

2. MÜLLER U, HORAT W, CONROY M, REISMAN RE. Anaphylaxis following Hymenoptera stings in three patients with urticaria pigmentosa. *J Allergy Clin Immunol* 1983;**72**:685–690.
3. JUAREZ C, BLANCA M, MIRANDA A, et al. Specific IgE antibodies to vespids in the course of immunotherapy with *Vespula germanica* administered to patients sensitised to *Polistes dominulus*. *Allergy* 1992;**47**:299–302.
4. VAN DER LINDEN PWG, HACK CE, VAN DER ZWAN, et al. Preliminary report: complement activation in wasp-sting anaphylaxis. *Lancet* 1990;**336**:904–906.
5. KÖNIG BE, RUEFF F, PRZYBILLA B. Generalized urticaria caused by sesame seed with negative prick test results and without demonstrable specific IgE antibodies. *J Allergy Clin Immunol* 1995;**96**:560–561.
6. OETTGEN HC, MARTIN TR, DRAZEN JM, et al. Active anaphylaxis in IgE-deficient mouse. *Nature* 1994;**370**:367–310.

Sublingual IT in OAS

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Key words: oral allergy syndrome; SLIT.

• SUBLINGUAL/swallow immunotherapy (IT) (SLIT) is now accepted as a viable alternative to the subcutaneous route, and its safety has been proven in both children and adults. The most common side-effects reported are gastrointestinal complaints

(especially when high doses are used) and oral itching.

The safety of SLIT in patients suffering from oral allergy syndrome (OAS) still represents a major concern and a matter of debate. OAS is characterized by oral itching and swelling, edema of the tongue/lips, and peroral urticaria, which appear within minutes after contact between certain foods and the oral mucosa. OAS is frequent in subjects

suffering from pollen allergy where fruits and vegetables (such as apple, carrot, kiwi, peach, and tomato) are the most common causal agents (1). In mite-allergic subjects, OAS is commonly due to shrimp and snail.

It has been hypothesized that in patients with OAS the sublingual administration of purified allergens may induce oral symptoms, but no study on the safety of SLIT in patients suffering from OAS is presently available.

We studied 30 patients suffering from OAS, and receiving SLIT for respiratory allergy; a matched group of 30 patients without OAS was also observed for oral side-effects, as internal control. The demographic and clinical data of the patients studied are summarized in Table 1. The diagnosis of OAS was established by clinical history, prick-by-prick, and open oral challenge with the fresh food. All patients received SLIT prepared as orosoluble tablets (LAIS, Lofarma, Milan, Italy) to be dissolved in the mouth for 1–2 min and then swallowed. The SLIT course was preseasonal for pollen allergy and continuous for mite allergy. The IT treatments were administered at the doses recommended by the manufacturer. None of

the subjects were taking antihistamines or corticosteroids at the beginning and during the IT course, since they were asymptomatic. All patients had to complete a record card for side-effects at each dose taken. The presence and grade (mild, moderate, severe) of itching, burning, edema of the tongue, edema of the lips, and peroral urticaria had to be recorded.

Twenty-eight patients with OAS suffered from pollen allergy (grasses, *Parietaria*, or birch), and their OAS was provoked mostly by kiwi, tomato, peach, watermelon, and cherry (also in association). The two patients with mite allergy had OAS induced by shrimp alone. The mean duration of the IT treatment in both groups was about 3 years (irrespective of the schedule). None of the patients herein observed reported oral side-effects during their multiple SLIT courses, and the treatment was optimally tolerated.

OAS is sustained by a type-I reaction and its coexistence with respiratory allergy is probably due to cross-reacting antigens or to superantigens such as prophylins or lipid transfer proteins (2). A few studies (usually in birch allergy) have been conducted on the efficacy of immunotherapy in OAS patients:

Table 1. Characteristics of patient population

	OAS group	Non-OAS group
Patients	30	30
Age (years) (mean SD)	24.5 ± 6	22.8 ± 5.5
Age range	16–41	15–34
Sex (M/F)	17/13	16/14
Disease (%)	21 Rhinoconjunctivitis (70%)	18 Rhinoconjunctivitis (60%)
	3 Asthma (10%)	2 Asthma (7%)
	6 Asthma + rhinoconjunctivitis (20%)	10 Asthma + rhinoconjunctivitis (33%)
Sensitization (%)	17 Grass (57%)	20 Grass (66.7%)
	9 <i>Parietaria</i> (30%)	5 <i>Parietaria</i> (20%)
	2 Mites (6.5%)	4 Mites (13%)
	2 Birch (6.5%)	1 Birch (0.3%)
Total SLIT courses	81 Preseasonal	74 Preseasonal
	5 Years continuous for mites	11 Years continuous for mites
Total doses	5640	5874
Oral side-effects	None	None

