

Component testing for food allergy

INTRODUCTION

The percentage of children in the United States with a reported food allergy has increased in the past 2 decades, to approximately 8% in 2018.¹ Allergies develop when a person has produced IgE antibody (ie, is sensitized) to specific food component proteins on initial exposure and is then re-exposed to the same food; a reaction can also occur when these IgE antibodies cross-react with similar component proteins in a different food. However, some children with a diagnosed allergy may be only sensitized to an antigen, without having a true allergy.

A true allergic reaction to a food is also called an IgE-mediated (ie, type I) hypersensitivity reaction. Symptoms occur within seconds of exposure to a food and can be severe; in rare cases, the reaction is fatal. It is important to realize that some individuals who are IgE-sensitized to a food will not

develop symptoms if the food is ingested again.² Therefore, patients with positive IgE test results for a specific food fall into 2 categories: (1) IgE-sensitized and allergic, and (2) IgE-sensitized but not allergic.

Whole-food IgE testing may not distinguish these 2 groups of patients. However, food component IgE testing detects IgE to different proteins within a food and can help better differentiate a patient with a true food allergy from an IgE-sensitized patient without a true allergy (**Table 1**).^{3,4}

DIAGNOSTIC TESTING

For patients with suspected food allergies (eg, peanut, tree nuts, milk, eggs), serum IgE tests or skin prick tests (SPTs) are recommended. Testing should focus on foods that are suspected of provoking a reaction or have been recently ingested and should be used in conjunction with the patient's clinical history (eg, recent ingestion, clinical reaction).⁵

Table 1. Whole Food and Components⁸⁻¹⁴

Whole food	Component proteins	Meaning of positive IgE reaction (component IgE profiles)
Peanut	Ara h 1, 2, 3, 6	High risk of systemic reaction including anaphylaxis (Ara h 2 nearly always associated with clinical allergy)
	Ara h 9	Variable risk of strong allergic reaction (often accompanied by sensitization to other peanut proteins)
	Ara h 8	Low risk of systemic reactions (associated with local reactions or no reaction at all)
Tree nuts		
Hazelnut	Cor a 9,14	High risk of systemic reactions including anaphylaxis
Cashew	Cashew Ana o 3	
Brazil nut	Brazil nut Ber e 1	
Walnut	Walnut Jug r 1	
	Hazelnut Cor a 8	Associated with mild local reactions, as well as systemic reactions
	Walnut Jug r 3	
	Hazelnut Cor a 1	
Milk	Casein (protein stable when heated)	High risk of reaction to all forms of cow's milk
	α-lactalbumin and β-lactoglobulin (proteins unstable when heated)	High risk of reaction to fresh cow's milk
		Low risk of reaction to baked foods containing milk
Egg	Ovomucoid (protein stable when heated)	High risk of reaction to all forms of egg
	Ovalbumin (protein unstable when heated)	High risk of reaction to fresh eggs
		Low risk of reaction to baked eggs

Serum IgE tests and SPTs are standard diagnostic tests, but these methods have limited positive and negative predictive values, which means that they do not reliably distinguish IgE sensitization from true allergy. This is reflected in a significant overlap in the distribution of food-specific IgE levels of patients with a true peanut allergy and those who are only sensitized.⁶ The oral food challenge (OFC), considered the gold standard in diagnostic testing for food allergies, can help diagnose food allergies if a clinical history or test results are insufficient to establish a diagnosis; however, OFC is expensive and puts the patient at risk for an anaphylactic reaction.⁷

Component testing, though not routinely recommended because its clinical utility has not been fully elucidated, can distinguish patients with a true food allergy from those who are only IgE-sensitized, without the risk of anaphylactic shock from an OFC.^{4,5} This approach measures IgE levels to individual food component proteins, synthesized by genetic engineering. Depending on the specific component target(s) of IgE reactivity (**Table 1**), a patient may be at low, variable, or high risk of a true allergy to the food of concern.

Structural similarities of proteins within food families may enable IgE cross-reactivity. Component testing can help determine the likelihood that a patient who is allergic to one food will also react to other potentially cross-reactive foods.

