

Anaphylactic reactions to sunflower seed

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We report on four patients sensitized to sunflower seed. Three of them developed anaphylaxis and one chronic bronchial asthma. All four patients reacted the first time sunflower seeds were ingested, and all had kept cage birds fed on sunflower seeds. Therefore, the route of sensitization was probably by inhalation of airborne sunflower seed allergens. Investigation of this type of hypersensitivity in 84 atopic patients showed that only three patients were RAST-positive, indicating that this allergy is fairly uncommon. On the other hand, when atopic persons are exposed to cage birds, the rate of sensitization is rather high, as indicated by the fact that in this category 79% were skin prick positive and 21% were unequivocally RAST positive to sunflower seed.

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Sunflower seeds are rich in oil, which, when extracted, is a common ingredient in margarine and cooking and salad oils. After oil extraction, the sunflower seed residues are used in forage for animals, and raw sunflower seeds are used as stock, poultry, and cage-bird feed. Peeled sunflower seeds, often roasted, are eaten as snacks, but may also be added to muesli or used as a bread condiment.

Like many other common pollen-allergen sources, e.g., mugwort and ragweed, the sunflower (*Helianthus annuus*) belongs to the Compositae family. Allergic reactions, in the form of contact dermatitis, and conjunctivitis with itching, linked to the forced labor of peeling sunflower seeds done by imprisoned prostitutes, were described as early as 1906 (4). As the sunflower is insect pollinated, there is only one case report on occupational respiratory allergy to sunflower pollen (1). In the current literature, more severe reactions, including generalized urticaria, dyspnea, and anaphylaxis, after ingestion of sunflower seeds have been reported (7, 9). Allergic reactions to sunflower seed are not common, and little is known about how the sensitization is induced. Therefore, the hypersensitivity is generally assumed to take place through an allergic cross-reactivity with other Compositae species (9, 12, 13).

In the present paper, we report on three patients in whom anaphylactic reactions and one patient in whom bronchial asthma occurred after ingestion of sunflower seeds. The patients had all kept cage birds, and the route of sensitization was probably inhalation of airborne sunflower seed allergens.

Material and methods

Skin prick tests (SPT) were performed with a standard panel of 14 common allergens (Phazet[®], Pharmacia Diagnostics AB, Uppsala, Sweden). SPT with sunflower seed allergen extract was done as described by Pepys (10). The test reactions were scored according to the Nordic Guidelines (11), with Phazet positive control (histamine-coated lancet) as the reference for 3+.

Sunflower seed allergen extract

Peeled sunflower seeds (1 g) were put in a hydraulic press, and a total pressure of 10 t (approximately 2 t/cm²) was applied to squeeze out the oil. The pressed sunflower seeds were then collected on a filter paper and transferred to a test tube, and 9 ml of physiologic saline solution was added (1:10 w/v). After extraction overnight, the sunflower seeds were sedimented by centrifugation at 1000 g for 10 min. The supernatant was transferred to another test tube and ultracentrifuged at 149000 g for 20 min. The middle fraction was carefully sucked off and sterilized through a 0.22-µm Millipore[®] filter. The total allergen extract yield was approximately 3 ml. When used in SPT, the extract was diluted with a saline solution containing 0.3% human serum albumin (Albumin Diluent[®], Pharmacia, Uppsala, Sweden).

RAST

The radioallergosorbent test (RAST) was performed, according to the instructions of the manufacturer (Pharmacia Diagnostics AB, Uppsala, Sweden), with a commercially available ^{125}I -labeled anti-IgE (Phadebas RAST). Sunflower seed disks were prepared by coupling 10 μl allergen extract to each CNBr-activated paper disk, as previously described (6). The disks were negative (<0.35 PRU/ml) in RAST with nonatopic serum samples with IgE concentrations of 10–7000 kU/l. The results were expressed in PRU/ml, as derived from the Phadebas RAST reference system.

Statistical analyses

The results in the control group were analyzed by Fisher's exact test for comparisons of two proportions.

Case reports

Case 1 was that of a 44-year-old woman who had smoked 15–20 cigarettes/day for 28 years. She had no family history of atopy, but had had conjunctivitis once as a child, when playing in hay. The patient had kept cage birds (budgerigars, parakeets, and finches) in varying numbers in her home for the last 15 years. She never experienced any respiratory symptoms that could be connected with the presence of her cage birds. For several years she had noticed itching and urticaria in her mouth when she ate egg and hazelnuts. She had also had a cat for 1 year, during which time she had periods of dyspnea and wheezing. The symptoms occurred mainly at home and during exercise. One year later, she ate a few sunflower seeds and suffered from dyspnea, heart palpitations, and a feeling of distress. The symptoms were relieved after salbutamol inhalation. About a year later, she ate bread flavored with sunflower seeds, and after a few minutes she experienced stiffness around her mouth and in her neck, and extreme dyspnea with rhonchi and heart palpitations, and generalized urticaria developed. She was taken to hospital, where the usual antishock treatment was given successfully, and she fully recovered after 2 h.

