

02.01.02 Allergy Testing

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This Medical Policy document describes the status of medical technology at the time the document was developed. Since that time, new technology may have emerged, or new medical literature may have been published. This Medical Policy will be reviewed regularly and updated as scientific and medical literature becomes available; therefore, policies are subject to change without notice.

Related Policies:

- [02.01.01 Allergy Immunotherapy](#)

Summary

Description

Allergic or hypersensitivity disorders may be manifested by generalized systemic reactions as well as localized reactions in any organ system of the body. The reactions may be acute, subacute, or chronic, immediate, or delayed and may be caused by numerous offending agents, e.g., pollen, molds, dust, mites, animal dander, stinging insect venom, food(s), and double-blind food challenge tests. Diagnosing allergies often involves testing serum and skin. Other diagnostic procedures have been developed to elicit and assess hypersensitivity reactions including but not limited to intradermal, patch and ingestion challenge tests.

Summary of Evidence

For individuals who have a suspected intolerance of environmental agents or food who receive the Antigen Leukocyte Antibody Test (ALCAT), the evidence includes a randomized controlled trial (RCT) and case series. Relevant outcomes are morbid events and medication use. There is a lack of published research on the diagnostic accuracy of ALCAT; therefore, it is not possible to determine the sensitivity, specificity, and/or predictive value of the test compared with alternatives. A few low-quality studies have reported improvements in outcomes following the use of ALCAT, but it is not possible to determine whether these changes occurred as a result of the test itself, bias, variation in the natural history of the condition, and/or the placebo effect. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a suspected intolerance to environmental agents, food(s), Hymenoptera (stinging insects), inhalants or drugs and receive skin testing (in-vivo) allergy testing utilizing any of the following methods: epicutaneous (scratch, prick, puncture), skin endpoint titration (SET), patch testing (skin patch testing), and photo-patch testing for the diagnosis of hypersensitivity (i.e., allergy), the evidence includes practice parameter systematic reviews. Relevant outcomes are morbid events and medication use. The current evidence regarding this skin testing in the diagnosis of allergic conditions is based on low strength evidence and the evidence is insufficient to determine that the technology results in an improvement in the net health outcome. However, even though there is a paucity in the scientific evidence regarding the use of this skin testing in diagnosing suspected allergies this testing is widely considered to be in accordance with generally accept standards of medical practice in the United States and will be considered medically necessary when the criteria below are met, see [Policy](#).

For individuals who have suspected intolerance to food and receive in-vivo allergy testing utilizing intradermal (intracutaneous) the evidence includes practice parameter systematic review. Relevant outcomes are morbid events and medication use. Based on this evidence review (Sampson et. al. 2014) intradermal (intracutaneous) allergy testing is “not recommended to aid in the diagnosis of food allergy due to a higher false-positive rate compared to epicutaneous (scratch, prick, puncture) skin testing. This testing would not only increase systemic reactions but also increases risks of inappropriate diagnosis and unnecessary dietary elimination of foods.” However, this evidence review provides one exception in which this testing would be appropriate to utilize in individuals with “delayed anaphylaxis associated with hypersensitivity to the carbohydrate moiety alpha gel found in mammalian red meats” as epicutaneous skin testing “does not reliably identify the culprit food(s).” Therefore, based on the scientific evidence regarding the use of intradermal (intracutaneous) allergy testing this testing will be allowed for individuals with delayed anaphylaxis associated to carbohydrate moiety alpha gel found in mammalian meats as this testing for this indication is widely considered to be in accordance with generally accepted standards of medical practice in the United States and will be considered medically necessary when the criteria below are met, see [Policy](#).

For individuals who have a suspected intolerance to environmental agents, food(s), Hymenoptera (stinging insects), inhalants or drugs and receive serum testing (in vitro) allergy testing the evidence includes practice parameter systematic reviews. Relevant outcomes are morbid events and medication use. The current evidence regarding in vitro allergy testing in the diagnosis of allergic conditions is based on low strength evidence and the evidence is insufficient to determine that the technology results in an improvement in the net health outcome. However, even though there is a paucity in the scientific evidence regarding the use of in vitro allergy testing (serum testing) in diagnosing suspected allergies this testing is widely considered to be in accordance with generally accepted standards of medical practice in the United States and will be considered medically necessary when the criteria below are met, see [Policy](#).

For individuals who have a suspected intolerance to environmental agents, food(s), Hymenoptera (stinging insects), inhalants or drugs and receive skin testing (in-vivo allergy testing) or serum testing (in vitro allergy testing) utilizing one of the allergy testing methods listed below in the [Policy](#) under investigational the evidence includes practice parameter systematic reviews, cohort studies, prospective and retrospective comparative case control studies. Relevant outcomes are morbid events and medication use. Currently there is a paucity in the evidence regarding these allergy testing methods, they remain unproven and have not yet been established to be in accordance with generally accepted standards for medical practice. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Additional Information

Not applicable

OBJECTIVE

The objective of this evidence review is to determine whether allergy testing improves the net health outcomes in individuals with suspected intolerance of environmental agents or food(s).

PRIOR APPROVAL

Not applicable

POLICY

Medically Necessary

Note: See [Policy Guidelines](#) for any applicable frequency limits.

Allergy testing using the following types of tests may be considered **medically necessary** for individuals with clinically significant allergic history of symptoms (i.e., the symptoms are not adequately controlled by empiric conservative therapy):

Note: Testing must correlate specifically to the individual's history, risk of exposure and physical findings.

- **Epicutaneous (scratch, prick or puncture)** testing may be considered **medically necessary** when immunoglobulin E (IgE)-mediated reactions occur (see [Policy Guidelines](#)) to any of the following:
 - Food(s); **or**
 - Hymenoptera (e.g., stinging insects; venom); **or**
 - Inhalants; **or**
 - Specific drugs (penicillins and macromolecular agents).
- **Intradermal (Intracutaneous)** testing may be considered **medically necessary** when immunoglobulin E (IgE)- mediated reactions occur (see [Policy Guidelines](#)) to any of the following:
 - Hymenoptera (e.g.,stinging insects; venom); **or**

- Inhalants; **or**
 - Specific drugs (penicillins and macromolecular agents).
- **Skin Endpoint Titration (SET)** testing (also known as intradermal dilutional testing (IDT) for determining the starting dose for immunotherapy) may be considered **medically necessary** for any of the following:
 - Individual is highly allergic to Hymenoptera venom allergy (stinging insects); **or**
 - Individual is highly allergic to inhalants.
 - **Skin Patch Testing** may be considered **medically necessary** for diagnosing contact allergic dermatitis.
 - **Photo-Patch Testing** may be considered **medically necessary** for diagnosing photo-allergic contact dermatitis in evaluation of photo-sensitivity disorders.
 - **Photo Tests** may be considered **medically necessary** for evaluating photo-sensitivity disorders.
 - **Serum (in-vitro) IgE Antibody Tests (RAST, MAST, FAST, ELISA, or ImmunoCAP)** testing may be considered **medically necessary** for any of the following indications:
 - Individual is receiving skin test suppressive medical therapy that cannot be temporarily discontinued (e.g., antihistamines or beta blockers).
 - Presence of widespread skin disease (e.g., dermatographism, ichthyosis, intensive dermatitis, or generalized eczema).
 - When clinical history suggests an unusually greater risk of anaphylaxis from skin testing.
 - Evaluating cross-reactivity between insect venoms.
 - As an adjunctive laboratory test for disease activity of allergic bronchopulmonary aspergillosis (ABPA); **AND**

The testing is being performed for any of the following indications:

- Allergic broncho-pulmonary aspergillosis (ABPA) and certain parasitic diseases; **or**
 - Food allergy; **or**
 - Hymenoptera venom allergy (e.g., stinging insects; venom); **or**
 - Inhalant allergy; **or**
 - Specific drugs.
- **Total Serum IgE (paper radioimmunosorbent test [PRIST], radioimmunosorbent test [RIST]) testing** may be considered **medically necessary** for the diagnostic evaluation in an individual with known or suspected allergic broncho-pulmonary aspergillosis (ABPA) and/or hyper IgE syndrome.
 - **Alpha-Gal Allergy (Meat Allergy) Testing** using in vivo intradermal (intracutaneous) **or** in vitro serum allergy testing may be considered **medically necessary** for individuals who present with documentation of either of the following after ingestion of mammalian meat, typically within 3 to 6 hours:
 - Urticaria, angioedema or anaphylaxis; **or**
 - Gastro-intestinal symptoms (e.g., abdominal pain, diarrhea and/or vomiting) accompanied by pre-syncope or syncope.

- **Ara h 2 Testing for Peanut Allergy** may be considered **medically necessary** for persons with suspected peanut allergy.

Not Medically Necessary

Allergy testing will be considered **not medical necessary** for the following indications:

- When the criteria above are not met.
- Individual with mild symptoms.
- Monitoring response to immunotherapy.
- Performance of both skin testing and serum allergy testing for the same allergens.

Allergy Retesting

Medically Necessary

Note: *With the exception of venom skin tests, which may require a repeat test at three-to-six-month intervals when the initial test is negative and would be considered **medically necessary**.*

Repeat allergy testing when the above criteria is met may be considered **medically necessary** for any of the following indications:

- Individual develops new sensitivities during or after allergy immunotherapy.
- Individual has failed to respond to allergen immunotherapy.

