Allergen Testing AHS – G2031

Description of Procedure or Service

Allergic disease is characterized by inappropriate or exaggerated immune reactions to foreign antigens (allergens) that are generally innocuous to most people, but when introduced into a genetically-predisposed individual, elicit a hypersensitivity reaction (R. Hamilton, 2017).

Hypersensitivity reactions can be classified into four types, two of which are associated with allergy, type I immediate immunoglobulin (IgE) reactions and type IV T cell mediated reactions (Chang & Guarderas, 2018).

Type I reactions involve the formation of IgE antibodies specific to the allergen. When the subject is re-exposed to that allergen, the allergen binds multiple IgE molecules, resulting in the release of an array of inflammatory mediators, including histamines, that precipitate the symptoms of allergic disease (R. Hamilton, 2017).

Allergen testing in serum is designed to detect the presence of allergen-specific IgE. A positive test for allergen-specific IgE confirms the presence of the antibody only. Actual reactivity must be determined by history or supervised challenge (Kowal & DuBuske, 2017).

Several diagnostic procedures have been developed to elicit and assess hypersensitivity reactions including epicutaneous, intradermal, patch, bronchial, exercise, and ingestion challenge tests (Bernstein et al., 2008).

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for allergen testing when it is determined the medical criteria or reimbursement guidelines below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Allergen Testing is covered

1. Reimbursement is allowed for specific IgE in-vitro allergy testing:
a. In lieu of skin testing for an INITIAL allergy screen. When in-vitro testing is ordered, the medical record must clearly document the indication and why it is being used instead of skin testing.

b. When skin testing is either contraindicated (see Policy Guidelines below for details), or when direct skin testing results are not consistent with the history of an anaphylactic or other severe reaction to an allergen and further treatment decisions would be impacted by confirmation of sensitivity, in the evaluation of:
   i. individuals with asthma or
   ii. individuals with suspected allergen-induced chronic rhinitis, or
   iii. individuals with suspected food allergy, or
   iv. individuals with suspected insect venom allergy, or
   v. individuals with suspected allergy to specific drugs

2. Reimbursement is allowed for specific in-vitro IgE testing when:
   a. Allergens chosen for testing are based on the individual’s history, physical examination, and environment, and
   b. It is limited to 20 allergen specific antibodies per year.

3. Reimbursement is allowed for in-vitro testing for total serum IgE for:
   a. Individuals with moderate to severe asthma being considered for Xolair therapy, or
   b. Individuals suspected of allergic bronchopulmonary aspergillosis

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**When Allergen Testing is not covered**

1. Reimbursement is not allowed for routine re-testing for allergies to the same allergens in the absence of a new clinical presentation.

2. Reimbursement is not allowed for in-vitro testing of allergen specific IgG or non-specific IgG, IgA, IgM, and/or IgD in the evaluation of suspected allergy.

3. Reimbursement is not allowed for basophil activation flow cytometry testing (BAT) for measuring hypersensitivity to allergens.

4. Reimbursement is not allowed for The Antigen Leukocyte Antibody test (ALCAT)

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**Policy Guidelines**

**Background**

Allergies affect over 50 million Americans, as many as 30 percent of adults and 40 percent of children (Jackson, Howie., Akinbami, & CDC, 2013; National Academies of Sciences, Health and Medicine, Food and Nutrition, & Committee on Food Allergies: Global Burden, 2016). The incidence of allergic disease is increasing (Pawankar, Holgate, Canonica, Lockey, & Blaiss, 2013), and are estimated to result in over $17 billion in health care costs and 200,000 emergency department visits annually (Adams, Kirzinger, & Martinez, 2013).

Allergic diseases, respiratory infections, and autoimmune conditions have similar clinical presentations and self-reported symptoms have a relative low PPV (Sampson et al., 2014). Thus, laboratory allergy and immunologic testing are useful in clarifying diagnosis and guiding treatment when the frequency, duration, and sequelae of upper respiratory infections exceed the norm or when rhinosinusitis or asthma symptoms persist despite treatment (Chow et al., 2012). Allergy testing is also useful in identifying causative allergen in atopic dermatitis (eczema), contact dermatitis, urticaria, angioedema, and food or drug allergies. Knowing the causal allergen helps provide clinically relevant information for avoidance and treatment (Chang & Guarderas, 2018).
A majority of environmental, food, and medication allergies with clinical significance are type I immunoglobulin E (IgE)-mediated allergies (Kowal & DuBuske, 2017). Diagnosis of an IgE-mediated allergy involves identification of the allergen, demonstration of IgE specific to that allergen, and confirmation that symptoms occur when the patient is exposed to the allergen. The IgE response to an allergen can be assessed using skin or serum testing. Patch testing is preferred for delayed T-cell mediated response (Chang & Guarderas, 2018; Zug et al., 2014).

