

intake of some fresh foods, namely fruits (apple), nuts (hazelnut), and vegetables (celery) (oral allergy syndrome [OAS]) (1, 2). We report on a case of OAS in a woman after a kiss from her boyfriend, who had just eaten a fresh apple.

A 24-year-old woman had suffered since the age of 12 years from mild seasonal rhinoconjunctivitis

A new test for food allergy: the single-blind kiss food challenge (SBKFC), an investigation perhaps most appropriate in the springtime.

in the months February to June due to tree and grass pollens. She also had a history of OAS after eating raw apples, carrots, celeriac, and hazelnuts, so that she strictly avoided these foods. She was referred to our allergy unit because after eating an Italian dish, pasta with green sauce (*spaghetti al pesto*), she immediately developed angioedema of the face, dyspnea, and generalized urticaria. The "pesto" sauce contained pine nuts, which had caused the allergic reaction (3). A few weeks before she had also experienced acute edema of the lips with itching in the mouth after a kiss from her boyfriend, who had just eaten a green apple. The last time she had eaten apples herself was about 5 years before.

By convention, allergists most often base the diagnosis of specific allergy on the patient's medical history, supplemented with allergy tests such as skin prick tests and allergen-specific serum IgE determinations. Several attempts have been made to facilitate the diagnostic procedures in patients with food allergy, but so far only the double-blind, placebo-controlled food challenge (DBPCFC) fulfills the criteria of a suitable diagnostic tool, "the gold standard" (4, 5). However, according to Bindslev-Jensen (6), it is important to emphasize that the existence of different protocols for performing DBPCFC often makes direct comparison difficult. The use of freeze-dried extracts in capsules is problematic, as the reactions occur in the mouth and throat in the presence of saliva. Therefore, in view of the above-described reaction, I propose to introduce in the allergy workup a "single-blind, placebo-controlled kiss food challenge" (SBPKFC), which offers some advantages (fresh food items, administration by mouth, etc.) and is easy to perform. Since, for an obvious reason, double-blind challenges cannot be performed, as for publication in peer-reviewed journals – such as *Allergy* – three positive challenges with verum and three negative results with placebo (kiss alone) are required.

Key words: oral allergy syndrome; single-blind, placebo-controlled kiss food challenge (SBPKFC).

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Occupational allergy to the housefly (*Musca domestica*)

A 35-YEAR-OLD female patient suffered conjunctivitis and rhinitis between May and July. Lung function and breathing were normal. Skin prick tests with various allergen extracts including pollens, molds, house-dust mites, and storage mites (Allergopharma, Reinbek, Germany) were negative. RAST measurements with cow dander allergen disks were negative. The patient showed no evidence of sensitivity to milk. Symptoms were most frequently experienced indoors. A nasal provocation test was therefore performed with a house-dust mite (*Dermatophagoides pteronyssinus*) extract, but the result was negative. The patient was asked to keep a careful record of when and where symptoms occurred, and this revealed an association with working in a barn infested by houseflies (*Musca domestica*).

A conjunctival test was performed by touching the eye with the wing of a housefly for a few seconds. A strong conjunctival response with reddening of the eyes and free-flowing tears developed almost immediately. A similar test in three control patients was negative. A rub test on the volar surface of the forearms with a housefly was negative.