COMPONENT TESTING EXAMPLES

Tree nuts and peanuts

Different nut component proteins may elicit systemic reactions, local reactions, or no reaction at all, depending on their resistance to heat and enzymatic digestion.^{15,16} In peanuts, for example, storage proteins (eg, Ara h 1, Ara h 2, Ara h 3, Ara h 6) are resistant to digestion and can trigger systemic reactions, whereas PR-10 (eg, Ara h 8) is heat- and digestion-labile. IgE reactivity to PR-10 alone usually results in no or local reactions (**Table 2**).^{17,18} Therefore, IgE reactivity to Ara h 1-3, 6 supports a diagnosis of a true peanut allergy and may require dietary restrictions and anaphylaxis precautions during meals, while sensitization to Ara h 8 alone would suggest a low risk for a true peanut allergy and continued peanut consumption would likely be appropriate.¹⁹

The structural similarities of proteins throughout the plant kingdom also affect their potential for IgE cross-reactivity (**Table 2**).²⁰ For example, walnuts, pecans, and hazelnuts form a group of strongly cross-reactive tree nuts²¹; thus, an individual with IgE to allergenic components in walnuts can also be allergic to pecans and hazelnuts. IgE cross-reactivity also explains why individuals can have IgE to certain foods, such as peanuts and tree nuts, but not exhibit true allergy: exposure to profilin or bromelain and its cross-reactive carbohydrate determinant (CCD) MUXF3—found throughout

Table 2. Component Protein Families in Tree Nuts and Peanuts

Protein family	Component protein	Source	Stability	Cross-reactivity to IgE
Storage protein	Ana o 3 Ara h 1, Ara h 2, Ara h 3, Ara h 6 Ber e 1 Cor a 9, Cor a 14 Jug r 1	Brazil nut, cashew, hazelnut, peanut, walnut	Stable to both heat and digestion; therefore, can give rise to systemic reactions	Relatively species-specific
Lipid transfer protein	Ara h 9 Cor a 8 Jug r 3 Pru p 3	Hazelnut, peanut	Stable to heat and digestion; therefore, can give rise to systemic reactions	Varies
PR-10 protein	Ara h 8 Bet v 1 Cor a 1 Mal d 1	Hazelnut, peanut	Heat and digestion labile. Primarily results in local clinical reactions	Varies
Profilin	Ara h 5 Bet v 2 Cor a 2 Gly m 3 Phl p 12	Brazil nut, cashew, hazelnut, peanut, walnut	Heat and digestion labile. Primarily results in no or local clinical reactions	Extensive

the plant kingdom—can cause sensitization, but these allergens are not associated with true allergy.²²

By identifying specific protein components that are common among certain nut or plant species, component testing may help guide dietary restrictions to include or exclude foods based on the potential for allergic reactions due to IgE cross-reactivity.

Milk and eggs

In their native conformations, milk and egg proteins may cause mild to severe allergic reactions in IgE-sensitized patients (**Table 1**).^{20,23} Patients with IgE reactivity to milk and egg proteins that are resistant to heat or digestion (eg, casein, ovomucoid) are most likely to have allergic reactions to these foods. However, many patients who are IgE-sensitized primarily to heat-labile milk and/or egg component proteins (eg, α -lactalbumin, β -lactoglobulin, ovalbumin) can tolerate eggs and/or milk in baked goods even though they react to these foods when uncooked or undiluted by other ingredients.²⁴

Test availability

Quest Diagnostics offers whole-food IgE testing with reflex to components if whole-food IgE testing is positive for certain foods (**Appendix**).