**Skin Testing**

Skin testing is the most rapid, sensitive, and cost-effective testing modality for the detection of immunoglobulin E (IgE)-mediated disease. The procedure lasts less than an hour with minimal patient discomfort. There are several published practice parameters for allergen skin testing (Bernstein et al., 2008; Chang & Guarderas, 2018; Kowal & DuBuske, 2017).

**Serum IgE**

Immunoassays measuring both total IgE and allergen-specific IgE in serum and other bodily fluids have been developed. Specific IgE immunoassays do not require patient cooperation, are not limited in patients with skin disease, are not blocked by antihistamines, and pose no risk of adverse reactions (Bernstein et al., 2008; Chang & Guarderas, 2018; Stokes & Casale, 2017).

**Other tests**

Patch testing is the gold standard for identification of a contact allergen (Mowad, 2006; Rietschel, 1997). Although occlusive patch testing is the most common technique, open, prophetic (provocative), repeated insult, photopatch, and atopy patch tests are also available if special situations indicate their use (Bernstein et al., 2008).

Cellular activation assays measuring the release of histamine from basophils (Kim et al., 2016; Santos & Lack, 2016) or mast cells (Bahri et al., 2018) as diagnostic or prognostic indicators of allergy have been the subject of intense research. Basophil and eosinophilic reactivity tests have been shown to be associated with food-induced allergic responses and have been shown in current research to be modified over time during immunotherapy (Sampson et al., 2014). The basophil activation test (BAT) in particular has emerged as having superior specificity and comparable sensitivity to diagnose food allergy, when compared with skin prick test and specific IgE (Santos & Shreffler, 2017). Histamine release from leukocytes of allergic persons is an excellent in vitro correlate of allergy, however is currently still considered a research test (Bernstein et al., 2008).

**Analytical Validity**

Variables that can influence the wheal size when performing SPT include multiple operators, extract concentrations and quality, skin test devices, time of day, location on the skin, and the measuring of results (Nelson, 2001; Werther et al., 2012).

In 2006, Oppenheimer and Nelson evaluated variability and analytical validity of skin testing finding that “Overall, a significant degree of variability was reported with regard to number of skin tests performed, extract concentrations, skin test devices, interpretation and documentation of results, and quality assurance procedures. The average number of skin prick tests performed ranged from 5.09 (grasses) to 10.9 (trees), whereas the average number of intradermal tests performed ranged from 2.03 (grasses) to 5.6 (perennial). The allergen extract concentrations used for intradermal testing varied widely. Expressed as a dilution of the concentrated extracts, 20.8% use 1:100 dilutions, 10.3% use 1:500 dilutions, and 59.4% use 1:1,000 dilutions. Significant variability also occurred regarding devices and the technique with which the devices were used. Most clinicians (92.1%) used the most concentrated extract available for skin prick testing. For reporting the results of skin testing, 53.8% used a 0 to 4+ scale, and only 28.3% measured orthogonal diameters. Of those using a 0 to 4+ scale, two thirds related the results to the size of the histamine control. Quality assurance testing was reportedly performed by 61.2% of responders. However, less than 10% of responders used an objective test protocol for this purpose.” (Oppenheimer & Nelson, 2006)
In 2012 Werther et al assessed variability in skin prick test results performed by multiple operators as “SPTs have previously been compared when performed multiple times by a single operator(Carr, Martin, Howard, Cox, & Borish, 2005). Quintip and Greer Pick were shown to have 95 and 98% sensitivity, respectively, with 100% specificity for both the devices. The previous studies show which device is most accurate if skin testing is performed by the same clinician on each occasion but has limited relevance in situations where testing is carried out by multiple operators. In many clinical and research settings, skin testing is performed by more than 1 operator” and found that “The devices using the "puncture" method (Staller genes Lancet, Quintip) provide less variability in results than those using a "prick" method when carried out by multiple users (Greer Pick and Feather Lancet). Testing on the back also gives less variable results compared with the arm.”(Werther et al., 2012)

CLSI has evaluated the analytical validity of serum IgE measurements and found that "Clinical/diagnostic sensitivity and specificity of IgE antibody assays cannot be accurately determined due to the absence of definitive gold standard methods for defining allergic disease. Total and allergen-specific IgE analyses achieve among the highest analytical performance of any antibody assay by following consensus procedures in CLSI-ILA20-A3” (R. G. Hamilton et al., 2016).

