Medical Policy Manual Laboratory, Policy No. 01

Allergy and Sensitivity Tests of Uncertain Efficacy

Effective: October 1, 2024

Next Review: June 2025
Last Review: August 2024

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Allergy and sensitivity tests of uncertain efficacy are not standard practice in the clinical setting.

MEDICAL POLICY CRITERIA

The following allergy and sensitivity tests are considered **investigational** as the scientific evidence does not permit conclusions regarding their effects on health outcomes:

A. Antigen leukocyte cellular antibody (ALCAT) automated food test
B. Applied kinesiology allergy test
C. Conjunctival challenge test (ophthalmic mucous membrane test)
D. Cytotoxic food tests
E. Electrodermal testing (also known as electro-acupuncture)
F. Hair analysis
G. IgA food panel tests
H. IgG/IgG4 allergen specific antibody test and food tests

I. Iridology

J. Lifestyle Eating and Performing-Mediator Release Test (LEAP-MRT)

K. Leukocyte histamine release test (LHRT)

L. Nasal challenge test

M. Passive transfer or P-X (Prausnitz-Küstner) test (now considered obsolete-and replaced by Radioallergosorbent tests)

N. Provocation-neutralization food or food additive allergy test

O. Rebuck skin window test (no longer in use)

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Sublingual Immunotherapy as a Technique of Allergen Specific Therapy, Medicine, Policy No. 121

BACKGROUND

Allergy refers to an acquired potential for developing adverse reactions that are mediated by the immune system (via immunoglobulin E [IgE] antibodies). Allergic disease represents the clinical manifestations of these adverse immune responses. An allergen is any substance that can cause an allergic reaction. Allergens are often common, usually harmless substances such as pollens, mold spores, animal danders, dust, foods, insect venoms, latex, and drugs.

The optimum management of the allergic patient should include a careful history and physical examination and may include confirming the cause of the allergic reaction by information from allergy tests. The following allergy tests are considered clinically useful for allergy confirmation by the American Academy of Allergy, Asthma, and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) in the diagnosis and management of the allergic patient.[1]

- Bronchial challenge test
- Double-blind food challenge test
- Intradermal skin testing
- Patch test
- Percutaneous skin tests such as the scratch, prick, or puncture tests
- Photo patch test
- Specific IgE in vitro tests such as Radioallergosorbent Test (RAST), Multiple Radioallergosorbent Tests (MAST), Fluorescent Allergosorbent Test (FAST), Enzyme-linked Immunosorbent Assay (ELISA), and the ImmunoCAP IgE test
- Total serum IgE concentration

Once an allergy-causing agent is identified, treatment is provided by avoidance, medication, or immunotherapy.

ALLERGY TESTS OF UNCERTAIN EFFICACY

This policy addresses only allergy tests of uncertain efficacy and those used primarily in research settings. Tests which may be considered useful in the clinical setting, as noted above, are not addressed in this policy.

Antigen Leukocyte Cellular Antibody (ALCAT) Automated Food Test

The ALCAT automated food test measures whole blood leukocytes by a proprietary process that identifies allergens which cause an increase in leukocyte activity. An electronic counter measures the change in number and size of white blood cells which have been incubated with purified food or mold extracts. A histogram is produced based on cell count and cell size. Individually processed test samples are compared with a "Master Control" graph. Scores are generated by relating these effective volumetric changes in white blood cells to the control curve.

Applied Kinesiology (or Muscle Strength Test)

Muscle strength in the extremities is measured before and after a person is exposed to an allergen. Strength in the opposing arm is measured as a person holds a container of allergen extract in the opposite hand or ingests an allergen. A decrease in strength is used to indicate the presence of disease and various nutritional supplements may be recommended.

Cytotoxic Food Tests

This test involves the response of collected white blood cells to the presence of food extracts to which the patient may be allergic. A technician observes the unstained cells for changes in shape and appearance of the leukocytes. Swelling, vacuolation, crenation, or other cytotoxic changes in cell morphology are taken as evidence of allergy to the food.

Electrodermal Testing (Also Known as Electro-acupuncture)

Electrodermal testing measures changes in skin resistance while a person is exposed to an allergen, either food or inhalant. This allergy-testing device uses a galvanometer to measure the electrical resistance of the skin. A drop in the resistance of the skin is believed to indicate the presence of allergy.

Hair Analysis

Hair is analyzed for the presence (or lack) of various minerals and toxins. Findings are correlated to nutritional deficiencies or disease. Recommendations for diet and supplements are provided based on the analysis.

IgA Food Panel Tests

Immunoglobulin A (IgA) is secreted by mucous membranes. Testing for a specific type of IgA, called tissue transglutaminase antibodies, can be useful in diagnosing celiac disease. Measurement of IgA antibodies have been used in research settings as diagnostic tests for various food allergies and prognostic tests to determine response to allergy treatments for other food types.

IgG/IgG4 Antibody Tests and Food Specific IgG/IgG4 Tests

There are four subclasses of immunoglobulin G (IgG). Selective deficiencies in one or more of the four IgG subclasses are seen in some patients with repeated infections. Measurements of

IgG and specifically IgG4 antibodies have been used in research settings as diagnostic and prognostic tests to determine response to allergy treatments.

