be a viable option for younger patients is of particular importance because many children are understandably fearful of injections and, thus, do not pursue treatment.

Allergies, whether secondary to foods, environmental allergens, stinging insects, or medications, can substantially affect the quality of life of pediatric patients. Thoughtful evaluation for pertinent clinical presentations is paramount because both false-positives and false-negatives with testing can lead to unnecessary lifestyle modifications or inappropriate treatment. Management should be a joint effort between the pediatrician and the allergist because these patients and their families require regular monitoring and ongoing education about changing recommendations as new discoveries are made in the field.

## Summary

- Based on practice guidelines, skin prick testing is currently the most commonly used method of allergy testing and is the preferred initial approach. (9)
- Long-term symptoms of allergic rhinitis or conjunctivitis, recurrent sinusitis (especially seasonal), or concern for allergic asthma are indications for environmental allergen testing when symptoms are persistent, refractory to standard care, or could be improved by proper allergen avoidance or when patients and families are curious about identifying potential triggers. (6)
- Testing for food allergens is clearly indicated when an anaphylactic reaction has occurred or symptoms suspicious of an immediate, immunoglobulin E (IgE)-mediated allergy are demonstrated with ingestion of a specific food. (6)
- Based on strong evidence, skin testing for penicillin is well validated and reliable. Investigation of penicillin allergy should be performed for any patient with a history of cutaneous reaction to aminopenicillins. (6)(12)
- Based primarily on consensus due to lack of relevant clinical studies and lack of evidence regarding validated testing for other agents, skin testing is performed with less frequency for medication classes other than penicillin.
- Based on practice guidelines, any patient who has experienced a life-threatening systemic reaction after an insect sting should have testing performed, and venom immunotherapy should be considered. Testing is not indicated for reactions limited to the skin in the pediatric population (<16 years of age). (15)(16)
- Based on practice guidelines, allergy immunotherapy is indicated for the treatment of patients with allergic rhinitis, allergic conjunctivitis, allergic asthma, or stinging insect hypersensitivity who demonstrate evidence of specific IgE antibodies with a relevant history and positive testing. (25)
- Subcutaneous immunotherapy consists of injecting gradually increasing doses of allergen extracts over a period (buildup phase) until the monthly target maintenance (therapeutic effective) dose is achieved. (25)(26)
- Sublingual immunotherapy is a relatively recent therapeutic development that may be a more convenient option for patients with environmental allergies. Administration of the specific allergen to the oral mucosa is done via fast-dissolving tablets placed underneath the tongue. (34)(35)

*References for this article are at <http://pedsinreview.aappublications.org/content/40/5/219>.*



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1. A 7-year-old boy was referred to a pediatric allergist for evaluation after having several episodes of hives following the consumption of various types of berries, including strawberries, blackberries, and raspberries in various combinations. The allergist advised the family that it is best to start with performing allergy skin and serum testing before proceeding to direct allergen challenge based on which of the following rationales?
  - A. Skin and serum testing are considered the gold standard.
  - B. Skin and serum testing are less expensive.
  - C. Skin and serum testing have a lower risk of adverse reactions.
  - D. Direct allergen challenge are less precise.
  - E. Direct allergen challenge are valid only for patients older than 12 years.
2. A 12-year-old girl with a history of asthma, allergic rhinitis, and recurrent sinusitis is being evaluated for possible penicillin allergy. She had been taking chronic nasal corticosteroids and loratadine at bedtime for the past 3 months. She was recently admitted to the hospital with asthma exacerbation and was discharged on a 5-day course of oral corticosteroids, which she completed a week ago. She recently had several episodes of sinusitis requiring antibiotic drug courses. Because of suspected penicillin allergy, her antibiotic drug choices have been gradually limited to cephalosporins and macrolides. Which of the following factors will most likely interfere with her skin testing?
  - A. Chronic nasal corticosteroid use.
  - B. Loratadine use.
  - C. Recent episode of asthma exacerbation.
  - D. Recent episode of sinusitis.
  - E. Recent 5-day course of oral corticosteroids.
3. A 3-year-old boy is brought to the emergency department by emergency medical services after he sustained an anaphylactic reaction to a bee sting while playing outside. The patient was stung over his left cheek. He immediately had diffuse swelling of the left side of his face, diffuse urticarial rash, and acute onset of cough, wheezing, and respiratory distress. The mother called 911, and emergency medical services arrived at the scene in 3 minutes, administered epinephrine, and placed the child on supplemental oxygen. There is no history of bee stings. The family is worried about future similar episodes. In addition to the immediate and acute management, which of the following is the most appropriate in management of this patient to prevent life-threatening reactions to insect envenomation?
  - A. Advise the family that a child younger than 5 years is too young for allergy testing and immunotherapy.
  - B. Discharge the patient with an epinephrine autoinjection device and consider referral for skin testing if he sustains future bee stings.
  - C. Reassure the family that the risk of a life-threatening reaction to insect envenomation is very low and is estimated to be less than 0.1% of the pediatric population.
  - D. Recommend venom testing of the 2 older siblings as a screening test.
  - E. Refer the patient for immediate skin testing and immunotherapy to reduce the risk of future anaphylaxis.

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4. A 12-year-old girl with a history of seasonal allergies and asthma is seen in the allergy clinic during her spring break for follow-up. She was diagnosed as having asthma at 4 years of age and had multiple exacerbations primarily triggered by seasonal changes and environmental allergens. She is well-controlled on daily inhaled corticosteroids and takes  $\beta_2$  agonists by inhaler as needed for exacerbations. She also takes antihistamines almost daily during high pollen count blooming season. Because she has not shown signs of outgrowing her asthma, allergy skin testing is being considered. Which of the following is a contraindication to allergy skin testing in this patient?
- A. Allergic rhinitis.
  - B. Current daily use of antihistamines.
  - C. Current daily use of inhaled corticosteroids.
  - D. No contraindications to allergy skin testing.
  - E. Occasional use of  $\beta_2$  agonists.
5. The patient in the vignette in question 4 was scheduled to come back for allergy skin testing in the summer season. Her skin testing was positive for several environmental allergens. She is to be started on immunotherapy. Which of the following is the optimal duration of allergy immunotherapy required to obtain a sustained response?
- A. 6–12 months.
  - B. 1–2 years.
  - C. 3–5 years.
  - D. 5–10 years.
  - E. Lifelong.

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