Knight et al “examined the qualitative concordance between SPT and sIgE as measured on the HYTETCM288 platform for 10 commonly encountered inhalant allergens in 232 subjects, and analysed the performance characteristics for the HYTETCM288. Overall concordance between SPT and sIgE was >70% for all allergens tested. Sensitivity ranged from 25% to 95%, depending on the allergen, while specificity was significantly higher for all allergens (78-97%). NPV was >85% for all allergens tested, while PPV was more variable, ranging from 22% to 88%. These results are similar to findings in other studies comparing SPT with sIgE. Lack of concordance in a percentage of samples might be partly attributed to differences in allergen preparations for SPT and HYTETCM 288.”

Clinical Validity and Utility

In 1998 Tschopp et all found that “To diagnose current allergic asthma (CAA) and current allergic rhinitis (CAR), the sensitivity of Phadiatop was significantly higher than that of SPT (72.5% vs 65.4%, 77.1% vs 68.4% respectively; P < 0.01 and < 0.001) and IgE (72.5% vs 56.9%, 77.1% vs 43.9%, respectively; both P < 0.001). The sensitivity of SPT was significantly higher (68.4% vs 43.9% P < 0.001) than that of IgE to diagnose CAR. When CAA and CAR were excluded, the SPT specificity was significantly higher than that of Phadiatop (77.8% vs 71.9% and 85.9% vs 80.5%, respectively; both P < 0.001): when CAR was excluded, SPT was significantly higher than IgE (85.9 vs 81.4%; P < 0.001). SPT had significantly the best positive predictive value for CAA (5.2% for SPT vs 4.6% for both IgE and Phadiatop; both P < 0.001) and CAR (48.7% for SPT vs 43.5% for Phadiatop and 31.6% for IgE; both P < 0.001). The three markers of atopy had roughly the same negative predictive value (NPV) for CAA, but IgE had a significantly lower NPV for CAR than SPT and Phadiatop (88.1% vs 93.3% and 94.7%, respectively; both P < 0.001). The diagnostic efficiency of SPT was significantly higher than that of Phadiatop (83.1% vs 79.9% and 77.6 vs 71.9%, respectively; both P < 0.001) to diagnose CAR and CAA. IgE and SPT had equal efficiency (77.6%), which was significantly higher than that of Phadiatop, to diagnose CAA (71.9%; both P < 0.001). In conclusion, SPT have the best positive predictive value and the best efficiency to diagnose respiratory atopic diseases. Furthermore, SPT give information on sensitivity to individual allergens and should therefore be used primarily by clinicians to assess respiratory allergic diseases” (Tschopp et al., 1998)

Usmani et al (2007) investigated the value of investigation of both immediate and delayed type hypersensitivity in latex contact uticaria. In Three hundred and thirty out of 1060 patients referred to the clinic were prick tested. 54.2% patients were referred from dermatologists. 26.6% were referred from occupational health, 68 patients had positive reactions on prick testing of whom 36 had positive patch tests (52.9%), which were of current relevance in 27 patients (39.7%). Nine out of 106 health workers referred to exclude latex contacturticaria had positive prick tests to latex. Fifty of these patients demonstrated delayed-type hypersensitivity with nickel, cobalt, rubber and its additives being the most common allergens found. Of the 262
patients who had negative prick tests, 121 had positive patch tests (46.1%) of current relevance to patient history in 92 subjects (35.1%). While none of the six patients referred for investigation of reaction to local anaesthetics had a positive prick test, one was allergic to local anaesthetic on patch testing. They concluded that omission of patch testing from the investigation of allergic skin disease, even when contact urticaria may be the sole suspected diagnosis, would result in the frequent missed diagnosis of contact allergy.