SPT was negative for mugwort and animal dander, but was 3+ for poultry feather and 2+ for soybean. RAST was positive for egg (2.6 PRU/ml), hazelnut (4.9 PRU/ml), dog (1.7 PRU/ml), cat (0.4 PRU/ml), budgerigar feather (43 PRU/ml), budgerigar droppings (1.1 PRU/ml), budgerigar serum (51 PRU/ml), and poultry feather (29 PRU/ml). However, none of these sensitizations could explain the life-threatening symptoms that were precipitated after the ingestion of sunflower seeds.

Case 2 was that of a 4-year-old girl without previous symptoms of atopy, but whose mother is allergic to birch pollen. The family had previously kept a parakeet, which was fed mainly sunflower seeds. When the girl was about 1 year old, she had developed conjunctivitis, dyspnea, and wheezing when in the room where the bird cage was kept. The family therefore got rid of the bird. From that time on until the present episode, the patient had had conjunctivitis only from down pillows. At the age of 4, she ate bread containing sunflower seeds. This was the first time that she had eaten sunflower seeds. About 10 min after the ingestion, she felt ill and complained of stomachache and dyspnea. On arrival at the hospital, the girl was pale and distressed, and the jugular was indrawn. On auscultation, rhonchi were audible over the lungs. The pulse rate was 124/min. Generalized urticaria developed. Salbutamol inhalations, intramuscular antihistamine, and oral cortisone were administered. The girl fully recovered within 45 min.

SPT for birch, timothy, mugwort, and animal dander were negative. RAST was positive for budgerigar feather (0.8 PRU/ml).

Case 3 was that of a 25-year-old, nonsmoking actress with hereditary predisposition to allergy. She had suffered from a mild egg allergy as a child. The family had kept from 1 to 15 canaries for about 8 years during her childhood. The first time she had eaten sunflower seeds was when she was 18 years old, and she almost immediately experienced itching in the mouth, ears, and eyes and vomiting. Generalized urticaria, facial angioedema, and a feeling of faintness developed. At the hospital emergency unit, she received conventional antishock treatment and recovered. After this episode she had experienced six similar reactions after eating muesli, snacks, salads, and bread containing sunflower seeds.

SPT was 3+ for mite and 2+ for cat. RAST was negative for mugwort, but was 1.2 PRU/ml for mite and 0.4 PRU/ml for cat.

Case 4 was that of a 66-year-old, nonsmoking woman with a 7-year history of mild asthma. She had often had "abronchitisa" and atopic dermatitis during her childhood, but had been symptom-free as an adult. Seven years before, she had pneumonia with a markedly prolonged course, which for several years was followed by short or longer periods of slight fever and pronounced fatigue with dyspnea, expectoration, coughing, and wheezing. The symptoms were initially interpreted as recurrent pneumonia in an asthmatic patient. Several chest radiographs revealed fluctuating unspecific pulmonary infiltrates. The cough and dyspnea were most severe during the evenings, nights, and mornings and were clearly associated with the home environment. The diagnosis was finally put down as allergic alveolitis.

because precipitating antibodies against budgerigar and dove allergens were positive. The patient had kept a parrot, fed mainly sunflower seeds, for the last 20 years. The patient had never, as far as she knew, eaten sunflower seeds. However, the first time she ate bread flavored with sunflower seeds, she reacted with asthmatic symptoms, rhinoconjunctivitis, and erythema in the face.

SPT for mugwort was 1+, but RAST was negative.

Control group

The frequency of hypersensitivity to sunflower seed was examined in 84 atopic (i.e., with a positive SPT for at least one common allergen) patients referred for allergologic investigation. The patients answered a questionnaire on allergy symptoms and cage birds at home. All were also skin prick tested with the standard panel of allergens and sunflower seed extract diluted 1:100 (w/v), and RAST for sunflower seed was performed when SPT was positive ($\geq 1+$).

Results

A summary of the results in the four cases is presented in Table 1.

Patient no. 1 underwent SPT with sunflower seed extract diluted 1:10 (w/v) on the volar aspect of the right forearm. After 10 min, there was a wheal reaction of 6+ (25 × 35 mm) with pseudopods at the SPT site, and the patient began to feel stiffness of her upper lip and show moderate shortness of breath. Urticaria developed on the right arm. No rhonchi could be heard on auscultation over the lungs. Subcutaneous epinephrine (0.5 mg) and oral histamine were immediately administered. After about 10 min, when intravenous hydrocortisone (100 mg) had also been given, her symptoms diminished. She fully recovered within 1 h and remarked that this allergic reaction was very mild in comparison with what she had experienced after having eaten bread flavored with sunflower seed. SPT for pure sunflower oil was negative. RAST for sunflower seed was 376 PRU/ml

Table 1. Summary of results of SPT and RAST for sunflower seed in four female atopic patients

Case no.	Age (years)	Extract dilution (w/v)	SPT	RAST (PRU/ml)	Total IgE (kU/l)
1.	44	1/10	6+	380	1500
2.	4	1/10000	4+	180	940
3.	25	1/1000	4+	100	770
4.	66	—	nd	10	120

nd: not done.

