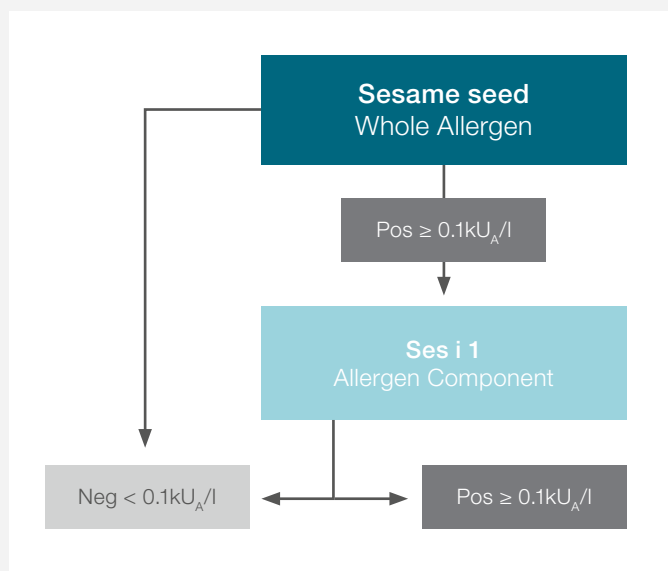


Component-Resolved Diagnostics in Sesame Allergy*

Introduction

Sesame (*Sesamum indicum*) is one of the oldest known cultivated oilseed plants and both the seeds and oil are commonly used ingredients in African, Asian, Mediterranean, and Middle Eastern cuisine. Sesame is a common trigger of allergic symptoms such as wheezing, dyspnea, asthma, atopic dermatitis and anaphylaxis, likely due to its widespread use in the food, pharmaceutical and cosmetic industries.^{1,2} Traditionally it is consumed as tahini paste or halva sweets, and it is also used as toppings on bread and crackers. It may be a hidden allergen in processed foods such as dips, spreads, bakery goods and cereals when added as flour, paste or oil, and it may occur unintentionally due to cross contamination during production. With the high risk of accidental intakes and reactions, many countries, including the USA, have recognized sesame as a major food allergen requiring labeling on the products.³

Figure 1. Sesame test algorithm



Overview

- Specific IgE testing to Ses i 1 can aid in improving the diagnosis of sesame allergy¹¹⁻¹⁸
- A quantitative ImmunoCAP™ Ses i 1 allergen component test is now available for component-resolved diagnostics
- This component test may minimize the need for oral food challenges¹¹⁻¹⁸ and offers improved diagnostic work up.

Sesame can cause severe allergic reactions. Among common seeds and nuts, it has been reported to cause allergic symptoms with the highest severity.⁴ Sesame allergy also commonly co-exist with peanut and tree nut allergy, with 50-60% of patients also being allergic to peanut and/or tree nuts.^{4,5}

Background

The prevalence of sesame allergy varies globally. In countries with high sesame consumption, such as Australia and Israel, sesame allergy confirmed by oral food challenge (OFC) has been reported to occur in 0.8%⁶ and 0.9%^{1,7} of children, respectively. It is considered the third and ninth most common childhood food allergy in Israel^{1,7} and the USA¹, respectively, and the second most common food to cause anaphylaxis in children in Israel.^{1,7} In Canada⁸, Mexico⁹ and the USA¹⁰, a prevalence of 0.1-0.2% in children and adults has been estimated, based on self-reported or probable diagnosis of sesame allergy evaluated by symptoms and sensitization. It is often lifelong, and only about 20-30% of children outgrow their sesame allergy.^{1,18}

Consequently, since sesame allergy often is lifelong and there is a high risk of severe reactions, appropriate diagnosis and management is very important, particularly as sesame may occur as a hidden allergen, causing a risk of accidental intake.¹

Diagnostic considerations

Studies have shown specific IgE to Ses i 1 to be a promising aid in the diagnosis of sesame allergy as compared to whole sesame specific IgE and skin prick testing (SPT), showing higher clinical specificity and better predictive value for positive outcomes of OFC.¹¹⁻¹⁸ Testing for Ses i 1 sensitization may therefore help facilitate decision when to perform OFC, especially in patients with high levels of specific IgE to Ses i 1 and a high probability to react.¹⁴⁻¹⁶

Protein characteristics

Ses i 1 is a major 2S albumin storage protein in sesame, and is stable to heat and proteases, which increases the risk of severe reactions and anaphylaxis.^{19,20} Ses i 1 has shown resistance to high heat (100°C) and to the digestive conditions of GI tract at both acidic and neutral pH, and it was found to remain intact after gastric as well as duodenal digestion.²¹ Such protein stability is believed to increase the risk of severe reactions and anaphylaxis and has been proposed to be a key player in allergic reactions to sesame.^{20,21}

