Clinical allergy induced by repeated challenges or by exposure to a cross-reactive food?

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**Background:** Sequence homology in IgE binding epitopes of proteins from different foods may cause cross-sensitivity and hereby also clinical cross-reactivity. A recent study investigating allergy towards pistachio nut and cashew nut found that 25/25 patients were double-allergic to the nuts. The levels of specific IgE (sIgE) may increase with age and new allergies may occur towards previously tolerated foods. Sensitization, on the contrary, can be present though the patient is tolerant to the food item, why diagnosis relies on oral food challenges (OFCs).

A study has shown that up to 13\% of OFCs can be negative, with a clinical reaction upon re-exposure. This can be due to priming or maturation of the immune system. But the course of events leading to reactivity or cross-reactivity towards a previously tolerated food item is not fully clarified.

**Report:** A 1-year-8-months-old girl was referred to an allergy center after an allergic reaction to hazelnuts. She had sIgE (Thermo Fisher Scientific, Uppsala, Sweden) towards other tree nuts that she had never ingested, and kept a nut-free diet until subsequent OFCs (see figure 1).

After two negative pistachio-OFCs, one positive cashew-OFC and one negative walnut-OFC, a 20 fold increase in sIgE was observed towards all nuts challenged with including hazelnuts (later hazelnut-OFC was positive).

Regular intake of the food tolerated in an OFC is normally recommended. But due to the increase in sIgE it was regarded unsafe. When re-challenged with pistachio nut, the patient reacted with grade-2-anaphylaxis (asthma, rhinitis and urticaria) to a dose much lower than the dose previously tolerated. Due to safety and ethical reasons the patient was not re-challenged with walnuts.

**Clinical Relevance:** The report suggests that allergy or cross-allergy towards pistachio nut may be induced by repeated exposure. It also stresses the importance of IgE testing close to the date before and shortly after an OFC. The natural course of allergic disease should be taken into consideration. But the timing of OFCs could be of importance to the challenge outcome.

**Statement of Consent:** A written consent for presentation and publication is obtained from the parents.
**Figure 1:** Summary of clinical and serological testing. OFCs were terminated at appearance objective symptoms or after tolerating 10 grams (g) of nut (the first pistachio-OFC was stopped at 0.45 g, due to time-shortage).

IgE (detection limit ≥ 0.35 kU/L) towards all listed nuts and components were measured on each blood sample. IgE is depicted on a logarithmic scale.