Table 2. Results of SPT and RAST for sunflower seed in 84 atopic patients

n	Sunflower seed		Mugwort-positive SPT	Cage bird at home	Food allergy
	SPT	RAST			
66	Negative	nd	17	3	4
13	Positive < 3+	0	6	8	2
5	Positive $\geq 3+$	3	3	3	5

nd: not done.

(class 5), and the total IgE concentration was 1500 kU/l.

The results from patients 2 and 3 are presented in Table 1.

Patient no. 4 had a RAST score of 10 PRU/ml for sunflower seed, but RAST was negative for parrot. Total IgE was 120 kU/l. The patient was persuaded to give away her parrot, and 6 months later her asthma symptoms were markedly improved and the airway hyperresponsiveness was reduced. RAST was 5.3 PRU/ml for sunflower seed, with a total IgE of 55 kU/l.

The results in the control group are summarized in Table 2. Eighteen of the 84 patients had positive SPT for sunflower seeds, while the remaining patients had negative SPT. In these 18 SPT-positive patients, only three were also positive for RAST (2.9, 3.4, and 1.4 PRU/ml, respectively). Positive SPT for sunflower allergen extract was strongly correlated to both cage bird at home and history of allergy to food ($P < 0.001$ and $P < 0.002$, respectively). There was a weak association with positive SPT for mugwort ($P < 0.09$).

Discussion

The habit of keeping cage birds, particularly parakeets, has increased markedly in Sweden during the last few decades. Sunflower seeds constitute their main food, and the birds deftly unshell the seeds before eating them. Down, epithelial scrapings, and droppings from the birds and peelings from the sunflower seeds are scattered outside the cage onto the floor. The smaller particles of this debris inevitably become mixed and airborne with the house dust. All four of our patients had kept cage birds in their homes for a long period of time, indicating that they had been continuously exposed to dust containing sunflower seed fragments. None of the patients had previously eaten sunflower seeds, and the first time they did so, their allergic response was severe and rapidly developed into an anaphylactic reaction, which in one patient was life-threatening.

Although we lack objective proof of the route of sensitization, it seems most likely that the sensitization occurred through the airways, resulting from

inhalation of sunflower seed allergens. The fact that only one of the patients exhibited a weak positive skin reaction to mugwort (the most common allergen source from the Compositae family in Sweden) supports the conclusion that the sensitization had been induced by sunflower seed aeroallergens and reduces the likelihood of cross-reactivity with allergens from plants botanically related to sunflower. Moreover, the proportions of specific IgE antibodies were very high in the four patients (25, 19, 13, and 8%, respectively). However, in the fraction of the control group that exhibited a positive RAST $\geq 3+$, the possibility of cross-reactivity is more likely, because the RAST scores for sunflower seed were low and there was a high incidence of food allergy and positive SPT for mugwort. There are epitopes shared by, e.g., mugwort and celery allergens (3). The fact that the SPT-positive patients significantly more often had cage birds at home contradicts the idea of a cross-reactivity between mugwort and sunflower seed in this group.

Patient no. 4 exhibited a more complex clinical picture with allergic alveolitis through long-standing exposure to airborne organic materials from her pet bird and an IgE-mediated bronchial asthma caused by the food of her pet bird, i.e., sunflower seeds. Thus, her history differed from those of the other three patients. This case also illustrates the importance of antigen avoidance in any allergic disorder. After the antigen sources had been removed, that is, when the patient no longer had a cage bird that was fed sunflower seeds in her home, her bronchial symptoms markedly improved. After 6 months, the RAST for sunflower seed and total IgE value were reduced by 50%.

Cross-reactions between inhaled and food allergens have been described earlier. Lybarger et al (8) have reported a case of occupation-related asthma caused by sensitization to garlic dust, documented by SPT, which some years later resulted in a rapid onset of dyspnea, after consumption of food containing garlic. Bush et al. (2) have described a case of anaphylaxis occurring after ingestion of one shrimp in a patient who had been exposed to aerosolized shrimp protein in a shrimp-processing factory.

The SPT reaction in patient no. 1 illustrates the hazard in performing SPT with an undiluted allergen extract in a patient with a history of anaphylaxis. Patients nos. 2 and 3 were therefore tested only with extract diluted 10 000 and 1000 times, respectively.

One additional observation that deserves mention is that sunflower seed allergens are apparently fairly stable to heat denaturation. Sunflower seed is often used as a bread condiment, and the heat stability of

the allergens is illustrated by the fact that when bread is being baked, the temperature in the oven is typically about 200°C for 30–60 min. Sunflower oil contains only infinitesimal amounts of the hydrophobic allergen proteins (5), a fact which explains why sunflower oil-containing products may be safely ingested by persons sensitized to sunflower seed.

The findings in this study indicate that if the investigation of allergic symptoms associated with cage birds is negative, it is important to focus attention on the bird feed, since exposure and sensitization to airborne bird feed allergens may induce life-threatening allergic reactions in the patient if this kind of seed is ingested.

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