There are seven sesame allergen components registered by the WHO/IUIS Allergen Nomenclature Subcommittee: four storage proteins including two 2S albumins (Ses i 1 and Ses i 2) and two 11S globulins (Ses i 6 and Ses i 7), two oleosins (Ses i 4 and Ses i 5) and one vicilin-like 7S globulin (Ses i 3).¹⁹

Ses i 1 is one of the major allergens in sesame seed and the majority of sesame allergic patients are sensitized to Ses i 1.^{14,20} It is considered a good predictor of clinical allergy to sesame and is commonly associated with allergic reactions of the skin, respiratory tract, gastrointestinal system, cardiovascular systems and anaphylaxis.^{14,20} Ses i 1 is also reported to be the most clinically relevant sesame allergen associated with severe allergic reactions.²⁰

Management considerations

Utility of specific IgE testing with Ses i 1 was examined in another study performed in Israel from the same research group, sesame oral immunotherapy (OIT) was evaluated in 75 children.¹⁸ Full desensitization was achieved in 88.4% of the patients. In a subset of these OIT patients (n=16) and controls (n=11), the levels of specific IgE to Ses i 1 was measured and was shown to decrease in the OIT-treated patients compared to controls.

Sesame Seed	Ses i 1	Management Considerations
+	+	<p>If clinical symptoms are present, high probability of clinical sesame allergy and severe, systemic reactions.^{13,20} Patient likely to react to Oral food challenge (OFC).^{13,15-16} Consider other co-sensitizations (e.g. peanut and tree nuts).^{4,5,14,16} Consider the following:¹⁸</p> <ul style="list-style-type: none"> • Avoiding contact or consumption of sesame seed and sesame products • Prescribing epinephrine auto-injector • Making family, colleagues, and teachers aware of the allergy and have a plan
+	-	<p>If clinical symptoms are present, consider further investigation to identify the primary allergen by investigating what other allergens your patient is exposed to. It's possible that cross reactivity is the cause of symptoms.^{4,5,14,16} Consider the following:</p> <ul style="list-style-type: none"> • Further testing for tree nuts and seeds. OFC with a specialist may be recommended¹²⁻¹⁶ • If patient passes an OFC, foods prepared with or around sesame may be consumed • Prescribing epinephrine auto-injector
-	-	<p>If there are no clinical symptoms and no detection of specific sIgE, primary sesame allergy and severe reactions are unlikely. OFC with a specialist may be recommended.¹²⁻¹⁶ Consider the following:</p> <ul style="list-style-type: none"> • If patient passes an OFC, foods prepared with or around sesame may be consumed

Note: As in all diagnostic testing, any diagnosis or treatment plan must be made by the clinician based on test results, individual patient history, the clinician's knowledge of the patient, as well as their clinical judgment. Patients can be sensitized to more than one allergen component.

In a Japanese study, 92 sesame-sensitized children were divided into symptomatic (positive sesame OFC or convincing clinical history, n=36) and asymptomatic (negative sesame OFC or known tolerance to sesame, n=56).¹⁴ Both groups were tested for Ses i 1, and Ses i 1 sensitization was found to be present in 92% (33/36) of the symptomatic group and in 32% (18/56) of the sensitized but asymptomatic group. Further, it was reported that a specific IgE level to Ses i 1 of 3.96 kU_A/L was identified as an optimal cut-off in that study population, yielding a sensitivity of 86.1% and a specificity of 85.7%. The study also reported Ses i 1 to be more diagnostically informative and useful than Ses i 2 (the other 2S albumin in sesame). Measurement of Ses i 1 specific IgE in patients with suspected sesame allergy may thus help in reducing the number of OFC needed to confirm clinical reactivity.

In another Japanese study of 90 sesame-sensitized children evaluating the results of OFC, the authors found higher levels of specific IgE to Ses i 1 in OFC-positive patients (n=18) compared to OFC-negative patients (n=72), and could demonstrate a reduced requirement of OFCs in patients with high Ses i 1 specific IgE levels.¹⁵ The study found 5% and 50% probability of a positive OFC with Ses i 1 specific gE levels below 0.13 kU_A/L and above 32.0 kU_A/L, respectively. Furthermore, the level of Ses i 1 specific IgE was proposed to be superior for predicting positive outcomes of OFC as compared to SPT or specific IgE to sesame extract.