Not Medically Necessary

Routine **annual** allergy re-testing utilizing the above allergy testing without a definite clinical indication is considered **not medically necessary**.

Investigational

Allergy testing including but not limited to the following is considered **investigational** because the evidence is insufficient in determining this testing results in improved net health outcomes:

- ALCAT test (Antigen Leukocyte Cellular Antibody Test, an automated food allergy test)
- Anti-Fc epsilon receptor antibodies testing
- Anti-IgE receptor antibody testing
- Bead-based epitope assay (VeriMAP Peanut DX)
- Basophil Activation Testing (BAT)
- Body chemical analysis (testing for idiopathic environmental intolerances" (IEIs) or multiple food and chemical sensitivities)
- Complement Antigen Testing when utilized for the diagnosis of delayed food allergies
- Cytotoxic food testing (Bryans Test)
- ELISA/ACT
- Eosinophil cationic proteic (ECP) test
- Food immune complex assays (FICA)

- Food specific IgG antibodies
- Leukocyte antibodies testing
- Mediating a protective anti-helminth (parasitic) immune response
- Mediator release test (MRT)
- Ophthalmic mucous membrane tests/conjunctival challenge test
- Panel testing for food sensitivities or food allergies including SAGE testing for food delayed sensitivity and Biotek food allergy panel
- Passive cutaneous transfer test – Prausnitz-Kustner or P-K testing
- Provocation testing (e.g., Rinkel test) either subcutaneously or sublingually
- Provocative nasal test (also known as nasal provocation testing)
- Precision diagnostics for food allergy with non-personalized large panel testing
- Pulse test (pulse response test, reaginic pulse test)
- Rebuck Skin Window test
- Sublingual allergy desensitization to aeroallergens
- Testing for other immunoglobulin (e.g., IgG, IgG4, IgA, IgM, IgD) or subclasses to determine allergies

POLICY GUIDELINES

Mediated Allergic Reaction

The most common signs and symptoms of a Type 1 IgE mediated (allergic) reaction includes the development of hives, pruritis, angioedema, flushing, wheezing, rhinitis, and abdominal cramping.

Severe Reaction

A severe reaction of a Type 1 IgE mediated (allergic) reaction causes anaphylaxis which may cause loss of consciousness, nausea, vomiting, tachycardia, and hypotension.

Limitations of Skin Testing:

- Age
 - Generally, not preferred less than 6 months of age due to potential for less accuracy since infant skin can be less reactive.
 - Patient cooperation in small children may be limited.
- Antihistamines either prescription (Hydroxyzine [Vistaril]) or over the counter (Claritin, Zyrtec, Allegra, or Benadryl) should be stopped for at least 5 days.
- Beta blockers (relative contraindication) should be stopped for at least 72 hours (if possible) since they interfere with treatment to the event of an allergic reaction.
- Tricyclic antidepressants may interfere with skin testing.
- Prednisone > 10 mg for more than 2 weeks may interfere with skin testing.

Frequency Limits

The number of max units for allergy testing will be limited to the following when the medical necessity criteria above are met:

Note: Frequency limits are calendar year January-December.

Code	Max Units
86003	70
86008	20
95004	80
95017	27
95018	19
95024	40
95027	90
95028	30
95044	90
95052	36
95056	1

Coding

See the [Codes table](#) for details.

BACKGROUND

Allergy tests are performed to verify or exclude the presence of IgE-mediated hypersensitivity and to identify the causative allergen(s). Testing can be broadly subdivided into in vivo and in vitro methodologies. In vivo methodologies, which determine the presence of specific IgE by administering an IgE-specific allergen into, on or near the individual and monitoring the individual's physiologic response(s) which may include skin allergy testing (e.g., skin prick testing, skin scratch testing, intradermal testing, skin patch testing, and skin endpoint titration), and food challenges. In vitro allergy tests determines the presence of specific IgE or elevated total IgE by analyzing the individual's serum which may include ELISA and RAST testing.

Skin prick testing and in vitro analyses of IgE are the most commonly performed allergy tests.

In-Vivo Allergy Testing

Skin Testing

Skin tests for IgE-mediated disease with allergenic extracts involve the introduction of small quantities of test allergens below the epidermis. Within 15 to 20 mins, a characteristic wheal and flare reaction occurs in individuals sensitive to one or more of the test allergens. The majority of allergists utilize prick or puncture and/or intracutaneous skin tests, since the amount of allergen delivered by these methods is better controlled than by scratch tests. Although skin testing is considered a safe procedure, adverse events, such as large local reactions and systemic symptoms may occur in extremely sensitive individuals. Prick or puncture tests are generally considered to be the most convenient, and most specific screening method for detecting the presence of IgE antibodies in individuals with appropriate exposure histories. Prick or puncture tests are generally less sensitive than intracutaneous tests. For inhalant allergens, prick or puncture tests are generally felt to correlate better with the presence of clinical allergy. However, intracutaneous (within the skin) testing may detect relevant sensitivity and should be considered when the prick or puncture test is negative or equivocal to allergens strongly suggested by the patient's history or exposure, or when skin sensitivity may be decreased such as in infants or older patients. Intracutaneous tests permit identification of a larger number of clinically reactive individuals, especially those with lower skin test sensitivity.

Skin testing to drugs is generally unreliable, except for the penicillin's and macromolecular agents, such as foreign antisera, hormone (e.g., insulin), enzymes (e.g., L-asparaginase, streptokinase, chymopapain), and egg-containing vaccines.

The Board of Directors of the American Academy of Otolaryngic Allergy (AAOA) endorsed strategies for testing for inhalant allergy, stating that "[m]embers should practice in ethical and fiscally responsible ways." The AAOA provided the following guidelines on the necessary number of tests for inhalant allergy (e.g., prick testing, intradermal testing, intradermal dilutional testing (IDT), and in vitro testing):

- **"Screening:** Screen with no more than 14 relevant antigens plus appropriate controls."
- **"Antigen survey:** If screening is positive and immunotherapy is contemplated, use no more than 40 antigens. More extensive testing may be justified in special circumstances."
- **"Quantification for safe starting point:** Use no more than 80 IDT tests routinely. More extensive testing may be justified in special circumstances."

Skin Endpoint Titration (SET)

Skin endpoint titration (SET) (also known as intradermal dilutional testing (IDT)) is intradermal testing of sequential and incremental dilutions of a single antigen. SET involves serial testing with several dilutions of a single treatment allergen or mixture of allergens to identify the lowest dilution that produces a positive skin reaction. In performing the test, wheals of identical size are made in the most superficial layers of the skin and measured for uniformity. The first wheal is made with approximately 0.1 ml of a dilution estimated to be too weak to produce symptoms. Successive wheals are made with serial dilutions, each generally five times stronger than the previous one, until negative responses are replaced by positive responses of increasing size. The "endpoint" is the weakest dilution that produces a positive skin reaction and initiates progressive increase in the diameter of wheals with each stronger dilution. Proponents of SET emphasize that it quantifies skin testing and replaces a single equivocal reaction with a progressive pattern easily identified.

In a guideline, the AAOA recommends for SET “that up to 80 injections are usually necessary to identify the offending antigen and find a safe starting point for immunotherapy.”

Provocation (Challenge) Testing

In provocation or challenge testing, a suspected allergen in a clinically relevant exposure is administered in an attempt to reproduce symptoms. Recognized forms of target-organ challenge testing (bronchial, ingestion, patch testing). Challenge tests have been broadly applied under research conditions for many years, but there also may be clinical situations in which they can be useful for confirmation of clinical disease. Considerable experience with these methods is required for proper interpretation and analysis.

Prausnitz-Kustner or P-K Testing

Prausnitz-Kustner testing has been used in patients with dermatographia or generalized skin eruptions. A control site on the forearm of a non-allergic recipient is selected. This site is injected intradermally with allergy serum from a patient on whom direct skin tests cannot be done. Allergenic extract is later injected intradermally into the initial injection site of the recipient and observed for the development of a wheal and flare. Because of the risk of transmitting hepatitis or AIDS, this test is contraindicated.

Patch Testing and Photo-Patch Testing

Allergy patch testing is an accepted method of differentiating allergic contact dermatitis and irritant contact dermatitis. Twenty to 30 antigens are used in the usual routine screening panel of patch tests. The patches have different suspected irritants (allergens) and are placed on the individuals’ back and left in place for 48 hours. After removing the patches an initial reading is at 96 hours (usually takes 48-96 hours for reaction to develop) examining the skin for any signs of a hypersensitivity reaction.

Photo-patch allergy testing is used to detect photoallergic reactions (photo contact dermatitis) to various antigens such as sunscreen, antiseptics, plant allergens and drugs. With photo-patch testing places two identical sets of allergens onto the patient’s back on day one, and at 48 hours only one of the sets is exposed to ultraviolet (UVA) light. The patches are read at 96 hours. Photocontact dermatitis is diagnosed when only the exposed allergen appears only to react on the light-exposed site.