Iridology

According to the AAAAI, iridology attempts to relate the anatomical features in the iris to various systemic diseases.

LEAP-MRT®

This procedure involves two test components. The first component, Lifestyle Eating and Performing (LEAP®), tests patients for multiple food and additive/chemical allergies. The patient is tested and then given a tailored eating plan. In the second component, the Mediator Release Test (MRT®) measures non-IgE mediated immune pathways using a blood test.

Provocative-neutralization Tests for Food (or Food Additive Allergy Test)

This procedure is performed by injecting (intradermal or subcutaneous), or placing under the tongue (sublingual), dilute extracts of the suspected food or inhalant allergen and observing the patient's response or reaction. A symptomatic response indicates an allergy to that food or inhalant, and the reaction can be neutralized by application of a similar extract of a lesser dilution.

ALLERGY TESTS IN THE RESEARCH SETTING

The following tests are primarily used in the research setting:

Conjunctival Challenge Test

With conjunctival testing, an allergenic extract is placed into the conjunctival sac of the eye followed by observation for redness, itchiness, tearing of the eye, and other similar symptoms. According to the AAAAI, these tests are often used in research protocols that require an objective standard for evaluating clinical sensitivity to an allergen.

Leukocyte Histamine Release Test (LHRT)

In this testing, leukocytes from the serum of an allergic individual are observed for histamine release in the presence of an antigen. The commercial availability of simplified and automated methods of laboratory analysis have renewed interest in the clinical applications of LHRT in the evaluation of food, inhalant, and drug allergies. The AAAAI guidelines for this test indicate it is primarily used in a research setting.

Nasal Challenge Test

This test provides precise measurements of changes in nasal airway resistance along with observations such as number of sneezes and measurement of inflammatory mediators in the nasal secretions after exposure to an allergen. The more commonly known "sniff test," uses a visual assessment of mucosal swelling and rhinorrhea after a small amount of dry pollen is inhaled.

EVIDENCE SUMMARY

This policy is based on appraisal of the current scientific evidence published in peer-reviewed

journals and AAAAI clinical practice guidelines for allergy diagnostic testing. The focus of this review is on randomized controlled trials (RCTs) that demonstrate how the tests in question impact treatment decisions and health outcomes in patients with allergies.

ALLERGY TESTS OF UNCERTAIN EFFICACY

The following tests have either not been evaluated in randomized, controlled trials (RCTs) examining the clinical utility of the test and/or have been evaluated in RCTs of low quality that report inconclusive or contradictory findings:[1-8]

- Antigen leukocyte cellular antibody (ALCAT) test
- Applied kinesiology
- Cytotoxic tests
- Electrodermal testing
- Hair analysis
- IgA food panel tests
- IgG and IgG4 allergen specific antibody or food test
- Iridology
- LEAP-MRT
- Provocation- neutralization

ALLERGY TESTS IN THE RESEARCH SETTING

Leukocyte Histamine Release Test (LHRT)

Overall, the evidence is not sufficient to permit conclusions on the diagnostic accuracy of LHRT. Studies are potentially prone to spectrum bias, referral bias, and ascertainment bias. Alternative tests were not performed in a blinded manner, or studies did not indicate whether there were blinded interpretations of the tests.[9, 10] Some studies included patients with known allergies, and thus these highly selected populations did not represent the same population with equivocal allergy histories that would undergo testing.[10-14] In some situations, results were compared with bronchial provocation testing, considered the gold standard for inhalant allergies. However, bronchial provocation may only be performed on a subset of patients with a limited number of allergens. For example, bronchial provocation may only be performed when there are discordant results between RAST and skin prick testing.[15] While it has been suggested that LHRT may be a valuable test in those patients with discordant results of skin prick testing and RAST testing, studies focusing on this subgroup of patients were not identified in a literature search.

Conjunctival and Nasal Challenge Tests

These tests are often the tools of research protocols and are used to determine clinical sensitivity to an allergen.[1] While it has been suggested that conjunctival and nasal challenge tests may be valuable to confirm diagnosis when skin tests are negative, the studies focusing on this subgroup of patients are small, nonrandomized trials which do not permit conclusions on the clinical utility of conjunctival or nasal challenge tests.[16-24]

PRACTICE GUIDELINE SUMMARY

AMERICAN ACADEMY OF ALLERGY, ASTHMA, AND IMMUNOLOGY (AAAAI)

In a summary titled, “What Primary Care Givers Need to Know About the New Guidelines for the Diagnosis and Management of Food Allergy in the US,” the following expert opinion-based recommendations are outlined for the diagnosis of food allergies:[25]

> Food allergy should be suspected when typical symptoms (e.g., urticaria, edema, wheezing, mouth itch, cough, nausea/vomiting, anaphylaxis) occur within minutes to hours of ingesting a food. The medical history/exam are recommended to aid in diagnosis. A detailed history of the reaction to each incriminated food is essential for proper diagnosis.
>
> Tests for food-specific IgE are recommended to assist in diagnosis but should not be relied upon as a sole means to diagnose food allergy. The medical history/exam are recommended to aid in diagnosis. A medically monitored feeding (food challenge) is considered the most specific test for food allergy.
>
> Food-specific IgE testing has numerous limitations, because positive tests are not intrinsically diagnostic and reactions sometimes occur with negative tests. Testing “food panels” without considering history is often misleading and not recommended
>
> Several tests are not recommended, including food-IgG/IgG4, total IgE, applied kinesiology, and electrodermal testing.