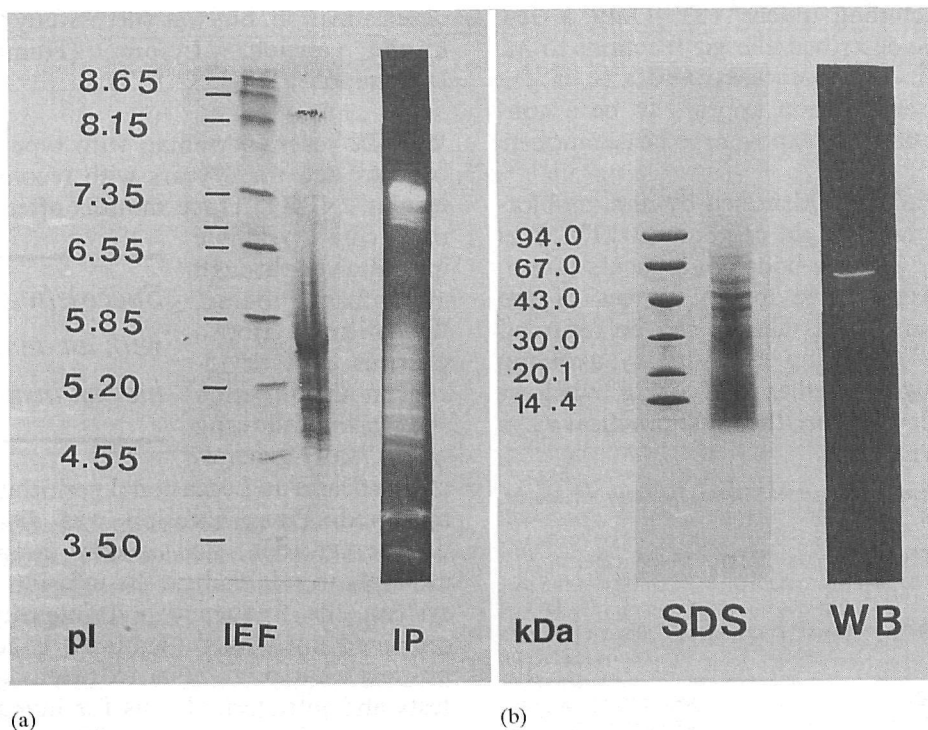


FIGURE 1. (a) IEF of housefly extract and immunoprint (IP) with patient's serum; left: marker proteins (pI: isoelectric points). (b) SDS-PAGE of housefly extract and Western blot (Wb) with patient's serum; left: marker proteins (kDa).

Skin tests were not performed. An allergen extract was prepared from houseflies caught in the barn where the patient worked. The houseflies were anesthetized with ether and mortared to a fine powder under liquid nitrogen. The powder was extracted in Coca's solution (5 g NaCl and 2.5 g NaHCO_3 /l distilled water) and stirred overnight at 6°C. The solution was centrifuged and filtered (0.22 μm), and the protein content was determined by a modified Lowry assay before storage at -20°C . Allergen disks, prepared by reacting 3 μg protein per disk (1), detected specific IgE in the patient's serum with a RAST class of 3, while a nonallergic control serum pool gave a RAST class of 0. Total serum IgE was 163 kU/ml as measured by ELISA (Allergopharma). The protein pattern of the housefly extract was determined by isoelectric focusing (IEF) of 50 μg protein in an agarose gel containing the Ampholine carrier Ampholyte pH 3.5–10 (Pharmacia, Freiburg, Germany). The protein bands were stained with Coomassie brilliant blue (E. Merck, Darmstadt, Germany). Most of the bands were found in the pI range 4.55–6.0 (Fig. 1a). An immunoprint was produced by capillary transfer of separated proteins onto a nitrocellulose membrane (Schleicher & Schüll, Dassel, Germany), incubation with the patient's serum (diluted 1:5), and incubation with ^{125}I -labeled anti-human IgE (Allergopharma 200 000 cpm/ml) at room temperature overnight. An autoradiograph,

produced by exposure to radiograph film (Kodak-X-Omat AR) over 14 days at -20°C , showed strong IgE binding in the pI ranges 4.6–5.8 and 6.8–7.5 (Fig. 1a).

The molecular weight profile of the extract was determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) of 25 μg protein in accordance with the method of Laemmli (2) (Fig. 1b). The molecular weights of the allergens were established by Western blotting of unstained proteins (electrotransfer) onto nitrocellulose membranes. An autoradiograph produced by the same procedure as for immunoprints after IEF identified allergens in the range 43–60 kDa. The most prominent band showed a molecular weight of 60 kDa (Fig. 1b). By SDS-PAGE, the protein pattern was about 14.4–70 kDa.