In 2014, a meta-analysis (Soares-Weiser et al., 2014) examined the clinical validity of SPT and IgE for food allergy and found that “For cows' milk allergy, the pooled sensitivities were 53% (95% CI 33-72), 88% (95% CI 76-94), and 87% (95% CI 75-94), and specificities were 88% (95% CI 76-95), 68% (95% CI 56-77), and 48% (95% CI 36-59) for APT, SPT, and sIgE, respectively. For egg, pooled sensitivities were 92% (95% CI 80-97) and 93% (95% CI 82-98), and specificities were 58% (95% CI 49-67) and 49% (40-58%) for skin prick tests and specific-IgE. For wheat, pooled sensitivities were 73% (95% CI 56-85) and 83% (95% CI 69-92), and specificities were 73% (95% CI 48-89) and 43% (95% CI 20-69%) for SPT and sIgE. For soy, pooled sensitivities were 55% (95% CI 33-75) and 83% (95% CI 64-93), and specificities were 68% (95% CI 52-80) and 38% (95% CI 24-54) for SPT and sIgE. For peanut, pooled sensitivities were 95% (95% CI 88-98) and 96% (95% CI 92-98), and specificities were 61% (95% CI 47-74), and 59% (95% CI 45-72) for SPT and sIgE.”

Klemans et al (2015) examined the diagnostic accuracy of using sIgE to peanut components to improve sensitivity and specificity of peanut allergen testing and found that “sIgE to Ara h 2 showed the best diagnostic accuracy of all diagnostic tests to diagnose peanut allergy. Compared to the currently used SPT and sIgE to peanut extract, sIgE to Ara h 2 was superior in diagnosing peanut allergy and should therefore replace these tests in daily clinical practice, especially in children.”(Klemans et al., 2015)

Sozmen et al (2015) examined the diagnostic accuracy of using the patch test to avoid oral food challenge. They found that in two hundred and forty-three children that underwent OFC to suspected food, clinically relevant food allergies in 40 (65%) children to egg and in 22 (35%) to cow's milk. The sensitivity of skin prick test for both milk and egg was 92%, specificity 91%, positive predictive value 35%, and negative predictive value of 93%. Sensitivity, specificity, positive predictive value, and negative predictive value of atopy patch test for both milk and egg were 21%, 73%, 20%, and 74%, respectively.

Santos et al (Santos et al., 2015) also studied the utility of the BAT to predict the severity and reactivity to peanut during oral food challenges. They found that of the 124 children submitted to OFCs to peanut, 52 (median age, 5 years) reacted with clinical symptoms that ranged from mild oral symptoms to anaphylaxis. Severe reactions occurred in 41% of cases, and 57% reacted to 0.1 g or less of peanut protein. The ratio of the percentage of CD63(+) basophils after stimulation with peanut and after stimulation with anti-IgE (CD63 peanut/anti-IgE) was independently associated with severity (P = .001), whereas the basophil allergen threshold sensitivity CD-sens (1/EC₅₀ × 100, where EC₅₀ is half maximal effective concentration) value was independently associated with the threshold (P = .020) of allergic reactions to peanut during OFCs. Patients with CD63 peanut/anti-IgE levels of 1.3 or greater had an increased risk of severe reactions (relative risk, 3.4; 95% CI, 1.8-6.2). Patients with a CD-sens value of 84 or greater had an increased risk of reacting to 0.1 g or less of peanut protein (relative risk, 1.9; 95% CI, 1.3-2.8). Basophil reactivity is associated with severity and basophil sensitivity is associated with the...
threshold of allergic reactions to peanut. CD63 peanut/anti-IgE and CD-sens values can be used to estimate the severity and threshold of allergic reactions during OFCs.

BAT has the potential of being a useful tool for measuring hypersensitivity to allergens, especially for patients who are not suitable for skin testing due to skin status or prior severe reactions, since it is an ex vivo, flow cytometry-based assay. BAT, for use as standard clinical practice, is currently limited by its lack of standardization in methodology as well as between systems used. A study by Depince-Berger and colleagues has proposed standardization between systems and instruments using whole blood-EDTA samples with instrumentation standardization. “BAT would strongly benefit from easy implementation [EDTA, one step stimulation/labeling, wash, full sample analysis over time parameter, B cell relative basophil count] and standardization of instrument settings on MFI targets whatever system or instrument is used (Depince-Berger, Sidi-Yahya, Jeraiby, & Lambert, 2017).” No international standardization of BAT has been implemented to date.