Nasal or Conjunctival Provocative Challenge Tests

Nasal or conjunctival provocative challenge tests are utilized for the diagnosis of either food or inhalant allergies and involve the direct administration of the allergen to the mucosa. The patient is then observed for signs and symptoms and the presence of symptoms is interpreted as a positive indication of allergies. These tests are time consuming, only 1 antigen may be administered per session, a non-standardized quantity of allergen is administered, and they have the potential of inducing severe symptoms. There is currently no standard of techniques for nasal or conjunctival challenge tests that can be applied to clinical practice.

Provocation-Neutralization (Rinkel Test)

Provocation-neutralization is a method of testing for the presence of food, inhalant or environmental chemical allergies by exposing the individual to test doses of these substances intradermally, subcutaneously, or sublingually with the purpose of either producing or preventing subjective symptoms. Provocation-neutralization evolved from the serial end-point titration skin testing procedure and is based on the concept that extremely small quantities of allergens can cause immediate disappearance (“neutralization”) of ongoing symptoms. Once a test is considered positive (results are interpreted either by subjective symptom provocation or objective skin whealing), a progressive series of lower concentrations are administered under the tongue or skin until a dose is reached at which the patient reports no sensations. The amount of the test substance is considered the “neutralizing dose”,

which is then used for future treatment. Sublingual testing has been used mainly in diagnosing food allergy, although extracts of chemicals, inhalant allergens, drugs, and hormones have been administered by the sublingual route. Since provocation-neutralization requires the provoking and neutralizing of symptoms to a single item at a time, the patient could be required to undergo hundreds of individual tests requiring weeks or months of full-day testing.

Sublingual provocative neutralization with hormones utilizes the same principles as noted above and involves preliminary extensive blood testing for allergies to hormones and the subsequent administration of small doses of hormones suspected of causing the allergic symptoms. There have been no well-controlled studies that have shown this procedure to be effective in the diagnosis and treatment of symptoms thought to be caused by allergy to hormones.

Provocation-neutralization must not be confused with the recognized forms of target-organ challenge testing (bronchial, ingestion, patch testing), which are proven modalities.

In-Vitro Allergy Testing

Ara h 2 Testing

Ara h 2 is a conglutin seed storage protein and member of the 2S albumin family and is considered one of the major peanut allergens. Individuals who are sensitized to Ara h 2 are at an increased risk for more severe symptoms and anaphylactic reactions.

Bead-Based Epitope Assay (BBEA)

A bead-based epitope assay (BBEA) has been proposed to diagnose and monitor individuals with food allergies. The test breaks down allergenic proteins into smaller components, called epitopes. It then measures the reactivity of an individual's IgE/IgG4 levels to each epitope to generate a detailed reactivity profile that can be used by clinicians to manage the allergy. There are several IgE epitope mapping methods based on the binding of IgE molecules to peptides that are derived from the allergen, thereby allowing for the identification of epitopes.

AllerGenis™ has developed multiplex immunoassay technology that is proposed to more precisely diagnose and monitor individuals with food allergies. According to the manufacturer's website, the diagnostic technology subdivides allergenic proteins into smaller peptides, called epitopes, and measures the reactivity of a patient's IgE to these epitopes. The platform uses a high-throughput, Luminex bead-based epitope assay (BBEA) to analyze IgE reactivity to discrete food allergen epitopes (e.g., VeriMAP™ Peanut Dx, VeriMAP™ Peanut Sensitivity). The VeriMAP Peanut Dx is a peanut allergen-specific IgE and quantitative assessment of 64 epitopes using enzyme-linked immunosorbent assay (ELISA) combined with Luminex's bead-based xMAP® Technology to measure the reactivity of a individual's antibodies to each epitope in order to generate a detailed reactivity profile.

Radioallergosorbent Test (RAST)

The discovery of the role of IgE in clinical allergy testing resulted in the development of in vitro diagnostic assays to test for allergen sensitivity. The first immunoassays were developed to quantify the serum concentration of total IgE. In normal individuals, IgE is usually present at low levels; 130 ng/ml represents the upper limit of the normal range. However, a significant number of asymptomatic normal individuals, such as those with parasitic diseases or with depressed cell mediated immunity, exceed this level. Also, some allergic individuals may exhibit normal total IgE levels in the presence of elevated levels of specific IgE. Methods were therefore developed to assay allergen specific IgE. The radioallergosorbent test (RAST) system was developed for in vitro measurement of specific IgE in a individual's serum. Other in vitro tests for specific IgE have been developed and employ the same principles as the RAST but use an enzymatic (MAST) or fluorogenic (FAST) detection system in place of a radioactive label.

In vitro tests that screen for multiple allergens in a single assay (Phadiatop®, Pharmacia Diagnostics) or that can be used in an automated system (ImmunoCAP®, Pharmacia Diagnostics) have been developed. The ImmunoCAP is designed as a "sandwich" immunoassay. The sensitivity and specificity of the ImmunoCAP compares favorably with those of the modified PhadezymRAST® system. Results from studies have indicated that, when compared to skin prick testing as the gold standard, the ImmunoCAP system has been shown to have a greater sensitivity (80–95%) than RAST and to have similar specificity (85%). Other modified versions of the RAST test include the PRIST, RIST, VAST) and ELISA IgE tests.

Antigen Leukocyte Antibody Test (ALCAT)

The Antigen Leukocyte Antibody Test (ALCAT) is intended to identify foods and other environmental agents for which an individual may be intolerant. It is not intended to diagnose food allergies. The test is based on the theory that a substantial increase in leukocyte size and number is characteristic of an intolerant response. Identifying the specific inciting agent facilitates avoidance of that agent, which may lead to a reduction in symptoms. In this regard, ALCAT has been used as a tool for developing an elimination diet that targets the most likely offending agents.

The test is performed by taking a sample of blood, which is first treated to remove the red blood cells and then tested to determine the baseline number and size of leukocytes and platelets. Measurement of size and count of cells is performed by the Coulter technique, which is a standard technique in clinical hematology. Next, a small quantity of blood is incubated with multiple agents. Following exposures, change in the number and size of cells is determined for each exposure. A 10% increase in the size of leukocytes is considered characteristic of a response to an intolerant agent.

The ALCAT website (Cell Sciences Systems) lists 11 separate panels consisting of various combinations of foods, herbs, food additives/coloring, and environmental chemicals. The total number of agents tested in these panels ranges from 70 to 357.

Cytotoxic Testing (Bryans Test)

Cytotoxic testing (Bryans Test) is based on the theory that the addition of a specific allergen to either whole blood or a serum leukocyte suspension from a suspected allergic patient will result in reduction of the white blood cell count or death of the leukocytes, thereby indicating the presence of an immune response.

ELISA/ACT

ELISA/ACT tests lymphocytes in a laboratory culture for their reaction to up to 300 purified foods, preservatives, chemicals, and minerals. This test is not FDA approved and is not established as a useful test in clinical practice.

Food Immune Complex Assays FICA

Food Immune Complex Assays (FICA) are based on the standard solid phase radioimmunoassay methodology. These assays quantify the presence of serum immune complexes containing both antigen and antibody and are counted.

Rebuck Skin Window Test

Rebuck skin window test is an immunologic test in which the skin is abraded with a scalpel. Laboratory cover slips are placed over the abraded areas for 24 hours. The cover slips are then stained and analyzed. An immune deficiency may be present if there is an abnormality of monocytes displayed either by their absence or their inability to migrate to intracellular sites of antigen within 12 hours.

Leukocyte Histamine Release Test

The leukocyte histamine release test is a measurement of the amount of histamine released in-vitro. Varying concentrations of an allergen extract are added to the individual's peripheral blood leukocytes and histamine is normally released as a consequence of the interaction of allergen with cell bound IgE antibodies. If an individual is atopic to a specific antigen, the leukocytes will not release the histamine in-vitro.

Body Chemical Analysis

Body chemical analysis is typically seen in the diagnosis of a condition known as "idiopathic environmental intolerances" (IEIs) or "multiple food and chemical sensitivities." Samples of whole blood, serum, erythrocytes, urine, fat and hair are tested for the presence of environmental chemicals. The most common chemicals measured are organic solvents, other hydrocarbons, pesticides and metals. Some proponents of this testing also recommend measurements of the quantity of vitamins, minerals and amino acids in blood and urine in a search for "environmental sensitivities." The concept of multiple food and chemical sensitivities manifested by numerous symptoms in the absence of objective physical findings lacks scientific foundation.

Mediator Release Test (MRT)

The mediator release test (MRT) has primarily been used to detect intolerance to foods and additives in individuals with irritable bowel syndrome (IBS). The MRT measures the aggregate release of inflammatory mediators from the individual's immunocytes in vitro after exposure to specific foods and food additives. The results of the MRT have been used to design a patient-specific diet to treat IBS by avoiding foods and additives that trigger significant inflammatory mediator release. For the MRT, the individual's blood sample is incubated with various extracts of foods and food additives and then analyzed for the presence and aggregate amount of release of inflammatory mediators from the individual's leukocytes. Results are compared to control samples of the individual's blood that have not been exposed to food extracts or additives.