Many insects, including bees, wasps, chironomids, fire ants, and cockroaches, are known to cause allergic reactions. Several authors have reviewed

*Allergic
rhinoconjunctivitis in a
farm worker with IgE
antibodies to several
allergens, especially one
of 60 kDa, as
demonstrated by IEF
and immunoblotting.*

this subject, including Fuchs (3). Only a few publications have described allergic reactions to *M. domestica* (4, 5). In those cases, and also in the present report, sensitization appears to be a consequence of occupational exposure to large numbers of houseflies.

The principal allergen identified by immunoblotting had a molecular weight of about 60 kDa. It is premature to say whether body components (dust), secretions, or excreta are major sources of the allergens. At present, this allergy can be regarded only as "exotic". Limiting exposure by avoiding areas infested by houseflies and using window-screens to exclude them are the most practical ways of minimizing symptoms.

Key words: conjunctival provocation test; EAST; housefly allergy; immunoblot; *Musca domestica*.

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Desensitization-resistant insulin allergy

THE PREVALENCE of insulin allergy has considerably decreased with the availability of human recombinant insulins, and the disorder is now rare, although well described (1). Insulin allergy may present as immediate-type IgE-mediated local or systemic anaphylactic reaction, as delayed-type hypersensitivity, or, more rarely, as serum sickness. We here describe non-IgE-mediated allergy to human recombinant insulin which resisted insulin

desensitization, but was successfully treated with an insulin analog, Lyspro (Humalog®, Lilly, Indianapolis, IN, USA) (2).

■ A 22-year-old woman with type I diabetes had been treated for 8 years with recombinant human insulin (NPH). Three months after starting treatment with crystalline insulin given through an infusion pump, the patient developed pruritus and erythema at the injection site. In the following weeks, daily generalized urticaria and occasional periorbital angioedema appeared. Pump infusion was discontinued and despite various s.c. insulin preparations and attempts to reintroduce the infusion pump delivery system, the frequency and intensity of urticaria remained unchanged (Table 1). Except for weakly positive skin prick tests to protamine, skin prick tests and intradermal tests for human, porcine, or bovine insulins (Actrapid, Monotard, Insulatard, Actrapid MC, Ultralente MC), as well as for various additives (phenol, metacresol, and zinc), and specific IgE (human and porcine insulins, protamine) (Phadebas CAP, Pharmacia, Uppsala, Sweden), were negative.

After a first unsuccessful desensitization with human insulin (Actrapid Novo), two further desensitization attempts, one with porcine Actrapid, and another with human Actrapid over 2 weeks, also failed. Steroids were stopped, and an analog of human insulin, Lyspro (Humalog®, Lilly) (2), with reversed positions of amino acids lysine 28 and proline 29 on the insulin β -chain, was first administered s.c. over 12 h in increasing doses up to a plateau of 4 U every 3 h. Urticaria disappeared within 3 days, and Lyspro could be administered by pump infusion. Urticaria never recurred over a follow-up of more than 18 months.

■ The pathogenesis of our patient's hypersensitivity reaction remained unclear. There was no indication of IgE-mediated hypersensitivity, according to negative skin prick tests, intradermal tests, and IgE assays with insulin and additives. Furthermore, on several occasions, the patient continued to develop daily urticaria despite therapy with protamine-free insulins. Urticaria has also been related in some patients to a type III hypersensitivity reaction to insulin (1, 3). In our patient, we detected only low amounts of IgG anti-insulin antibodies (8-10% by radioimmunoassay, Sanofi-Pasteur, Marne-la-Coquette, France), within ranges which did not differ from those of asymptomatic patients, and

Successful treatment with an analog of human insulin.

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