they studied the possible effects of the treatment on oral symptoms, and provided controversial results (3–5). As far as SLIT is concerned, no data are available, but the sublingual administration of purified allergens (vaccines) could be expected to elicit oral symptoms in patients with OAS. Indeed, in none of our patients did the SLIT treatment provoke oral symptoms; therefore, we can hypothesize that no cross-reacting allergen is contained in the commercial vaccine used, and that fresh food has probably a different immunologic behavior with respect to purified allergens. We conclude that the presence of OAS should not be considered a contraindication or a risk factor for SLIT, at least with pollen extracts, in patients suffering from respiratory allergy.

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References

1. ORTOLANI C, ISPANO M, PASTORELLO E, BIGI A, ANSALONI R. The oral allergy syndrome. *Ann Allergy* 1988;**61**:47–52.
2. SANCHEZ-MONGE R, LOMBARDERO M, GARCIA-SELLES FJ, BARBER D, SALCEDO G. Lipid transfer proteins are relevant in fruit allergy. *J Allergy Clin Immunol* 1999;**103**:514–519.
3. HERRMANN D, HENZGEN M, FRANK E, RUDESCHKO O, JAGER L. Effect of hyposensitization for tree pollinosis on associated apple allergy. *J Invest Allergol Clin Immunol* 1995;**5**:259–267.
4. ASERO R. Effects of birch-pollen specific immunotherapy on apple allergy in birch pollen hypersensitive patients. *Clin Exp Allergy* 1998;**28**:1368–1373.
5. MOLLER C. Effect of pollen immunotherapy on food hypersensitivity in children with birch pollinosis. *Ann Allergy* 1989;**62**:343–345.

Nitrate intolerance

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Key words: food additives; food allergy; oral challenges; pruritus; sodium nitrate.

● A PATIENT with chronic generalized pruritus caused by nitrate intolerance was recently described (1). Another, nearly identical case induced by the same food additive is reported here.

A 40-year-old woman presented because of a 9-month history of severe, unremitting pruritus of her back and arms. She had a long history of perennial rhinitis, but had never experienced urticaria, eczema, or any visible rash. The daily use of cetirizine in 10-mg tablets produced little relief. The pruritus was continuous, was

not enhanced by contact with cold water or by exercise, and was not associated with the use of drugs or with specific food intake. Physical examination revealed severe scratching lesions at both shoulders and arms but no skin abnormality. Several dermatologists had excluded infestations such as scabies or pediculosis during the previous months.

Laboratory analyses (blood cell counts; ESR; glucose levels; urinalysis; liver, renal, and thyroid function tests; thyroid autoantibodies; and stool tests for ova and parasites) were normal, as was the chest roentgenogram. By contrast, total IgE levels were high (1250 IU/ml).

SPT with a large panel of commercial food extracts (Dome-Hollister/Stier,

Spokane, WA, USA 1:20 w/v) were negative, whereas SPT with airborne allergens (Allergopharma, Reinbek, Germany) revealed hypersensitivity to house-dust mite. The intradermal injection of autologous serum did not elicit any wheal and flare reaction (2), and patch tests with a standard panel of 29 common haptens (GIRDCA) were negative at the 72-h reading. An additive-free diet was started; on day 10 of the elimination diet, the pruritus completely disappeared. After 1 month of additive-free regimen, during which the woman remained symptom-free, an open challenge (unrestricted diet) was carried out. Pruritus relapsed 3 days after the reintroduction of foods containing additives and, again, totally disappeared some days after the additive-free diet was resumed. After 1 month without symptoms, double-blind, placebo-controlled peroral challenges with food additives were carried out. The patient continued the elimination diet throughout the whole challenge period. Additives (tartrazine 10 mg, erythrosin 10 mg, sodium metabisulfite 25 mg, sodium benzoate 100 mg, sodium glutamate 100 mg, sorbic acid 100 mg, sodium nitrate 10 mg, and butylated hydroxyanisole 10 mg) were given in opaque capsules in a randomized sequence. Multiple placebos (talc capsules) were used in order to minimize possible bias (3). Consecutive substances were challenged 1 week apart, and the patient remained under controlled conditions for at least 2 h after each challenge.

About 3 h after the ingestion of sodium nitrate 10 mg, generalized pruritus appeared and lasted for 4 days. None of the other substances or the placebos induced pruritus. Nitrate intolerance was diagnosed.

This case of nitrate intolerance, characterized by chronic unremitting pruritus in the absence of any cutaneous rash, was virtually identical to the one we recently reported (1). This suggests that:

A case of chronic pruritus caused by nitrate intolerance that confirms a previous report.