The mediator release test has also been promoted for use in individuals with chronic fatigue syndrome, metabolic conditions (e.g., diabetes, obesity), gastrointestinal disorders (e.g., gastroesophageal reflux disease, chronic ulcerative colitis, and Crohn's disease), neurologic disorders (e.g., migraine headaches, cluster headaches), rheumatologic disorders (inflammatory arthritis, arthralgias, fibromyalgia), otolaryngologic disorders (e.g., perennial rhinitis, chronic sinusitis, chronic otitis media with effusion), dermatologic conditions (e.g., eczema, urticaria, dermatitis), and in individuals with behavioral conditions (e.g., attention deficit disorder, hyperactivity, frequent mood swings, inability to concentrate).

Eosinophil Cationic Protein

Eosinophil cationic protein (ECP) is an eosinophil-specific mediator that can be measured in bodily fluids to estimate the extent of eosinophil activation, although it provides no information about the presence of IgE-mediated allergy.

Anti-IgE and Anti-Fc Epsilon Receptor Antibodies

These antibodies trigger mast cell and basophil degranulation by the engagement of the Fc epsilon receptor. The anti-IgE antibody will quantify autoantibodies to IgE which will aid in the diagnosis and management of autoimmune chronic urticaria.

Complement Antigen Test

This test combines IgE, IgG, IgG4, and complement C3d reactions to common foods found in the diet. IgE mediated food allergies can lead to hives, anaphylaxis or digestive issues while delayed food sensitivities IgG and IgG4 are linked to sinus problems, acne, gas, bloating, fatigue, constipation, autism, irritable bowel syndrome and depression. Eliminating food sensitivities may assist with the healing of intestinal permeability.

Alpha-Gal Allergy (Meat Allergy Testing)

Alpha-gal syndrome is a type of food allergy that makes individuals allergic to meat and other products made from mammals. In the United States this condition is usually caused by a bite by the Lone Star tick. The Lone Star tick is found mainly in the southeastern United States. Most cases are reported in the south, east and central United States, but this condition appears to be spreading farther north and west as deer are carrying the Lone Star tick to other parts of the United States. Alpha-gal syndrome can cause serious allergic reactions such as anaphylactic reactions. There is no treatment other than avoiding red meat and other products made from mammals.

Alpha-gal allergy testing may be performed by blood or skin testing. The treatment for alpha-gal syndrome involves avoiding the foods with red meat or meat-based ingredients.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory

Improvement Amendments. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this testing.

RATIONALE

This evidence review was created in November 2003 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through February 2026.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

In-Vivo Allergy Testing

Clinical Context and Test Purpose

The purpose of the allergy testing in individuals with a suspected intolerance of environmental agents or food(s) is to inform a decision whether to pursue additional diagnostic testing, initiate treatment, or lifestyle and diet management.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with suspected intolerance to environmental agents or food(s).

Interventions

The tests being considered is allergy testing.

In vivo allergy testing determines the presence of specific IgE by administering an IgE-specific allergen into, on or near the individual and monitoring the individual's physiologic response(s) which may include the following:

- Nasal or conjunctival provocative challenge test
- Patch testing
- Photo-patch testing
- Prausnitz-Kustner or P-K testing

- Provocation-neutralization (Rinkle Test)
- Skin endpoint titration (SET)
- Skin testing
 - Epicutaneous
 - Intradermal (intracutaneous)

Comparators

The following tests and practices are currently being used to make decisions about diagnosing suspected intolerance of environmental agents or food: antigen or allergen skin testing, antigen or allergen in vitro assays, and elimination dietary changes.

Outcomes

The general outcomes of interest are confirming intolerance to an environmental agent or food and selecting an appropriate intervention. The timing of interest may range from 4 weeks to evaluate test results to 1 to 2 years to evaluate reductions in morbid events and medication use.

Study Selection Criteria

For the evaluation of allergy testing, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard (describe the reference standard)
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

Review of Evidence

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Nasal or Conjunctival Provocative Challenge Test

Dykewicz et. al. (2020) in an evidence review regarding rhinitis which states the following: “Nasal challenge for vasomotor rhinitis (VMR), to determine nasal hyperresponsiveness (e.g., using cold dry air or hypertonic saline in a challenge chamber), may be used in research to assess drug efficacy but is rarely used for clinical diagnosis.” Also, in this evidence review it was noted that conjunctival challenge to grass pollen was completed, however, “throughout the early part of 20th century skin tests, both puncture and intradermal were the rule once IgE was discovered, and in vitro laboratory tests could identify antibodies to specific allergens.” This evidence review refers to Bernstein et. al. (2008) evidence review regarding allergy diagnostic testing. See [Practice Guideline and Position Statements](#).

Patch Testing and Photo-Patch Testing

Fonacier et. al. (2015) in an evidence review regarding contact dermatitis stated that the majority of the practice parameter summary statements (recommendations) are based on descriptive and retrospective studies and there is an absence of validated positive control data to confirm a diagnosis of acute contact dermatitis (ACD) which is a limitation of these studies reporting on patch and photo-patch data. The evidence supporting the summary statements (recommendations) in this evidence review is considered low strength. See [Practice Guideline and Position Statements](#) regarding the summary statements (recommendations) related to diagnosis of contact dermatitis using patch testing and the diagnosis of photo-allergic contact dermatitis (CD) using photo-patch testing.

Prausnitz-Kustner or P-K testing

The Prausnitz-Kustner or P-K testing is now considered obsolete and has been replaced by Radioallergosorbent testing.

Provocation-Neutralization (Rinkle Test)

Sampson et. al. (2014) in an evidence review regarding food allergy the authors noted “provocation neutralization is unproven and should not be utilized in the evaluation of food allergy.”

Skin Endpoint Titration (SET)

Skin endpoint titration (SET) has been used as an alternative to skin prick testing or in vitro testing and has also been used to guide initiation of immunotherapy, with the endpoint dilution used as the starting dose. Although not considered a replacement for skin testing, SET may be indicated for determination of a safe starting dose for testing or immunotherapy when there is potential for the specific allergen in

question to produce a severe systemic reaction or anaphylaxis (such as with bee venom or allergic inhalants). Bernstein et. al. (2008) in an evidence review regarding allergy diagnostic testing stated the following: “In the case of natural allergens (e.g., pollen, molds, house dust mite), there are no clear guidelines for the initial concentration of allergen or exposure time to be used for testing. Standardized (AU or BAU) or conventional (wt/vol or protein nitrogen units [PNU]) allergenic extracts can be used. A prior intracutaneous skin test SET may be performed to estimate the initial challenge dose.”

Skin Testing

Sampson et. al. (2014) in an evidence review regarding food allergy this review included an update regarding intradermal (intracutaneous) skin testing for food allergy which states “intradermal skin testing for food allergy is not recommended to aid in the diagnosis of acute IgE mediated food allergy caused by an increased risk of systemic reactions. Intradermal skin testing with food extracts has also been shown to have significantly higher false-positive rates compared with SPTs. Therefore, if relied on, intradermal testing would not only increase systemic reaction risks but also increase risks associated with inappropriate diagnosis and unnecessary dietary elimination of foods. One exception to this is the use of intradermal (intracutaneous) testing related to delayed anaphylaxis associated with hypersensitivity to the carbohydrate moiety alpha gal found in mammalian red meats, SPTs do not reliably identify the culprit food or foods.” See [Practice Guideline and Position Statements](#).

Bernstein et. al. (2008) in an evidence review regarding allergy diagnostic testing advised this review was based on the following: “medical literature using a variety of search engines, such as PubMed, published clinical and basic studies were rated by categories of evidence and used to establish the strength of recommendations.” Comments were also solicited from the following societies: Joint Task Force and subsequently by the American Academy of Allergy, Asthma and Immunology (AAAAI), the American College of Allergy, Asthma and Immunology (ACAAI), and the Joint Council of Allergy, Asthma and Immunology and it was noted “this document represents an evidence-based broadly accepted consensus opinion.” Based on this evidence review the following was noted “prick/puncture tests or intracutaneous tests are the preferred techniques for IgE-mediated hypersensitivity such as inhalants, foods and drugs. Intracutaneous tests are generally used for specific allergens (i.e., Hymenoptera venoms and penicillin), but they may also be applied if prick/puncture test results are negative and there is a strong historical likelihood of clinical allergy to specific allergens.” See [Practice Guideline and Position Statements](#).

Golden et. al. (2016) in an evidence review regarding stinging insect hypersensitivity the authors advised this evidence review is based on observational studies states, case series, basic laboratory reports, and expert review articles to develop this practice parameter. See [Practice Guideline and Position Statements](#) regarding the recommendations related to allergy testing for stinging insect hypersensitivity.

In-Vitro Allergy Testing

Clinical Context and Test Purpose

The purpose of the allergy testing in individuals with a suspected intolerance of environmental agents or food(s) is to inform a decision whether to pursue additional diagnostic testing, initiate treatment, or lifestyle and diet management.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with suspected intolerance to environmental agents or food(s).

Interventions

The tests being considered is allergy testing.

