Improved sesame allergy diagnosis with Ses i 1

Sesame food allergy

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, such as Australia, New Zealand, Canada, Europe, Morocco, Taiwan and the USA, have recognized sesame as priority food allergen requiring labelling on the products.[3]

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]

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 USA[1], respectively, and the second most common food to cause anaphylaxis in children in Israel.[1,7] In Canada[8], Europe[3], Mexico[9] and the USA[10], 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]

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]

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 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]

Ses i 1 may cause severe systemic reactions

Ses i 1 is a major 2S albumin storage protein in sesame, and is stable to heat and proteases, which increase 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

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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]

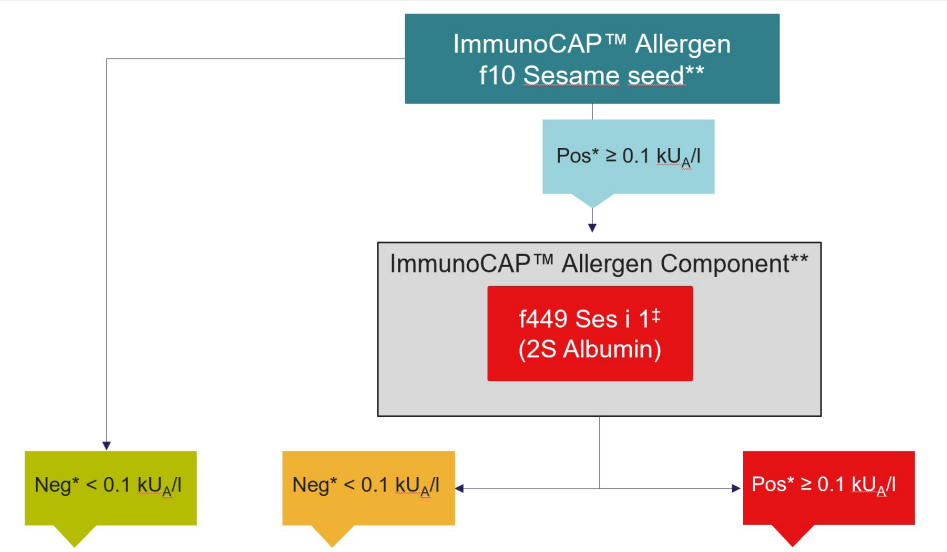
Ses i 1 is a marker for primary sesame allergy and severity

Ses i 1 is one of the major allergens in sesame seed and 55-100% 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]

Utility of specific IgE testing with Ses i 1 as an alternative to the OFC was investigated in a study from Israel on 42 children with suspected sesame allergy.[17] Levels of specific IgE to Ses i 1 differed significantly between allergic (n=27) and tolerant (n=15) patients, and correlated to results of the basophil activation test (BAT). Used together, specific IgE to Ses i 1 and BAT yielded correct positive classifications for 25 of 27 sesame allergic patients and could decrease the need for OFC in sesame allergic patients. 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.

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 of 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.

Figure 1. Sesame test algorithm



Primary sesame allergy unlikely

Diagnostic considerations: If suspicion of allergy persists, investigate what other allergens your patient is exposed to, which may cause symptoms. Consider further testing as appropriate.

Low probability of primary sesame allergy

Diagnostic considerations: Consider further sIgE testing with ImmunoCAP Whole Allergen tests for pollens, which may explain the sensitization to sesame extract. If suspicion of a food allergy persists, consider further sIgE testing for tree nuts and seeds, or consider alternative investigations such as sesame OFC.

High risk of severe, systemic reactions[14-18]

Management considerations: Consider prescribing adrenaline auto-injector and further testing with ImmunoCAP Whole Allergen tests **Cashew** (f202), **Hazelnut** (f17), **Walnut** (f256), **Brazil nut** (f18), **Macadamia nut** (f345), **Pistachio** (f203), **Pumpkin seed** (f226) and **Rape seed** (f316) as sesame allergy commonly co-exists with seed and tree nut allergy. Full product names available below.

* Results should be interpreted in the context of a patient's clinical symptoms and history. Patients can be sensitized to more than one component.

** Full product names available on page 4.

‡ Available on ImmunoCAP™ $ISAC_{E112i}$ multiplexing test.

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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 kUA/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%).

Key messages:

New quantitative and recombinant **ImmunoCAP Allergen Component f449 rSes i 1*** IVD test

Help **improve diagnosis and management** of sesame allergy

Stable 2S Albumin associated with **severe reactions.**

Hidden allergen, **high risk of accidental sesame intake.**

Sesame allergy is often **severe, life-long** and **co-exists with tree nut allergy.**

* Full product name on page 4.

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. The level of amino acid sequence identity between a variety of 2S albumins from seeds, nuts and legumes (sesame seed, castor seed, mustard seed, buckwheat and other tree nuts, peanut and soybean) ranges from 14% to 40%.[14,21] 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]

Ses i 1 for improved diagnosis of sesame allergy

The current gold standard 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 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]

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 decision on when to perform OFC thereby possibly contributing to minimize 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.

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Product List

ImmunoCAP™ Allergens:
ImmunoCAP Allergen f10, Sesame seed; ImmunoCAP Allergen f449, Allergen Component rSes i 1 Sesame seed; ImmunoCAP Allergen f13, Peanut; ImmunoCAP Allergen f202, Cashew nut; ImmunoCAP f17, Hazelnut; ImmunoCAP Allergen f256, Walnut; ImmunoCAP Allergen f18, Brazil nut; ImmunoCAP Allergen f345, Macadamia nut; ImmunoCAP Allergen f203, Pistachio; ImmunoCAP Rare Allergen f226, Pumpkin seed; ImmunoCAP Allergen f316, Rape seed;
Multiplex test:
ImmunoCAP ISAC$_{E112i}$

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