Although the ALCAT machine is FDA registered and there are a few papers published, results are not reproducible when subject to rigorous testing and do not correlate with clinical evidence of allergy (Beyer & Teuber, 2005; Hammond & Lieberman, 2018; Wuthrich, 2005).

**Applicable Federal Regulations**

The FDA has cleared 40 assays for total IgE, and 58 assays for allergen specific IgE.

Other assays are considered a laboratory developed test (LDT); developed, validated and performed by individual laboratories.

LDTs are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA’88).

As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

**Guidelines and Recommendations**

**Practice Guidelines and Position Statements**

The American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) published practice parameters in 2008 for allergy testing (Bernstein et al., 2008) which noted that “For individual patients, the choice of test allergens is guided by the history and physical examination and the physician’s knowledge, training, and experience.” The guidelines recommended that “Specific IgE immunoassays may be preferable to skin testing under special clinical conditions, such as widespread skin disease, patients receiving skin test suppressive therapy, uncooperative patients, or when the history suggests an unusually greater risk of anaphylaxis from skin testing.” They also note that for both skin testing and in-vitro specific IgE testing, “the allergens selected … should be determined based on the patient’s age, history, environment and living conditions (eg, region of the country), occupation, and activities.” Also, “The best indicators in the selection of appropriate pollens for clinical use are extensive prevalence in the air and concurrent allergy symptoms during annually recurrent seasons when such pollens are expected to be present in the ambient air.”

They AAAAI and ACAAI guidelines also state, “As is the case with skin tests, a direct correlation cannot be assumed between the presence of specific IgE (sIgE) antibodies and clinical disease.” Additionally, “sensitivity and the positive predictive value of both prick/puncture and specific IgE tests generally tend to be higher among pollens, stable anaphylactogenic foods, house dust mite, certain epidermals, and fungi compared with venoms, drugs, and chemicals.”
With regards to total IgE testing, these groups indicate, “Measurements of total serum IgE concentration are of modest clinical value when used as a screen for allergic disease or for predicting the risk of allergic disease.”

The AAAAI and ACAAI also note that “IgG and IgG subclass antibody tests for food allergy do not have clinical relevance, are not validated, lack sufficient quality control, and should not be performed.”

In regard to basophil activation assays they state “Histamine and leukotriene release measurements from human basophils after incubation with allergen are valuable research tools for in vitro investigations of allergy.”

Their practice parameter on drug allergy (2010) also states that “The basophil activation test is a recently described method of evaluating expression of CD63 on basophils after stimulation with an allergen. There are limited data using this method to evaluate patients.”

They also recommend, “Because anaphylactic reactions cannot be distinguished from anaphylactoid, nonimmune occurrences, it has been recommended that plasma histamine, tryptase, and specific IgEs (if available) may be ordered at the time of reaction and skin tests be performed later.”

In their 2014 practice parameter on food allergy (Sampson et al., 2014) they acknowledge: “Basophil and eosinophilic reactivity tests have been shown to be associated with food-induced allergic responses and have been shown in current research to be modified over time during immunotherapy.”

Their 2014 practice parameter on rhinosinusitis also recommends to “Perform an evaluation for specific IgE antibodies to airborne allergens in patients with RARS or CRS.”

In their 2015 practice parameter on anaphylaxis (Lieberman et al., 2015), they recommend “Skin tests and/or in vitro tests for specific IgE and challenge tests might be appropriate to help define the cause of the anaphylaxis.”

They also recommend against routinely obtaining total serum IgE levels for the diagnosis of food allergy, however because of the low PPV of self-reported symptoms and lack of pathognomonic signs on physical examination, they recommend that the accurate diagnosis of IgE-mediated food allergy should be aided by laboratory allergy testing, including skin prick and/or serum IgE testing. 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.