In vitro allergy tests determine the presence of specific IgE antibodies in serum to determine the presence of specific IgE or elevated total IgE and may include the following:

- Alpha-Gal allergy testing
- Antigen Leukocyte Antibody Test (ALCAT)
- Ara h 2 testing
- Basophil activation testing (BAT)
- Bead-based epitope assay (BBEA)
- Body chemical analysis
- Complement antigen test
- Cytotoxic testing (Bryans Test)
- Eosinophil cationic protein testing
- Food immune complex assay (FICA)
- Immunoglobulin subclasses (IgG, IgG4, IgA, IgM, IgD)
- Leukocyte histamine release test (LHRT)
- Mediator Release Test (MRT)
- Panel testing
- Radioallergosorbent test (RAST)
 - A variety of modifications have been made related to the RAST Test including the following:
 - Multiple – Antigen Simultaneous Test (MAST)
 - Paper Radioimmunosorbent Test (PRIST)
 - Radio-Immuno-Sorbent- Test (RIST)
 - Food Allergy and Sensitivity Test (FAST)
 - Modified Rast Test (MRT)

- VAST
- Enzyme-Linked Immunosorbent Assay (ELISA)
- ImmunoCAP
- Rebut window test

Comparators

The following tests and practices are currently being used to make decisions about diagnosing suspected intolerance of environmental agents or food: antigen or allergen skin testing, antigen or allergen in vitro assays, and elimination dietary changes.

Outcomes

The general outcomes of interest are confirming intolerance to an environmental agent or food and selecting an appropriate intervention. The timing of interest may range from 4 weeks to evaluate test results to 1 to 2 years to evaluate reductions in morbid events and medication use.

Study Selection Criteria

For the evaluation of allergy testing, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
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- Patient/sample clinical characteristics were described
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Review of Evidence

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Antigen Leukocyte Antibody Test (ALCAT)

There is not a widely accepted criterion standard test for food and environmental intolerance. The double-blind food challenge test may be considered an appropriate reference standard but there are deficiencies in the definitions and interpretation of food challenge results. No published studies identified have reported on the sensitivity and specificity of ALCAT compared with a double-blind food challenge. One study by Buczylo et al (1995) compared ALCAT with cytotoxic testing, which is not a test routinely used in clinical care at present, in 56 children between the ages of 6 months and 16 years. This study reported that the results of the 2 tests were consistent in two-thirds of patients.

No RCTs evaluating the clinical utility of ALCAT in a population with suspected intolerance of environmental agents or food were identified.

Randomized Controlled Trials

An RCT by Kaats et al (1996) evaluated the use of ALCAT in facilitating weight loss, changes in body composition, and health symptoms. One hundred patients were recruited through an advertisement in a fitness newspaper. Eligibility criteria included at least 2 symptoms that had a “severe effect,” as measured by the Disease Symptoms Inventory (DSI). Patients were randomized to ALCAT testing followed by dietary modifications or to a control group instructed to pursue a diet of their choosing. The ALCAT group received dietary guidance on dietary changes that were recommended based on ALCAT results. Outcomes were measured after 4 weeks of the intervention and included changes in weight, body composition, and symptoms on the DSI. Eight participants were lost to follow-up, 7 in the control group and 1 in the ALCAT group.

There was a greater reduction in weight in the ALCAT group than in the control group (-1.04 kg vs +0.32 kg; $P<.001$), as well as a greater reduction in the percent body fat (-1.2% vs +0.7%, $P<.001$). There were also significantly better scores on the final DSI outcomes for the ALCAT group. Of 20 symptoms included on the DSI, the final scores were significantly better for the ALCAT group on 18 of 20 symptoms. The results of this trial have limited clinical relevance because the outcomes reported (weight loss, body composition) are not applicable to the main clinical use of the test or relevant to the population assessed in this review. Additionally, the validity of the results was reduced due to limitations in patient selection, lack of blinding, and the provision of dietary guidance to the ALCAT group but not the control group.

Case Series

A small number of case series have reported on outcomes following an ALCAT evaluation and treatment based on ALCAT results. These studies are not sufficient to establish efficacy because case series do not control for the natural history of the disorder or for nonspecific factors such as the placebo effect. An example of such a study is Solomon (1992). In this publication, 172 patients with a range of symptoms were tested with ALCAT. Treatment was a food elimination diet and/or allergy immunotherapy, based on ALCAT results. Follow-up allergy testing was performed with serial endpoint titration at 3 to 6 months after

treatment. Outcomes were measured at 1 to 2 years posttreatment by an independent reviewer who asked individuals to rate the effectiveness of treatment on a 1-to-10 scale. For elimination diets, a range of improvement in individual symptoms of 20% to 82% was reported, and for immunotherapy, a range of improvement of 9% to 75% was reported.

Another uncontrolled study that used ALCAT as the basis for an elimination diet is that by Mylek (1995). This study enrolled 72 individuals with a range of symptoms considered to be the result of food intolerance. The largest percentage improvement in symptoms was reported for arthritis (83%), urticaria (75%), bronchitis (70%), and gastroenteritis (70%). A smaller degree of improvement was reported for the symptoms of hyperreactivity (32%), rhinitis (47%), and atopic dermatitis (49%).

Section Summary: Antigen Leukocyte Antibody Testing (ALCAT)

There is a lack of published research on the diagnostic accuracy of ALCAT; therefore, it is not possible to determine the sensitivity, specificity, and/or predictive value of the test compared with alternatives. A few low-quality studies have reported improvements in outcomes following the use of ALCAT, but it is not possible to determine whether these changes occurred as a result of the test itself, bias, variation in the natural history of the condition, and/or the placebo effect. Because the clinical validity of ALCAT has not been established, a chain of evidence supporting the clinical utility of the test cannot be constructed.

Alpha-Gal Allergy (Meat Allergy Testing)

Sampson et. al. (2014) in an evidence review regarding food allergy recommended the testing for IgE antibodies specific for the immunogenic oligosaccharide galactose-alpha-1, 3-galactose (alpha-gal) in patients who report a delayed systemic reaction to red meat or unexplained anaphylaxis, particularly if they have a history of previous tick bites. Recently, delayed allergy to mammalian meats has been linked to the production of IgE to alpha-gal in susceptible subjects, the vast majority of whom report tick bites. Urticaria, angioedema, and anaphylaxis can occur 3 to 6 hours after eating beef, pork, lamb, and venison, and the mechanisms for this delay remain poorly understood. Results of epicutaneous testing to the above foods might not be strongly positive, but in vitro assays for alpha-gal IgE are now commercially available. Alpha-gal– specific IgE (sIgE) will recognize epitopes present in all of these animals, and thus all of these meats should be eliminated from the diet.”

Ara h 2 Testing

Greenhawt et. al. (2020) in an evidence review on peanut allergy diagnosis included the following recommendation regarding Ara h 2 testing: “We suggest in favor of Ara h 2 diagnostic testing in a patient presenting for evaluation of suspected peanut allergy for which a single diagnostic test is to be used, as Ara h 2 would provide the best diagnostic accuracy as determined by virtue of more optimal positive/negative likelihood ratios. However, while Ara h 2 has the greatest specificity, it has lower sensitivity than SPT and sIgE, and in a patient with a high prior probability, the clinician may use Ara h 2, SPT, or sIgE to confirm the diagnosis of peanut allergy.”

Basophile Activation Testing (BAT)

Suarez-Farinas et. al. 2024 in a multicenter phase III clinical trial evaluated the utility of basophil activation testing (BAT) to predict double-blind placebo-controlled food challenge (DBPCFC) outcomes, including peanut eliciting dose (ED) thresholds and the severity of induced reactions as measured by epinephrine use, leveraging samples collected at baseline of the eligibility criteria. In total 362 subjects, distributed among clinical sites located in North America (United States and Canada) and Europe were

included in the study, and fifteen of the North American sites collected samples for BAT resulting in the evaluation of 241 pediatric patients (n=241). The primary end points were the ED obtained at DBPCFC and the severity of the elicited allergic reaction at DBPCFC. The severity of the allergy reaction was defined by the use of epinephrine at the DBPCFC. In addition, both the total PRACTALL score (sum of 8 domains) and the maximum PRACTALL grade (0-3) across all symptom domains were calculated as further proxy measures of severity of the reaction at DBPCFC. Using a machine learning approach that incorporated BAT derived features, clinical characteristics, and peanut-specific immunoglobulin E, the ability to predict outcomes of interest ED $\leq$ 300 mg or $>$ 300 mg and use of epinephrine was assessed using data randomly split into training (n=182) and validation (n=59) subsets). Expressions of basophil activation markers CD203c and CD63 correlated with ED and severity outcomes in term of either epinephrine use or maximum PRACTALL grade across all domains both by median fluorescence intensity and as a percentage of cells expressing the markers. Basophil expression of CRTH2 also discriminated between individuals with high and lower ED and the most informative concentrations of peanut extract in the BAT assay for these associations were 1 and 10 ng/mL. Using machine learning to assess the ability to predict outcomes of DBPCFC the best models using BAT derived features provided relatively high sensitivities 0.86 and 0.85 for predicting ED and epinephrine use, respectively, whereas specificities were lower ranging from 0.60 to 0.80. Including specific immunoglobulin E and skin prick testing data in addition to BAT testing did not improve the ability to identify individuals at risk for severe reactions, but did improve the ability to identify individuals with ED greater than 300 mg use of epinephrine. While these data may be promising the study authors concluded these results need to be confirmed and verified in additional cohorts and there were several limitations associated with this study: study focused only on peanut allergy leaving questions related to the use of BAT for other food allergies, study focused on only infants and children and it will need to be evaluated in older children and adults to verify this approach is valid regardless of cohort characteristics and the highest allergen dose of DBPCFC administered was 300 mg and for future cohorts a wider range of EDs will need to be included ideally from very low dose of allergic food to relatively large amounts.

