



# Testing for Allergy

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# Clinical Perspective

An allergy is a bodily reaction to a variety of otherwise harmless substances, resulting in the production of specific IgE antibodies. Allergic reactions can range from mild to severe. Anaphylaxis is the most severe form of an allergic reaction—one that may even result in death. Allergic reactions can manifest themselves as allergic asthma, allergic rhinitis, allergic conjunctivitis, atopic eczema/atopic dermatitis, or anaphylaxis, and these manifestations may vary between adults and children.

Allergies are common, with incidence rising over the past several years. The WHO estimates that 20% of the global population suffers from IgE-mediated allergic diseases, placing heavy financial strains on clinician and hospital resources, particularly in emergent situations.<sup>1</sup>

In the United States alone, allergy ranks as the sixth-leading cause of chronic illness. Each year, approximately 50 million Americans report experiencing some form of allergy, and 30,000 of them seek help at an emergency room.<sup>2,3</sup>

19% of patients in the U.S. have self-diagnosed as having food allergies, despite only 10.8% of those who undergo testing having confirmatory results. This point proves that it is crucial for adults with suspected food allergies to receive appropriate confirmatory testing and counseling to ensure food is not unnecessarily avoided and quality of life is not overly impaired.<sup>4</sup>



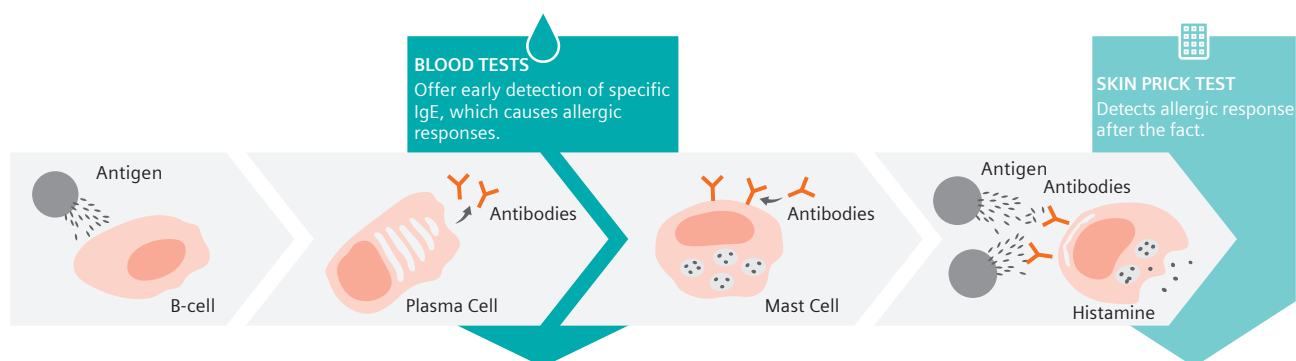
## Diagnostic workup for allergy diagnosis

Allergy testing can be performed by in vivo or in vitro methods. There are benefits and limitations to both methods, and it is recommended that the testing be performed in conjunction with a clinical history and physical examination. The clinical scenario should determine the appropriate test for each patient.<sup>5</sup> In vivo testing involves a skin prick test (SPT), which is often the first-line approach to determine the release of allergen-specific IgE antibodies. However, in vitro testing with highly purified allergens or recombinants can be used as an alternative or complementary diagnostic tool.<sup>6</sup>

Progression to an allergic reaction can be illustrated in four distinct phases, as shown below. In phase 1, an allergen enters the body and is recognized by a B-cell as a foreign substance. Phase 2 involves plasma cells producing IgE antibodies in response to the allergen

detected in phase 1. In phase 3, specific IgE antibodies attach to mast cells, which then proceed to release histamines, leukotrienes, and prostaglandins, seen in phase 4. The release of these inflammatory modulators results in a localized or systemic reaction called the allergic reaction, which can be measured by in vivo testing, such as SPT, or by in vitro blood testing.

The in vitro method measures specific IgE antibodies in the patient's serum that are produced by the plasma cells in phase 2 of the cycle. Therefore, serum testing may detect one's likelihood to react to an allergen(s) and potentially predict the severity of the reaction without the need to induce an allergic reaction—a key differentiator between these two methods.



The quality of allergen material used in testing remains paramount for both in vitro and in vivo testing methods,<sup>7</sup> and the accuracy and reliability of allergy tests are critical to diagnosis and treatment planning. Siemens Healthineers offers diagnostic tools and IMMULITE® 2000/2000 XPi 3gAllergy™ reagents in whose quality clinicians can be confident.