National Institute of Allergy and Infectious Diseases (NIAID) convened an expert panel to review current information and to make recommendations related to the evaluation of food allergy (FA), including the use of specific IgE (sIgE) testing (Boyce et al., 2010). With regards to allergen-specific serum IgE determination, NIAID recommended that “sIgE tests for identifying foods that potentially provoke IgE-mediated food-induced allergic reactions, but alone these tests are not diagnostic of FA.” It stated that “sIgE testing and skin prick testing both depend on the presence of allergen-specific antibodies. Because the former test measures sIgE in the serum and the latter reflects IgE bound to cutaneous mast cells, their results may not always correlate. Serum testing can be especially useful when SPTs cannot be done (for example, due to extensive dermatitis or dermatographism), or when antihistamines cannot be discontinued.” The NIAID also recommended not using the combination of skin prick test (SPT), sIgE tests and atopy patch test (ATP) for the routine diagnosis of food allergy.

Additionally, the NIAID notes that “the routine use of measuring total serum IgE should not be used to make a diagnosis of FA.”
“Non-standardized tests” such as basophil histamine release/activation, lymphocyte stimulation, allergen-specific IgG, cytotoxicity assays, and mediator release assays should not be used in the routine evaluation of FA, according to the NIAID guidelines.

**American Academy of Pediatrics (AAP)**

In 2012, AAP released a clinical report on allergy testing in childhood. It stated that “Both serum sIgE tests and SPT are sensitive and have similar diagnostic properties.” AAP summary included the following:

- “Treatment decisions for infants and children with allergy should be made on the basis of history and, when appropriate, identified through directed serum sIgE or SPT testing. Newer in vitro sIgE tests have supplanted radioallergosorbent tests.”
- “Positive sIgE test results indicate sensitization but are not equivalent to clinical allergy. Large panels of indiscriminately performed screening tests may, therefore, provide misleading information.”
- “Increasingly higher levels of sIgE (higher concentrations on serum tests or SPT wheal size) generally correlate with an increased risk of clinical allergy.”
- “Use of a multiallergen serum test can be helpful for screening for atopic disease if there is a clinical suspicion. If positive, allergen-specific testing may be considered.
- “Tests for allergen-specific IgG antibodies are not helpful for diagnosing allergies.”

**Xolair (FDA, 2007)**

The availability of Xolair for treatment of allergic asthma also has implications for allergy testing. According to the package insert, “Xolair is indicated for adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. Determine doses (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg).” The prescribing information also notes that “Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during Xolair treatment cannot be used as a guide for dose determination.”

**Medicare Regulations and Coding Guidelines (CMS, 2017)**

- Evaluation and management codes reported with allergy testing or allergy immunotherapy are appropriate only if a significant, separately identifiable service is administered.
- Allergy testing is not performed on the same day as allergy immunotherapy in standard medical practice. These codes should, therefore, not be reported together. Additionally, the testing becomes an integral part to rapid desensitization kits (CPT code 95180) and would therefore not be reported separately.

**International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis**

The authors reviewed the existing evidence behind various aspects of evaluation and diagnosis of the AR patient, and developed the following recommendations (Wise et al., 2018).

History taking is essential in the diagnosis of AR. Physical examination is recommended in the diagnosis of AR, and when combined with patient history, it increases diagnostic accuracy and excludes alternative causes. Making a presumptive diagnosis of AR on history (ideally combined with physical examination) is reasonable and would not delay treatment initiation. Confirmation with diagnostic testing is required for progression to AIT, or desirable with inadequate response to initial treatment.
SPT is recommended for evaluation of allergen sensitivities in appropriately selected patients. Regular use of the same SPT device will allow clinicians to familiarize themselves with it and interpretation of results may therefore be more consistent. The use of standardized allergen extracts can further improve consistency of interpretation. Patients can benefit from identification of their specific sensitivities. SPT is a quick and relatively comfortable way to test several antigens with accuracy similar to other available methods of testing.

Total IgE assessment is an option to assess atopic status. However, the evidence does not support a routine use.

Serum sIgE testing may be used in the evaluation of AR. Using standardized allergens and rigorous proficiency testing on the part of laboratories may improve accuracy. Patients can benefit from identification of their specific sensitivities. Further, in some patients who cannot undergo skin testing, sIgE testing is a safe and effective alternative.