AMERICAN ACADEMY OF ALLERGY, ASTHMA, AND IMMUNOLOGY (AAAAI) AND AMERICAN COLLEGE OF ALLERGY, ASTHMA AND IMMUNOLOGY (ACAAI)

The AAAAI and ACAAI guidelines, “Allergy Diagnostic Testing: An Updated Practice Parameter,” (2008) outline the following recommendations:[1]

> “With regard to evaluations for IgE antibody-associated food allergies, tests for food specific IgE antibody include percutaneous skin tests (prick/puncture tests) and serum assays. In general, these tests are highly sensitive (generally 85%) but only modestly specific (approximately 40% to 80%) and therefore are well suited for use when suspicion of a particular food or foods is high. They are not effective for indiscriminate screening (eg, using panels of tests without consideration of likely causes) and therefore generally should not be used for that purpose. (B)
>
> Intracutaneous skin tests for foods are potentially dangerous, are overly sensitive, increase the chance of a false-positive test result, and are not recommended. (D)
>
> A trial elimination diet may be helpful to determine if a disorder with frequent or chronic symptoms is responsive to dietary manipulation. (D)
>
> Graded oral food challenge is a useful means to diagnose an adverse reaction to food. (B)
>
> A number of additional diagnostic tests are under investigation, including APTs and tests for IgE binding to specific epitopes. (B)”

Level B evidence is based on evidence from at least one controlled study without randomization or at other type of quasi-experimental study. Level D evidence is based on expert committee reports, the opinion or clinical experiences of respected authorities, or both.

AMERICAN THORACIC SOCIETY (ATS), JAPANESE RESPIRATORY SOCIETY (JRS), AND ASOCIACIÓN LATINOAMERICANA DE TÓRAX (ALAT)

The ATS, JRS, and ALAT Clinical Practice Guideline for the Diagnosis of Hypersensitivity Pneumonitis in Adults (2020) states the following regarding serum IgG testing for potential antigens associated with HP:[26]

> For patients with clinical and radiographic manifestations suggestive of non-fibrotic or fibrotic HP, the guideline "suggests performing serum IgG testing that targets potential antigens associated with HP (suggestion, very low confidence in the estimated effects)."

This ATS/JRS/ALAT clinical practice guideline was informed by a systematic review of evidence, which included a comparison of serum IgG testing to questionnaires for the identification of HP-associated antigens.[27] The clinical practice guideline discussion concluded:

> "The evidence synthesis estimated that serum IgG testing against HP-associated antigens distinguishes HP from other interstitial lung diseases with a sensitivity and specificity of 83% and 68%, respectively. Included studies were limited by incorporation bias, absence of appropriate controls, and inadequate validation of questionnaires. The committee was unanimous in the opinion that both test characteristics are suboptimal. Most committee members considered testing convenient and adequate for generating supportive data; however, they acknowledged that testing is insufficient for confirming or excluding a diagnosis of HP because the test characteristics are inferior to most screening tests currently in use."

SUMMARY

There is not enough research to show that some tests used to diagnose and manage allergies are effective. Further, there are no evidence-based clinical practice guidelines that recommend these allergy tests. Therefore, the following allergy tests are considered investigational:

- Antigen leukocyte cellular antibody (ALCAT) test
- Applied kinesiology
- Cytotoxic tests
- Electrodermal testing
- Hair analysis
- IgA food panel tests
- IgG and IgG4 allergen specific antibody or food test
- Iridology
- LEAP-MR
- Passive transfer or P-X test
- Provocation- neutralization
- Rebuck skin window test
- Leukocyte Histamine Release Test (LHRT)
- Conjunctival Challenge Tests
- Nasal Challenge Tests

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CODES

NOTE: It is not appropriate to report CPT 95060 for the Schirmer test for dry eye, as this test is included as a part of a general ophthalmologic exam and is not separately reimbursable.

Codes	Number	Description
CPT	83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method
	86001	Allergen specific IgG quantitative or semiquantitative; each allergen
	86003	Allergen specific IgE; quantitative or semiquantitative, crude allergen extract, each
	86005	Allergen specific IgE; qualitative, multiallergen screen (eg, disk, sponge, card)
	86008	Allergen specific IgE; quantitative or semiquantitative, recombinant or purified component, each
	86343	Leukocyte Histamine Release Test (LHR)

Codes	Number	Description
	86486	Skin test; unlisted antigen, each
	95060	Ophthalmic mucous membrane tests
	95065	Direct nasal mucous membrane test
	95199	Unlisted allergy/clinical immunologic service or procedure
HCPCS	None	

Date of Origin: *January 1996*