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. 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 to similar component proteins in a different food. However, some children with a diagnosed allergy may only be 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 many individuals who are IgE-sensitized to a food will never develop symptoms when the food is ingested again. Therefore, patients with positive IgE test results for a specific food fall into 2 categories:
1) IgE-sensitized and allergic
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.

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 recently been ingested, and should be used in conjunction with the patient’s clinical history (eg, recent ingestion, clinical reaction). 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. 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.

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. 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. In peanuts, for example, storage proteins (eg, Ara h 1, Ara h 2, Ara h 3) 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). Therefore, IgE reactivity to Ara 1-3 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.

The structural similarities of proteins within each protein family also affect their potential for IgE cross-reactivity. For example, over a third (37%) of individuals who are allergic to...
walnuts are also allergic to Brazil nuts, cashews, and/or hazelnuts; thus, individuals who are allergic to one tree nut may have an allergic reaction upon first exposure to another tree nut (Table 2). Similarly, individuals who have been sensitized to lipid transfer proteins (LTPs) from previous exposures to fruits, grass, or tree pollens have an increased risk of systemic reactions to tree nuts due to IgE reactivity to tree nut LTPs (Table 2). By identifying specific protein components that are common among certain nut or plant species, component testing may help guide dietary restrictions to include foods that can trigger 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). Patients with IgE reactivity to milk and egg proteins that are resistant to heat or digestion (e.g., 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 (e.g., α-lactalbumin, β-lactoglobulin, ovalbumin) are able to tolerate the ingestion of egg and/or milk in baked goods even though they react to these foods when uncooked or undiluted by other ingredients.

**TEST AVAILABILITY**
Quest Diagnostics offers whole-food IgE testing with reflex to components if whole-food IgE testing is positive for certain foods. For testing options, consult the Quest Diagnostics online Test Directory (testdirectory.questdiagnostics.com). Components of panels and reflex tests may be ordered individually.
<table>
<thead>
<tr>
<th>Protein Family</th>
<th>Component Proteins</th>
<th>Source</th>
<th>Stability</th>
<th>Cross-reactivity to IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Storage Protein</td>
<td>Ana o 3, Ara h 1, 2, Ara h 3, Ber e 1, Cor a 9, Cor a 14, Jug r 1</td>
<td>Brazil nut, cashew, hazelnut, peanut, walnut</td>
<td>Stable to both heat and digestion; therefore, can give rise to systemic reactions</td>
<td>Relatively species-specific</td>
</tr>
<tr>
<td>Lipid Transfer Protein</td>
<td>Ara h 9, Cor a 8, Jug r 3, Pru p 3</td>
<td>Hazelnut, peanut</td>
<td>Stable to heat and digestion; therefore, can give rise to systemic reactions</td>
<td>Varies</td>
</tr>
<tr>
<td>PR-10 Protein</td>
<td>Ara h 8, Bet v 1, Cor a 1, Mal d 1</td>
<td>Hazelnut, peanut</td>
<td>Heat and digestion labile. Primarily results in local clinical reactions</td>
<td>Varies</td>
</tr>
<tr>
<td>Profilin</td>
<td>Ara h 5, Bet v 2, Cor a 2, Gly m 3, Phl p 12</td>
<td>Brazil nut, cashew, hazelnut, peanut, walnut</td>
<td>Heat and digestion labile. Primarily results in no or local clinical reactions</td>
<td>Extensive</td>
</tr>
</tbody>
</table>

References