Sampson et.al. (2014) in an evidence review regarding food allergy in which included basophil reactivity testing the authors found that the role of cellular in vitro as a diagnostic or prognostic indicator of a food allergy is currently under investigation and has not been well established to date.

Bead-Based Epitope Assay (BBEA)

The VeriMAP Peanut Dx is a peanut allergen-specific IgE and quantitative assessment of 64 epitopes using enzyme-linked immunosorbent assay (ELISA) combined with Luminex's bead-based xMAP® Technology to measure the reactivity of a patient's antibodies to each epitope in order to generate a detailed reactivity profile.

Most epitope studies focus on peanut, egg and milk allergies. The evidence in the published peer-reviewed medical literature regarding bead-based epitope assay (BBEA) consists of cohort studies and prospective and retrospective comparative case control studies with small sample sizes (Suprun et. al. 2019; Surez-Farinas et. al. 2019; Shen et. al. 2018; Chen et. al. 2016; Bogh et. al. 2014). Additional randomized comparative studies are needed to establish that BBEA improves outcomes compared to alternative testing modalities.

Observational Study

Grinek et al (2023) evaluated the prognostic ability of epitope-specific antibodies to predict the result of an oral food challenge (OFC) at 5 years. The LEAP and COFAR studies were registered on clinicaltrials.gov (NCT00329784 and NCT00356174) and subjects from these trials were utilized for evaluation. A Bead-Based Epitope Assay was used to quantitate IgE and IgG4 to 64 sequential (linear) epitopes from Ara h

1–3 proteins at 4–11 months, 1 and 2.5 years of age in 74 subjects (38 of them with a positive OFC at 5-years). Specific IgE (sIgE) to peanut and component proteins was measured using ImmunoCAP. Machine Learning methods were used to identify the earliest time point to predict 5-year outcome, developing prognostic algorithms based only on 4–11 months samples, 1-year or 2.5 years, and a combination of them. Data from 74 children were iteratively split 3:1 into training and validation sets and machine learning models were developed to predict the 5-year outcome. A test set (n=90) from an independent cohort was used for final evaluation. Elastic-Net algorithm combining ses-IgE and IgE to Ara h 1,2,3 and 9 proteins could predict the 5-year peanut allergy status of LEAP participants with an average validation accuracy of 64% at baseline. Samples taken at 1 year accurately predicted a 5-year OFC outcome with 83% accuracy. This performance remained consistent when evaluated on an independent CoFAR2 cohort with an accuracy of 78% for the 1-year model. Limitations included only subjects randomized to peanut avoidance arm of the LEAP trial and the sample size was further limited by the available sample volumes. Allergy status was determined at the 5-year OFC visit, however, some of the trial subjects may have developed the allergy prior to this visit. The study authors concluded while epitope-specific IgE profiles obtained at about 1 year of age in high risk children avoiding peanut may show promising results as prognostic biomarker for peanut OFC outcome at 5 years of age, limitations still remain epitope-specific IgE profiles in predicting allergy status and further prospective studies with larger sample sizes are needed

Body Chemical Analysis

Body chemical analysis is usually seen when diagnosing “idiopathic environmental intolerances” or “multiple food and chemical sensitivities.” The concept of multiple sensitivity testing in the absence of objective physical findings lacks scientific foundation. Currently there is no evidence to suggest these individuals suffer from an immunological abnormality. The existence of this condition is based on anecdotal reports with no verification using well-designed RCTs. Also, there is no evidence to support the utilization of this testing provides value in diagnostic allergy testing associated with idiopathic environmental intolerances or multiple food and chemical sensitivities using body chemical analysis.

Complement Antigen Test

Complement antigen testing (SAGE; Sage Medical Laboratories) has been utilized to identify delayed food allergies, however, there is insufficient evidence in the medical literature using this testing approach.

Cytotoxic Testing (Bryans Test)

In 1985 the U.S FDA determined that “cytotoxic testing remains an unproven diagnostic procedure unsupported by the scientific literature or well-controlled studies and clinical trials. While there are several reports of uncontrolled studies in the literature which advocate the use of cytotoxic test, the consensus of the scientific option is that the cytotoxic test is unreliable as a diagnostic tool and is not generally recognized by qualified experts as effective.”

Sampson et. al. (2014) in an evidence review regarding food allergies included the following regarding cytotoxic assays: “cytotoxic assays for the routine evaluation of IgE mediated food allergies is “unproven and should not be used because the results can lead to misdiagnosis or a missed diagnosis of IgE-mediated food allergy, thus leading to inappropriate or unnecessary dietary elimination of foods. This testing could result in a delay of appropriate diagnostic evaluation and management of IgE-mediated food allergies.”

Eosinophil Cationic Protein Testing

Sampson et.al. (2014) in an evidence review regarding food allergy which included eosinophilic reactivity testing the authors found that the role of cellular in vitro as a diagnostic or prognostic indicator of a food allergy is currently under investigation and has not been well established to date.

Food Immune Complex Assay (FICA)

Clinical studies to date indicate circulating immune complexes can be found in a normal population of individuals having no food allergy and the value of the measurement of FICA toward the diagnosis of food allergies remains unproven and does not have place in current clinical practice.

Immunoglobulin Subclasses

Sampson et. al. (2014) in an evidence review regarding food allergies included the following regarding immunoglobulin subclasses (IgA, IgM, IgG and IgA) the current understanding of the specific role in immunity of these immunoglobulin subclasses related to food allergies has not been demonstrated. The use of specific IgG measurement is an unproven test for the evaluation of food allergy.

In their Choosing Wisely Campaign, the American Academy of Allergy, Asthma and Immunology recommends against immunoglobulin G (IgG) testing in the evaluation of allergy. The American Academy of Allergy, Asthma & Immunology (AAAAI) states that appropriate diagnosis and treatment of allergies requires specific IgE testing (either skin or blood tests) based on the patient's clinical history.

Leukocyte Histamine Release Test (LHRT)

Boyce et. al. (2010) in an evidence review regarding food allergies included the following regarding leukocyte histamine release test (LHRT): "The EP recommends not using leukocyte histamine release test (LHRT) for the routine evaluation of IgE mediated food allergies." The authors concluded there is a lack of evidence demonstrating this testing provides any value in the diagnosis of food allergies.

Mediator Release Test (MRT)

There are, however, no studies of the mediator release test (MRT) reported in the peer-reviewed published medical literature that demonstrate improvements in clinical outcomes by incorporating MRT and associated dietary modifications into the clinical management of patients with the following conditions: irritable bowel syndrome (IBS), chronic fatigue syndrome, metabolic conditions (e.g., diabetes, obesity), gastrointestinal disorders (e.g., gastroesophageal reflux disease, chronic ulcerative colitis, and Crohn's disease), neurologic disorders (e.g., migraine headaches, cluster headaches), rheumatologic disorders (inflammatory arthritis, arthralgias, fibromyalgia), otolaryngologic disorders (e.g., perennial rhinitis, chronic sinusitis, chronic otitis media with effusion), dermatologic conditions (e.g., eczema, urticaria, dermatitis), and in patients with behavioral conditions (e.g., attention deficit disorder, hyperactivity, frequent mood swings, inability to concentrate).

Radioallergosorbent Testing (Rast)

Bernstein et. al. (2008) in an evidence review regarding allergy diagnostic testing "the first assay for allergen specific IgE was reported in 1967 and was termed radioallergosorbent test (RAST)." The RAST system was developed for in vitro measurement of specific IgE in an individual's serum and based on guidelines and current practice standards RAST testing is recommended for the diagnosis and

management of allergic broncho-pulmonary aspergillus (ABPA), food allergy, venom allergy, inhalant allergy and drug allergy.

Other in vitro tests for specific IgE have been developed and employ the same principles as the RAST but use an enzymatic (MAST) or fluorogenic (FAST) detection system in place of a radioactive label. Additional modified versions of the RAST test include the PRIST, RIST, MRT (modified RAST) and ELISA IgE tests.

In vitro tests that screen for multiple allergens in a single assay using an automated system ImmunoCAP® results from studies have indicated that, when compared to skin prick testing as the gold standard, the ImmunoCAP system has been shown to have a greater sensitivity (80–95%) than RAST and to have similar specificity (85%).