Unlike traditional skin prick testing (SPT), the measurement of quantitative IgE antibody levels in serum may be capable of “accurately identifying the specificity of the allergic response for targeting immunotherapy, predicting allergic symptom severity after allergen exposure, and attempting to distinguish tolerance from a food allergy.”<sup>8</sup>

### Situations in which in vitro specific IgE testing may be indicated over SPT include:<sup>6,18</sup>

- Negative SPT test with a high clinical suspicion
- Patients with eczema
- Patients taking tricyclic antidepressants
- Very young or older patients who may have a reduced histamine response
- Patients with an increased risk of anaphylaxis
- Pregnant women



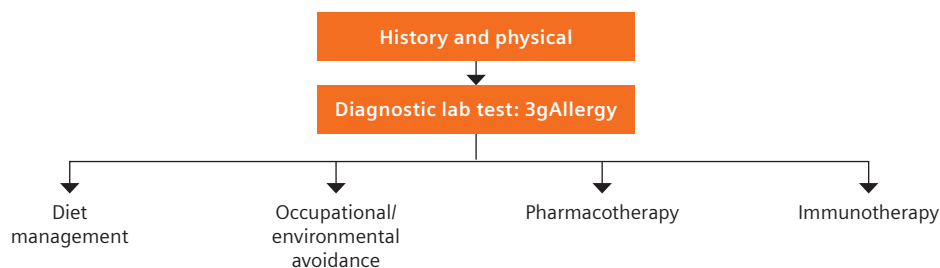
## Allergy in primary care

Patients first report the onset of a new allergic reaction while seeking help in a primary care setting. A well-informed clinician with access to the appropriate diagnostic resources can reduce the time to referral and/or differential diagnosis. In cases requiring an allergist referral, conducting serum IgE testing with IMMULITE 2000/2000 XPi 3gAllergy (alongside intradermal testing) during the primary care visit may assist the allergist in determining the correct allergen dilutions to start with when pursuing injection immunotherapy.<sup>9</sup>

### In vitro allergy blood testing supports improved patient outcomes

- Easy to perform, with one simple blood draw to obtain multiple determinants
- Reduced risk of anaphylaxis
- No skin reactions
- No need to stop patient's medications, as there is no interference with medications such as antihistamine H1 blockers, H2 antagonists, or tricyclic antidepressants<sup>10</sup>
- Good correlation with patient clinical history and skin tests<sup>5</sup>
- Readily available to primary care physicians
- Convenient method for monitoring decreases in sensitization resulting from a medical intervention such as allergen avoidance
- Valuable diagnostic tool for following development and prognosis of sensitization in childhood
- Convenient for patients suffering from eczema, atopic dermatitis, and other skin conditions
- Practical for geriatric and pediatric patients affected by dermatographism
- Convenient method for pediatric and geriatric patients

## Allergic disease-management paradigm



### Allergy treatments



**Avoidance.** This entails the conscious removal of allergens from the diet and/or environment and a hygiene and skin-care regimen. This is the mainstay treatment for food or chemical allergies, for which there is no known cure.<sup>11</sup>



**Pharmacotherapy.** This includes second-generation antihistamines, known as no-sedative antihistamines (NSA). The primary advantage of most of these second-generation allergy drugs is that they do not cross the blood-brain barrier and, unlike those of the first generation, do not cause sedation and drowsiness. Both first- and second-generation antihistamines have been shown to be effective in controlling typical allergy symptoms, such as rhinorrhea, congestion, itch, skin rashes, hives, and watery eyes.<sup>11</sup>



**Immunotherapy.** This is an effective treatment option for insect venoms and many kinds of aeroallergens. While results vary with the individual, immunotherapy is the only treatment that has been effectively used to cure certain types of allergic diseases.<sup>12</sup> Historically, only allergists/allergologists performed immunotherapy. In recent years, however, a few pharmaceutical companies have begun offering an innovative prescription service, which has enabled general practitioners to offer immunotherapy to their allergy patients.<sup>13</sup>

### Allergy in children

Accurate and timely diagnosis of pediatric and childhood allergies presents unique challenges to clinicians. Clinical presentation may be nonspecific, with symptoms ranging from coughing, sneezing, stomachaches, cramps, and nausea.<sup>14</sup> Pairing traditional methods of allergy testing with 3gAllergy sIgE serum testing may provide validation or challenge one's differential diagnosis in complex, nonspecific cases.

The impact of early and precise allergy identification, monitoring, and treatment reaches more than the millions of children diagnosed with food and skin allergies each year alone—it is a matter of quality of life and achieving developmental milestones.<sup>16,17</sup> Reducing the severity of allergy symptoms and preventing the progression to chronic disease has been proven to reduce the number of school days missed, essential to childhood development.<sup>10</sup>

### Common types of food allergies in children

90% of food allergies in children are caused by the following foods: cow's milk, egg (white), peanuts, wheat, soybean, and tree nuts (almond, cashew, etc.).<sup>10</sup>

### Common aeroallergens that cause allergies in children

Cat dander-epithelium, dog dander, cockroach, *Dermatophadoides pteronyssinus* and *Dermatophagoides farina* (house dust mites), *Aspergillus fumigatus*, and *Alternaria alternata*.<sup>15</sup>





## Allergy Testing and Diagnosis Made Simple, Fast, and Affordable

In vitro allergy testing is designed to provide value to clinicians and their patients, making testing and diagnosing simple, fast, and affordable, regardless of case complexity.