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Appendix. Food Allergy Panels and Tests^{a,b}

Test name	Test code
Brazil Nut (f18) IgE With Reflex to Component	94464
Cashew Nut (f202) IgE With Reflex to Component	94465
CCD (o214) IgE	39152
CCD and Profilin IgE Cross-Reactivity Panel	39151
Childhood Allergy (Food and Environmental) Profile With Reflexes Includes <i>Alternaria alternata</i> (m6, 2706), cat dander (e1, 2601), <i>Cladosporium herbarum</i> (m2, 2702), cockroach (i6, 2736), codfish (f3, 2803), cow's milk (f2, 37900) with reflex to milk components, <i>Dermatophagoides farinae</i> (d2, 2722), <i>Dermatophagoides pteronyssinus</i> (d1, 2721), dog dander (e5, 2605), egg white (f1, 37906) with reflex to egg components, mouse urine proteins (e72, 2658), peanut (f13, 91747) with reflex to peanut components, shrimp (f24, 2824), soybean (f14, 2814), walnut (f256, 3489), wheat (f4, 2804), and total IgE.	91683
Childhood and Tree Nut Allergy Panel With Reflex to Components Includes <i>Alternaria alternata</i> (m6, 2706), almond (f20, 2820), Brazil nut (f18, 94464) with reflex to Brazil nut components, cashew nut (f202, 94465), cat dander (e1, 2601), <i>Cladosporium herbarum</i> (m2, 2702), cockroach (i6, 2736), codfish (f3, 2803), cow's milk (f2, 37900) with reflex to milk components, <i>Dermatophagoides farinae</i> (d2, 2722), <i>Dermatophagoides pteronyssinus</i> (d1, 2721), dog dander (e5, 2605), egg white (f1, 37906) with reflex to egg components, hazelnut (f17, 94468) with reflex to hazelnut components, macadamia nut (rf345, 38475), mouse urine proteins (e72, 2658), peanut (f13, 91747) with reflex to peanut components, shrimp (f24, 2824), soybean (f14, 2814), walnut (f256, 94467) with reflex to walnut components, wheat (f4, 2804), and total IgE.	36766
Cow's Milk (f2) IgE With Reflex to Milk Component Panel	37900
Egg White (f1) IgE With Reflex to Egg Component Panel	37906
Food Allergy Profile With Reflexes Includes almond (f20, 2820), cashew nut (f202, 2608), codfish (F3, 2803), cow's milk (f2, 37900) with reflex to milk components, egg white (f1, 37906) with reflex to egg components, hazelnut (f17, 2817), peanut (f13, 91747) with reflex to peanut components, salmon (f41, 2841), scallop (f338, 273), sesame seed (f10, 2810), shrimp (f24, 2824), soybean (f14, 2814), tuna (f40, 2840), walnut (f256, 3489), and wheat (f4, 2804) IgE.	91682
Food and Tree Nut Allergy Panel With Reflex to Components Includes almond (f20, 2820), Brazil nut (f18, 94464) with reflex to Brazil nut components, cashew nut (f202, 94465) with reflex to cashew nut components, codfish (f3, 2803), cow's milk (f2, 37900) with reflex to milk components, egg white (f1, 37906) with reflex to egg components, hazelnut (f17, 94468) with reflex to hazelnut components, macadamia nut (rf345, 38475), peanut (f13, 91747) with reflex to peanut components, salmon (f41, 2841), scallop (f338, 273), sesame seed (f10, 2810), shrimp (f24, 2824), soybean (f14, 2814), tuna (f40, 2840), walnut (f256, 94467) with reflex to walnut components, and wheat (f4, 2804) IgE.	36763
Hazelnut (f17) IgE With Reflex to Component	94468
Peanut Component Panel	91681
Peanut, Total With Reflex to Peanut Component	91747
Profilin (t216) IgE	39153
Tree Nut Allergy Panel With Reflex to Components Includes almond (f20, 2820), Brazil nut (f18, 94464) with reflex to Brazil nut components, cashew nut (f202, 94465) with reflex to cashew nut components, hazelnut (f17, 94468) with reflex to hazelnut components, macadamia nut (rf345, 38475), peanut (f13, 91747) with reflex to peanut components, pecan (f201, 2864), pistachio (f203, 2726), and walnut (f256, 94467) IgE with reflex to walnut components.	94463
Walnut (f256) IgE With Reflex to Component	94467

^a Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).

^b Component panels or tests can be ordered separately.