The average pooled sensitivity of SPT is 85% which is often slightly higher than that of serum sIgE testing; however, this is not universally true depending on the allergen tested and the characteristics of the patient. Based on accuracy, convenience, cost, and promptness of results, SPT is often chosen as the first line diagnostic instrument to detect sensitivity to aeroallergens. Intradermal testing can be used as a second line test to exclude reactivity if the clinical suspicion is very high. In cases where dermatographism is present and/or patients are unable to wean off medications that affect skin testing, sIgE testing may be a better choice.

BAT is an option for AR diagnosis when first-line tests are inconclusive or for measuring response to AIT. Basophil sensitivity may be a useful marker for following response to immunotherapy.

The National Academies of Science, Engineering and Medicine

The National Academies of Science, Engineering and Medicine convened an expert committee to review the science and management practices of food allergy. Overall, they found that:

Currently, no simple diagnostic tests exist for food allergy.

Food allergy evaluation procedures include a medical history and physical examination, and also may include food-specific skin prick test, food-specific serum immunoglobulin E test, diagnostic food elimination diet, and oral food challenge (OFC). Selection of the specific tests needs to be individualized based on the medical history of each patient.

The BAT shows promising preliminary data, the potential utility is recognized and will require additional validation and standardization. “Guidelines suggest not using the BAT clinically on the grounds that it is nonstandardized, but recognize its use as a research tool (National Academies of Sciences et al., 2016).”

American Academy of Family Physicians

AAFP’s recommendations for practice state: Allergy and immunologic testing can help clarify the diagnosis and guide treatment. Immediate immunoglobulin E (IgE) and delayed T cell–mediated reactions are the main types of allergic responses. The allergens suspected in an immediate IgE-mediated response are identified through serum IgE-specific antibody or skin testing. For patients with an inhalant allergy, skin or IgE-specific antibody testing is preferred. In patients with food allergies, eliminating the suspected allergenic food from the diet is the initial treatment. If this is ineffective, IgE-specific antibody or skin testing can exclude allergens. An oral food challenge should be performed to confirm the diagnosis. Patients with an anaphylactic reaction to an insect sting should undergo IgE-specific antibody or skin testing. Skin testing for penicillin has a high negative predictive value and can help when penicillin administration is indicated and there are limited alternatives. Testing for other drug allergies has less well-determined sensitivity and specificity, but can guide the diagnosis. Patch testing can help identify the allergen responsible for contact dermatitis.
Policy Guidelines

Skin testing is contraindicated in the following situations:

- Patients who have certain skin conditions (for e.g. dermatographism, urticaria, cutaneous mastocytosis, atopic dermatitis, severe diffuse psoriasis)
- Patients who are taking medications that may interfere with the treatment of anaphylaxis (for e.g. Beta-blockers and Angiotensin Converting Enzyme inhibitors) or may impair skin test sensitivity (for e.g. tricyclic antidepressants, antihistamines)
- Patients who are at high risk to testing (for e.g., poorly controlled asthma, clinical history of severe reaction to minute amounts of allergen, cardiac arrhythmia, unstable angina)
- Patients who have experienced an anaphylactic event within the past one month
- Uncooperative patients (e.g., small children, individuals with mental or physical impairments)

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 82784, 82785, 82787, 83316, 83520, 86001, 86003, 86005, 86008, 88184

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources


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Specialty Matched Consultant Advisory Panel review 11/2019

Medical Director review 11/2019

**Policy Implementation/Update Information**

1/1/2019  BCBSNC will provide coverage for allergen testing when it is determined to be medically necessary because the medical criteria and guidelines are met. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (jd)

10/1/19  Policy statement revised to read:  BCBSNC will provide coverage for allergen testing when it is determined the medical criteria or reimbursement guidelines below are met. Wording revised in the Covered Section to change “medically necessary” to “reimbursement is allowed.” Wording revised in the Not Covered section. “Not Medically Necessary” and “investigational” changed to read “Reimbursement is not allowed…” Deleted coding grid. Notification 10/1/2019 for effective date 12/2/2019. (an)

12/10/19  Reviewed by Avalon 3rd Quarter 2019 CAB. Removed “Additional testing beyond this number will require individual review for coverage criteria” from the When Covered section. Added “or non-specific IgG, IgA, IgM, and/or IgD” to the When Not Covered section. The following codes: 88346, 86352, 86021, and 86434 along with the code table were removed from the Billing/Coding section. Specialty Matched Consultant Advisory Panel review 11/2019. Medical Director review 11/2019. (jd)

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