Rebuck Skin Window Test

Based on review of the current evidence this test is not reliable in documenting allergies since other immunodeficiencies can be found in individuals with allergic conditions.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Allergy, Asthma and Immunology (AAAAI)

In 2008, the American Academy of Allergy, Asthma and Immunology (AAAAI) updated their 1999 guideline regarding allergy diagnostic testing: This updated practice parameter includes the following recommendations:

Summary Statement 1. “Skin tests (prick/puncture and intracutaneous) have evolved as reliable, cost effective techniques for the diagnosis of IgE mediated diseases.” (B)

Summary Statement 2 “Prick/puncture tests are used to confirm clinical sensitivity indicated by allergens, foods, some drugs and few chemicals.” (B)

Summary Statement 20 “Intracutaneous tests are useful for evaluation of anaphylaxis, particularly drug (i.e. penicillin) and Hymenoptera venom anaphylaxis.” (A)

Summary Statement 35 “Prescreening with prick/puncture tests is a practical way to avoid life-threatening reactions to intracutaneous tests.” (C)

Summary Statement 43 “The number of skin tests and the allergens selected for skin testing should be determined based on the patient’s age, history, environment and living conditions (e.g., region of the country), occupation and activities. Routine use of a large number of skin tests or routine annual tests without a definite clinical indications are clearly not justified.” (D)

Summary Statement 78 “When clinical evaluations suggest that exposure to a specific contactant has occurred either in an occupational or nonoccupational clinical setting, patch testing can be used to confirm the diagnosis.” (C)

Summary Statement 81. If photocontact sensitivity is suspected, the appropriate allergens should be subjected to photopatch tests primarily in the UV-A range of 320-400 nm.” (C)

- If photosensitization is suspected, photo patch tests should be performed by a physician with expertise in UV radiation.

Summary Statement 84 “Although patch tests are indicated in any patient with a chronic eczematous dermatitis if ACD is suspected, patch tests are especially important in identifying both ICD and ACD in the occupational setting.” (C)

Summary Statement 85 “Other important exposures associated with ACD include the use of topical medication, including corticosteroids, plant-induced ACD, and dermatitis occurring after use of cosmetics and personal hygiene products.” (C)

Summary Statement 88 “Patch tests are most effective when the patients are selected on the basis of a clear-cut clinical suspicion of contact allergy and they are tested with the chemicals relevant to the problem; these conditions satisfy the prerequisites of high pretest probability.” (C)

Summary Statement 89 “Although the diagnostic accuracy of contactants cannot be compared with other in vivo or in vitro tests, diagnostic concordance between patch sensitivity and the outcomes of repeated open provocation tests has been demonstrated for some contactants.” (B)

Summary Statement 168 “Chemicals, plant resins and lipid constituents are the chief causes of ACD which requires patch testing for confirmation.” (A)

Summary Statement 172 “The skin prick/puncture test is superior to intracutaneous testing for predicting nasal allergic symptoms triggered by exposure to pollen.” (B)

Summary Statement 173 “A skin prick/puncture test is superior to intracutaneous testing for predicting allergic rhinitis and allergic asthma triggered by cat allergen exposure.” (B)

Summary Statement 174 “The skin prick/puncture can be used to rule out allergic rhinitis and allergic asthma triggered by cat allergen exposure.” (B)

Summary Statement 176 “In general S“In general Skin prick/puncture testing is more sensitive for identifying sensitization to inhalant allergens and confirming clinical allergy. However, specific IgE assays with defined quantifiable threshold levels can also predict positive respiratory responses after allergen exposure.” (B)

Summary Statement 187 “Graded oral food challenge is a useful means to diagnose and adverse reaction to food.” (B)

Summary Statement 190 “Diagnostic skins and/or specific IgE tests are used to confirm specificity of venom sensitization, they do not reliably predict severity of the sting reaction.” (B)

Summary Statement 201 “If Hymenoptera venom sensitivity is suspected, initial prick/puncture tests followed by serial endpoint titration with intracutaneous tests may be required.” (B)

Summary Statement 202 “Venon skin test may be repeated once or twice at 3- to 6-month intervals to confirm the diagnosis in patient who initially had negative tests results.” (D)

Summary Statement 204 “Evaluation of drug-specific IgE antibodies induced by many high-molecular-weight and several low-molecular-weight agents is often highly useful for confirming the diagnosis and prediction of future IgE mediated reactions such as anaphylaxis and urticaria. (B)

Summary Statement 209 “Atopy patch tests, lymphocyte proliferation tests, and basophil activation tests are additional diagnostic tests for drug allergy. Further studies are required to confirm their clinical utilization in the evaluation of drug and allergic patients.” (B)

Summary Statement 210 “Penicillin skin testing is the most reliable method for evaluating IgE mediated penicillin allergy provided that the necessary reagents are available. When performed with both major and minor determinants, the negative predictive value of penicillin skin testing for immediate reaction approaches 100%, whereas the positive predictive value is between 40% and 100%.” (B)

Summary Statement 217 “A presumptive diagnosis of aspirin exacerbated respiratory disease (AERD) can often be made by history; however, in some cases, aspirin provocation tests might be considered for a definitive diagnosis. (B)

Summary Statement 233 “Epicutaneously applied patch tests are the standardized diagnostic procedures to confirm ACD.” (A)

The American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI)

In 2022, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) jointly accepted responsibility for developing the drug allergy practice parameter update that included the following:

- “In the United States, diagnostic tests for drug allergies are based primarily on immediate skin testing.”
- Consensus-based Statement 6: “We suggest penicillin skin testing for patients with a history of anaphylaxis or a recent reaction suspected to be IgE mediated.” Strength of Recommendation: Conditional; Certainty of Evidence: Low

In 2020, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) updated their practice parameter regarding peanut allergy diagnosis and included the following recommendations:

- “Recommendation 1, A. We suggest in favor of diagnostic (SPT or sIgE) testing for peanut allergy (1) when patients have physician-judged high pretest probability of peanut allergy, or (2) prior to an OFC for patients with moderate pretest probability of peanut allergy. For both situations, shared decision making has been employed to arrive at the final decision. Conditional recommendation. Certainty of evidence: Very low.”
- “Recommendation 1, B. We suggest against diagnostic testing in patients where there is low or very low pretest probability of peanut allergy. Conditional recommendation. Certainty of evidence: Very low.”
- “Recommendation 2, A. We suggest in favor of Ara h 2 diagnostic testing in a patient presenting for evaluation of suspected peanut allergy for which a single diagnostic test is to be used, as Ara h 2 would provide the best diagnostic accuracy as determined by virtue of more optimal positive/negative likelihood ratios. However, while Ara h 2 has the greatest specificity, it has lower sensitivity than SPT and sIgE, and in a patient with a high prior probability, the clinician may use Ara h 2, SPT, or sIgE to confirm the diagnosis of peanut allergy. Conditional recommendation. Certainty of evidence: Low.”

- “Recommendation 2, B. We suggest against routine use of component testing in addition to either SPT or sIgE to whole peanut to increase diagnostic accuracy. Conditional recommendation. Certainty of evidence: Very low.”
- “Recommendation 3. We suggest against the clinician using the results of a SPT, sIgE to whole peanut extract, or sIgE to peanut components to determine the severity of an allergy phenotype or to predict the severity of a future reaction. Conditional recommendation. Certainty of evidence: Very low.”

In 2016, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) updated their practice parameter regarding insect sting hypersensitivity that included the following recommendations:

- “Perform skin tests and/or serum tests for IgE to stinging insect venoms on patients who are candidates for VIT. (Strong Recommendation; A evidence).”
- “If initial test results are negative in a patient with a clear history of systemic sting reaction, further testing (in vitro testing, repeat skin testing, or both) should be performed, as well as basal serum tryptase measurement. (Strong Recommendation; C evidence).”
- “Use skin tests as the preferred test for initial demonstration of venom specific IgE. In vitro measurement of serum IgE should be used as a complementary or alternative test. Test for all 5 venoms, with the possible exception of individual patients in whom a single culprit is definitively known. (Recommendation; C evidence)”

In 2014, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) updated their practice parameter regarding food allergy which stated the following summary statements:

- “Summary Statement 9: Manage non-IgE-mediated reactions to foods with appropriate avoidance and pharmacotherapy as indicated with the understanding that the specific role of immunity (eg, IgA, IgM, IgG, and IgG subclasses) in these forms of food allergy has not been demonstrated. [Strength of recommendation: Strong; B Evidence].”
- “Summary Statement 23: The clinician should use specific IgE tests (skin prick tests, serum tests, or both) to foods as diagnostic tools; however, testing should be focused on foods suspected of provoking the reaction, and test results alone should not be considered diagnostic of food allergy. [Strength of recommendation: Strong; B Evidence].”
- “Summary Statement 24: Component-resolved diagnostic testing to food allergens can be considered, as in the case of peanut sensitivity, but it is not routinely recommended even with peanut sensitivity because the clinical utility of component testing has not been fully elucidated. [Strength of recommendation: Weak; C Evidence].”
- “Summary Statement 30: The clinician should consider the diagnosis of oral allergy syndrome (pollen-food allergy) and obtain specific IgE testing to pollens in patients who experience limited oropharyngeal symptoms after ingestion of food antigens that cross-react with pollen antigens. [Strength of recommendation: Strong; B Evidence].”

