Molecular Peanut Component Diagnostics Differentiate Peanut Allergic from Peanut Sensitized Patients

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Peanut allergy is one of the most common food allergies, affecting approximately 1% of the US population [1], and the prevalence of peanut allergy is thought to be increasing [2]. In allergic individuals, anaphylaxis following exposure to peanuts can be fatal, requiring these individuals to carry epinephrine injectors at all times. Perhaps due to the serious nature of peanut allergies and its wide recognition, as many as 3 in 4 individuals are misdiagnosed as having peanut allergies [3], when in fact they have either asymptomatic to mild peanut sensitization or no sensitization at all. Recently peanut molecular component testing has been developed as an improved *in vitro* blood test to predict the likelihood of an allergic reaction. Molecular component testing represents a major step forward in differentiating peanut allergic individuals.

Summary Statements

Statement 1: Not all patients with positive skin test or serum results to whole peanut (F13) have an equal risk of severe systemic reactions following peanut exposure. Additional testing is required to determine the relative risk of potentially life threatening reactions.

Statement 2: Positivity to Ara h 2, Ara h 1 and/or Ara h 3 correlates strongly with a risk of severe systemic reactions to peanut exposure. An oral food challenge in these patients may potentially result in life threatening reactions.

Statement 3: The range of risk for Ara h 9 positivity varies more widely in studies compared to other components; however, at minimum, positivity to Ara h 9 suggests a moderately increased risk of severe reactions following peanut exposure.

Statement 4: Positivity to Ara h 8 correlates to a low risk of severe systemic reactions to peanut exposure, and may be due to cross-reactivity to other sources such as birch pollen.

Resolving Risk of Systemic Reaction

Misdiagnosis of peanut allergies can have negative repercussions. Individuals who are falsely diagnosed as being allergic to peanuts (or assume they have peanut allergy without diagnosis) unnecessarily undergo life-style changes and avoidance of a food that is exceedingly common. Alternatively, individuals who are not accurately identified as being at risk for severe, potentially life-threatening reactions to peanut will not have the appropriate knowledge and preparation to deal with an exposure and the resulting life threatening reaction.

Due to the potentially fatal impact of peanut allergy, accurate diagnosis is important. The double-blind placebo control food challenge (i.e. oral food challenge or OFC) is the gold standard for establishing a diagnosis [4]. However, this method of establishing a diagnosis presents a significant risk of life threatening reaction as a result of the challenge, in addition to being both time-consuming and expensive to perform. Because of these factors two other diagnostic methods, skin testing and IgE testing to whole peanut extract (F13), have been used. However, these

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methods have a poor ability to differentiate peanut sensitized patients from peanut allergic individuals; only 22.4% of patients with either a positive skin test or IgE test fail an oral food challenge and are therefore truly allergic [5].

Similar to testing with whole peanut extract, component testing detects IgE, but to specific antigen components of peanut. Positivity to specific peanut components provides significantly improved information to predict the risk of allergic reactions, and is particularly useful for patients with an unclear history, a history of mild reactions, or when allergic reactions to peanuts are suspected but not confirmed. As shown in Table 1 below, a positive result to the component known as Ara h 2 carries the highest risk [3], especially for individuals with results > 3.5 kU/L, while a positive result to Ara h 8 carries the lowest risk [5]. Positivity to Ara h 1 and/or Ara h 3 are at the higher end of the risk spectrum, in addition to being additive in risk when the same individual is positive to Ara h 2 [7]. Positivity to the final component, Ara h 9, represents a moderate relative risk [8] that is likely greater than Ara h 8, but less than Ara h 2, 1 and/or 3. However, clinical research studies of Ara h 9 currently vary in the exposure risk associated with individuals sensitized to this component. Interestingly, individuals in different geographical regions may vary widely in overall positivity rates to each component [8,9].

Table 1. Association of molecular peanut component antigen results with risk of allergic reaction

		Ara h 2	**Ara h 1** and/or **Ara h 3**	**Ara h 9**	**Ara h 8**	
		(+) Result is a value > 0.35 kU/L*				**Research Findings**
Relative Risk of Systemic Reaction	Very High	+	+	+/-	+/-	97% of patients positive to Ara h 2 and Ara h 1 or Ara h 3 have severe reactions than those positive to Ara h 2 alone [7].
	High	+	-	+/-	+/-	≥90% of patients positive to Ara h 2 fail oral food challenges [3]. Ara h 2 is heat and digestion stable.
	Moderate	-	+	+/-	+/-	Ara h 1 and/or Ara h 3 positivity is often associated with Ara h 2 positivity. Moderate risk is possible in patients only positive to Ara h 1 and/or Ara h 3 irrespective of Ara h 8 and Ara h 9 status [11]. Ara h 1 and Ara h 3 are heat and digestion stable.
		-	-	+	+/-	Ara h 9 is cross-reactive with peach pollen and related rosacea foods and often leads to oral symptoms, while representing a low to moderate risk for systemic allergic reactions [8]. Ara h 9 is heat and digestion stable.
	Low	-	-	-	+	99% of patients sensitized to Ara h 8 alone are peanut tolerant [5,6]. Ara h8 is cross-reactive with birch pollen, often leading to oral symptoms, while representing the lowest risk for systemic reactions. Ara h 8 is heat and digestion labile.

* Detectable IgE between 0.1 and 0.35 kU/L may be clinically significant

Conclusion

Molecular component testing represents a major step forward in diagnosing and assessing risk for peanut allergic individuals. The full extent of clinically utility from results following testing of peanut component is now emerging. Clearly, positivity to Ara h 2 places the individual in a high risk category, which is further enhanced with positivity to Ara h 1 and/or Ara h 3. In these individuals additional diagnostic efforts such as an OFC should be evaluated with caution and may not be advisable for all patients. Conversely, positivity only to Ara h 8 may suggest the individual is a good candidate for OFC, depending on other variables of the individual case. Additional studies and subsequent practice guidelines are likely to emerge in the near future now that component testing is in clinical use.

Author's Discolsure of Potential Conflicts of Interest

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