Similarly, a retrospective study conducted in the USA evaluated OFC results in 341 patients with suspected sesame allergy.¹⁶ In a subset of 30 patients, levels of specific IgE to Ses i 1 was measured. Positive OFC outcomes were seen in 40% (n=12) of these patients, and the level of specific IgE to Ses i 1 was significantly associated with a positive OFC outcome. In contrast,

the level of specific IgE to sesame extract or SPT did not show an association with a positive OFC outcome. It was further observed that 30% of the patients with specific IgE levels to Ses i 1 above 0.1 kU_A/L had a negative OFC result, which was considerably less compared to those with specific IgE to sesame extract (69%) or a positive SPT (61%).

Cross-reactivity between nuts and seeds

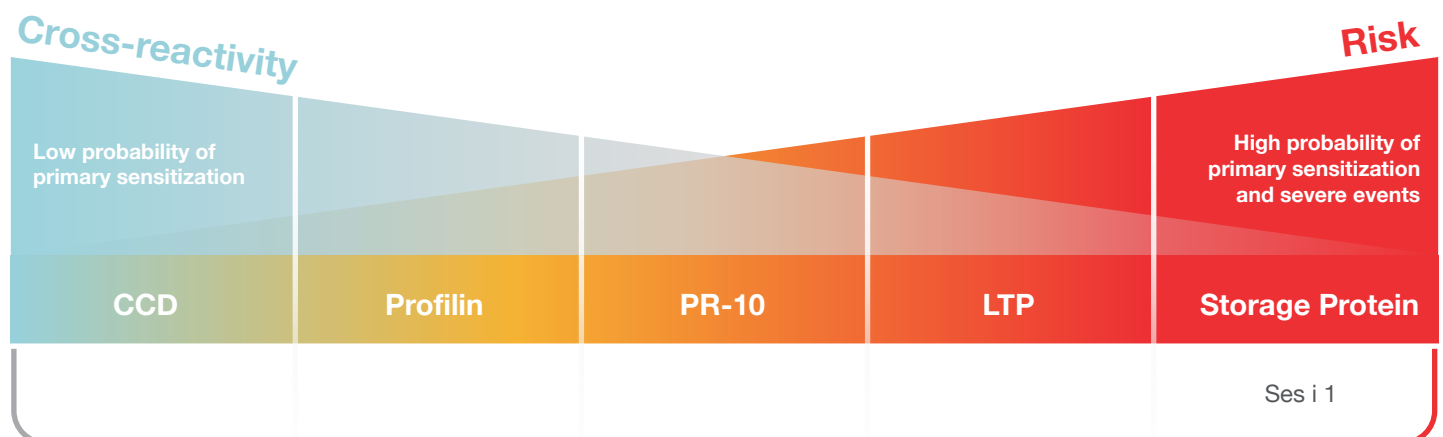
2S albumins differ considerably between species as compared to many other allergens and display low or no cross-reactivity except between botanically related species.²¹⁻²³ Therefore, among botanically distant foods, 2S albumins can be considered more species specific than most other components. Limited but highly variable immunological cross-reactivity has also been observed with other 2S albumins allergen components, such as Cor a 14 (hazelnut), Ara h 2 (peanut), Jug r 1 (English walnut), Ber e 1 (Brazil nut), Ana o 3 (Cashew nut), Pis v 1 (pistachio), and Bra n 1 (rapeseed).^{14,23}

Conclusions

The current optimal method for diagnosis of sesame allergy is OFC, which can be unpleasant and may potentially cause a severe reaction requiring immediate medical intervention. Other tests to help aid in the diagnosis of sesame allergy include measurement of sensitization by skin prick testing (SPT) and in-vitro blood testing for specific IgE to whole sesame.

As described earlier, studies have shown sensitization to Ses i 1 to be a better candidate to aid in the diagnosis of patients with primary sesame allergy, due to higher clinical specificity and better predictive value for positive outcomes of OFC, compared to whole sesame specific IgE tests and SPT.¹⁴⁻¹⁶

Sesame risk ramp^{12,15,16,20,23}



In conclusion, Ses i 1 sensitization seems to be a good indicator of primary sesame allergy. Specific IgE testing to Ses i 1 can aid in improving the diagnosis of sesame allergy, help understand patient risk for severe reactions, and may help facilitate decisions on when to perform OFC thereby possibly decreasing the need for OFC.¹¹⁻¹⁸ A quantitative ImmunoCAP Ses i 1 allergen component test, produced as a highly purified recombinant protein, is now available for component-resolved diagnostics, offering improved diagnostic work-up (Figure 1), especially for patients at risk for severe reactions to sesame.

*Official product names mentioned within this document: *ImmunoCAP Allergen f10, Sesame seed; ImmunoCAP Allergen f449, Allergen component rSes i 1 Sesame seed*

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