- “Summary Statement 33: Do not perform intracutaneous testing for the diagnosis of food allergy. [Strength of recommendation: Strong; B Evidence].”
 - “One possible exception to the use of intradermal testing in IgE mediated food allergy includes the use of intradermal testing in delayed anaphylaxis associated with hypersensitivity to the carbohydrate moiety alpha-gal found in mammalian red meats. This syndrome is characterized by delayed onset of anaphylactic symptoms, and SPTs do not reliably identify the culprit food or foods.”
- “Summary Statement 34: Unproven tests, including allergen specific IgG measurement, cytotoxicity assays, applied kinesiology, provocation neutralization, and hair analysis, should not be used for the evaluation of food allergy. [Strength of recommendation: Strong; C Evidence].”
- “Summary Statement 38: Measurement of food-specific IgG and IgG4 antibodies in serum are not recommended for the diagnosis of non-IgE-mediated food-related allergic disorders. [Strength of recommendation: Strong; B Evidence].”

In 2014, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) updated their practice parameter in the diagnosis and management of rhinosinusitis which included the following recommendation:

- “Perform an evaluation for specific IgE antibodies to airborne allergens in patients with recurrent acute rhinosinusitis (RARS) or chronic rhinosinusitis (CRS).”

In 2020, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) updated their practice parameter regarding rhinitis and included the following recommendations:

- “We recommend that aeroallergen skin prick tests or sIgE testing be completed to confirm the diagnosis of AR in a patient with a history consistent with acute rhinitis (AR).” Strength of recommendation: Strong; Certainty of evidence: High

American Academy of Allergy, Asthma & Immunology (AAAAI), American College of Allergy, Asthma & Immunology (ACAAI), and the Joint Council of Allergy, Asthma and Immunology (JCAAI)

In 2015, the American Academy of Allergy, Asthma and Immunology (AAAAI), the American College of Allergy, Asthma and Immunology (ACAAI), and the Joint Council of Allergy, Asthma, and Immunology updated practice parameters regarding contact dermatitis that included the following recommendations:

- “Summary Statement 2: In patients suspected of ACD, patch testing is the gold standard to confirm the diagnosis. [Strength of Recommendation: Strong; C Evidence].”
- “Summary Statement 9: In patients presenting with dermatitis that involves the scalp and neck, consider patch testing for common causative sensitizers in cosmetics, hair products, and jewelry. [Strength of Recommendation: Moderate; C Evidence].”
- “Summary Statement 10: Consider irritant and ACD in all patients presenting with acute or chronic hand eczema. All such patients suspected of CD should undergo patch testing. [Strength of Recommendation: Moderate; C Evidence].”
- “Summary Statement 16: Avoid or reduce doses of immunosuppressant medications such as systemic CS and other systemic immunosuppressants before patch testing. Avoid application of

TCS, TCI, or ultraviolet radiation to the PT site, because these may reduce allergic PT responses. [Strength of Recommendation: Moderate; C Evidence].”

- “Statement 24: Consult physicians with expertise in patch testing to household cleaning or industrial products if testing to the actual product suspected of containing the relevant allergen(s) is necessary, because false-positive and severe irritant reactions can occur. [Strength of Recommendation: Moderate; C Evidence].”
- “Summary Statement 25: : Consult physicians with expertise in UV radiation and photo-patch testing to confirm a suspected diagnosis of photo-allergic CD. [Strength of Recommendation: Strong; C Evidence].”
- “Summary Statement 34: If an eruption worsens, rather than improves, after the topical application of certain medications, or fails to respond to TCS, patch testing should be performed to the suspected product and/or ingredients known to be contact sensitizers. [Strength of Recommendation: Moderate; C Evidence].”
- “Summary Statement 36: Consider preoperative patch testing for metal sensitization in patients with a significant history of metal allergy. [Strength of Recommendation: Moderate; C Evidence].”
- “Summary Statement 37: In patients with joint replacement failure, patch testing to components of the implant may be helpful after infection and biomechanical causes have been excluded. [Strength of Recommendation: Moderate; C Evidence].”
- “Summary Statement 38: ACD and ICD are significant clinical problems in children. Patch testing should be performed and remains the gold standard for the diagnosis of ACD in children. [Strength of Recommendation: Strong; C Evidence].”

American College of Gastroenterology

A 2021 guideline on the management of irritable bowel syndrome from the American College of Gastroenterology notes that: "Multiple tests are marketed to diagnose food intolerances; however, none have been validated, and most have not been subjected to rigorous, blinded trials." The guideline goes on to state that: "Results of a leukocyte activation test are intriguing but need to be confirmed."

Canadian Society of Allergy and Clinical Immunology

In 2024 the Canadian Society of Allergy and Clinical Immunology issued a position statement addressing the critical concerns and the recommended practices surrounding the use of panel food testing for diagnosing food allergies. This position statement included the following:

- “Panel food tests have not been adequately validated as screening tests and carry a considerable false positive that result in unnecessary dietary restrictions, increased healthcare costs, and significant psychosocial distress for patients and their families.”
- “Oral food challenges remain the gold standard for diagnosing food allergy.”

Summary and Recommendations

- Due to the potential for significant long-term harm, panel food testing for food that have not been eaten should be actively discouraged.
- Testing should not be performed for foods that are being consumed on a regular basis without immediate symptoms consistent with IgE mediated allergy.
- If such testing is performed despite the strong recommendations against doing so, there must be clear communication to the patient about the reason for testing, along with a plan to proceed with more definitive testing (i.e. oral food challenge) should the testing be positive.
- Increase access to and support for oral food challenges.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

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CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	82784	Gammaglobulin (immunoglobulin); IgA, IgD, IgG, IgM, each
	82787	Gammaglobulin (immunoglobulin); immunoglobulin subclasses (e.g., IgG1, 2, 3 or 4), each
	83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method (when utilized for ALCAT)
	86001	Allergen specific IgG quantitative or semiquantitative, each allergen
	86003	Allergen specific IgE; quantitative or semiquantitative, each allergen (may be utilized RAST, MAST, FAST, PRIST, RIST, ELISA or ImmunoCAP) (May also be utilized for Alpha-gal allergy [meat allergy testing] and Ara h 2 testing)
	86005	Allergen specific IgE; qualitative, multiallergen screen (e.g., disk, sponge, card) (RAST, MAST, FAST, PRIST, RIST, ELISA or ImmunoCAP)
	86008	Allergen specific IgE, quantitative or semiquantitative, recombinant or purified component (RAST, MAST, FAST, PRIST, RIST, ELISA, or ImmunoCAP) (May also be utilized for Alpha-gal allergy [meat allergy testing] and Ara h 2 testing)
	86343	Leukocyte histamine release test (LHR)
	86849	Unlisted immunology procedure
	95004	Percutaneous tests (scratch, puncture, prick) with allergenic extracts, immediate type reaction, including test interpretation and report, specify number of tests (Epicutaneous [scratch, prick or puncture])
	95017	Allergy testing, any combination of percutaneous (scratch, puncture, prick) and intracutaneous (intradermal), sequential or incremental, with venoms. Immediate type reaction, including test interpretation and report, specify number of tests (Epicutaneous [scratch, prick or puncture])

	95018	Allergy testing, any combination of percutaneous (scratch, prick or puncture) and intracutaneous (intradermal), sequential or incremental, with drugs or biologicals, immediate type reaction, including test interpretation and report, specify number of tests (Epicutaneous [scratch, prick or puncture])
	95024	Intracutaneous (intradermal) tests with allergenic extracts, immediate type reaction, including test interpretation and report, specify number of tests
	95027	Intracutaneous (intradermal) tests, sequential and incremental, with allergenic extracts for airborne allergens, immediate type reaction, including test interpretation and report, specify number of tests (Skin Endpoint Titration [SET])
	95028	Intracutaneous (intradermal) tests with allergenic extracts, delayed type reaction, including reading, specify number of tests
	95044	Patch or application test(s) (specify number of tests)
	95052	Photo patch test(s) (specify number of tests)
	95056	Photo tests
	95060	Ophthalmic mucous membrane tests
	95065	Direct nasal mucous membrane test
	95199	Unlisted allergy/clinical immunologic service or procedure
	0165U	Peanut allergy-specific quantitative assessment of multiple epitopes using enzyme-linked immunosorbent assay (ELISA), blood, individual epitope results and probability of peanut allergy (VeriMAP Peanut DX)
	0178U	Peanut allergen-specific quantitative assessment of multiple epitopes using enzyme-linked immunosorbent assay (ELISA), blood, report of minimum eliciting exposure for a clinical reaction (VeriMAP Peanut DX)
HCPCS		
	None	
Type of Service	Laboratory	
Place of Service	Outpatient/Physician's Office	

POLICY HISTORY

Date	Action	Action
February 2026	Annual Review	Policy Revised
February 2025	Annual Review	Policy Renewed
February 2024	Annual Review	Policy Revised
February 2023	Annual Review	Policy Revised
November 2021	Interim Review	Policy Revised
February 2022	Annual Review	Policy Revised
February 2021	Annual Review	Policy Revised
February 2020	Annual Review	Policy Revised
February 2019	Annual Review	Policy Revised
February 2018	Annual Review	Policy Revised
February 2017	Annual Review	Policy Revised
April 2016	Annual Review	Policy Revised
May 2015	Annual Review	Policy Revised
June 2014	Annual Review	Policy Revised
August 2013	Annual Review	Policy Revised
September 2012	Annual Review	Policy Revised
September 2011	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

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