A zero-calibrator combined with chemiluminescent instrumentation and liquid-allergen technology allows for an analytical sensitivity of 0.1 kU/L and a functional sensitivity of 0.2 kU/L.

There are two key components that comprise IIMMULITE 2000/2000 XPi 3gAllergy Specific IgE.

### The assay provides the following clinical benefits:

- Aids in the detection of sensitized patients, which allows for monitoring and therapeutic intervention
- Supports clinical decision making when monitoring patients with low IgE levels with analytical sensitivity of 0.1 kU/L and functional sensitivity of 0.2 kU/L
- Assists in differential diagnosis of allergic diseases:
  - Sinusitis
  - Rhinitis
  - Conjunctivitis

### 1 Specific allergens and panels

When a patient with an allergy is tested, a reactive result may indicate a response to a specific allergen or a mix of allergens. Specific allergens and mixes require the Universal Kit.

### 2 Universal Kit

All specific allergens and mixes run with the Universal Kit to provide a result from the patient sample. One master curve applies to all specific allergy tests and mixes.

## 3gAllergy sIgE method performance

### Clinical utility of the IMMULITE 3gAllergy sIgE assay

The 3gAllergy sIgE method provides a quantitative measurement of specific IgE for the purpose of:

- Identifying offending allergens
- Supporting precise and timely therapeutic intervention
- Improving patient diagnosis and management

Diagnostic accuracy of different allergen components was measured using the IMMULITE 2000/2000 XPi 3gAllergy sIgE assay in serum samples of 195 allergic patients and 20 negative controls.<sup>21</sup> Skin prick test (SPT) was used for selection of allergic patients. Table 1 illustrates sensitivity, specificity, and agreement relative to SPT for results obtained by the IMMULITE 2000/2000 XPi 3gAllergy sIgE assays for each of the 11 allergens studied. SPT was used for clinical comparison.

**Table 1.** Diagnostic accuracy of IMMULITE 2000/2000 XPi allergen components compared to skin prick test (SPT) results. For the IMMULITE 3gAllergy sIgE assay, the usual 0.35 kU/L cutoff was used.<sup>21</sup>

IMMULITE 2000/2000 XPi 3gAllergy Assay			
Sensitizer	Allergen	Sensitivity	Specificity
Olive	Ole e 1	35/35 (100%)	0/20 (100%)
Birch	Bet v 1	35/35 (100%)	0/20 (100%)
HDM	Der p 1	27/35 (77.1%)	0/20 (100%)
	Der p 2	33/35 (94.3%)	0/20 (100%)
	Der f 1	25/35 (71.4%)	0/20 (100%)
	Der f 2	33/35 (94.3%)	0/20 (100%)
Shrimp	Pen m 1/Pen a 1	15/20 (75.0%)	0/20 (100%)
Peach	Pru p 3 (nsLTP)	34/35 (97.1%)	0/20 (100%)
	Pru av 3 (nsLTP)	34/35 (97.1%)	0/20 (100%)
	Pru av 1 (PR-10)	0/35 (0%)	0/20 (100%)
	Pru av 4 (profilin)	0/35 (0%)	0/20 (100%)

Results from case studies are not predictive of results in other cases. Results in other cases may vary.

### Clinical benefits of the IMMULITE 2000/2000 XPi 3gAllergy sIgE assay

The use of liquid allergens on polymer solid phase, unique to 3gAllergy, allows higher testing accuracy compared to the cellulose solid-phase method. This methodology provides a broader working range, ability to report results quantitatively and categorized, use of liquid allergens, and automation features that reduce labor requirements, total assay time, and possibility of error.<sup>11</sup>





## Clinical advantages of detecting IgE levels at concentrations lower than 0.35 kU/L

Studies indicate that earlier detection of allergies in children allows for prompt intervention, which may stop the progression of allergies to more-morbid conditions such as pulmonary obstructive disease.<sup>18</sup>

Detection of IgE levels below 0.35 kU/L is also useful in monitoring a patient's allergic threshold. Allergic sensitization is based on a cumulative process. When the allergen load accumulates beyond the patient's threshold, clinical allergic symptoms appear. It is therefore important to monitor accumulations of low-level allergens to prevent allergic symptoms. Timely identification of allergens and subsequent avoidance therapy are important for maintaining a patient's allergic threshold.<sup>20,21</sup>

## Conclusion

Allergy prevalence, morbidity, and mortality continue to rise globally, and while traditional in vivo testing remains common, in vitro testing has been proven to empower clinicians and elevate the standard of care. Despite the challenging nature of allergy diagnosis and management, 3gAllergy testing remains a simple and intuitive approach to allergy diagnosis.

IMMULITE 3gAllergy offers a broad range of tests to address various clinical needs related to quantitative determination of allergen-specific IgE. The assay provides reliable results as an aid in the clinical diagnosis of IgE-mediated allergic disorders.

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