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Whole bee for diagnosis of honey allergy

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Key words: honey allergy; IgE antibody; whole-bee body.

● POLLEN PROTEINS, mainly from *Compositae* plants, and glandular proteins from *Hymenoptera* insects are, as far as we know, the main allergens involved in allergy to honey (1–4). Honey, sac bee venoms, and honeybee heads are the main extract sources to prepare them (1,3,4). Apart from the bee venom extracts which can be found as high quality standardized reagents, the other two sources are raw materials; these are difficult to extract because of the relatively low protein content and variability in the composition of honeys, or difficulty in manipulating the bees in order to separate the structures containing the glandular tissues.

A 12-year-old patient was referred to our department (Hospital de Terrassa, Barcelona) with a clinical history of rhinitis. Allergen-specific IgE antibody and skin prick tests were positive to grass

pollens and *Chenopodium*, *Olea* and *Parietaria* pollens.

The patient's mother referred to two different episodes of angioedema with dysphagia, dysphonia, and dyspnea a few minutes after the ingestion of honey.

IgE antibody to honey and bee venom could not be found, but prick-by-prick with artisan honey was positive (>3 mm wheal diameter).

Honey extract was obtained from local artisan honey as previously reported (1), and the protein fraction was obtained by ammonium sulfate precipitation (DIATER Laboratories).

Prick test with the above-mentioned honey extract elicited a positive response (4 mm wheal diameter).

Whole-body bee extract was obtained from exhaustively washed frozen bees without venom sacs, by mechanical homogenization, aqueous extraction, dialysis and lipophilization (DIATER Laboratories).

SDS-PAGE IgE-immunoblot (Fig. 1) with honey extract using serum from a patient allergic to honey, and serum from a patient allergic to pollen, showed in both cases two components of 57 kDa and 29 kDa, respectively. Bauer et al. (4) found similar results to those described here with honey extracts. However, results of de la Torre et al. (1) do not coincide with ours regarding the size of components revealed, but they do report a similar phenomenon of IgE binding in serum from a patient allergic to honey and in controls. Inhibition of the immunoblotting to honey with whole-body extract becomes negative, indicating antigenic similarity

between the honey components revealed and proteins of the honeybee.

SDS-PAGE IgE-immunoblot with whole-body extract showed a high number of IgE binding components (57, 52, 38, 28, 26, 23, 20, 18 and 16 kDa). A similar pattern was found by Bauer et al. (4) in one patient when sunflower honey extract was used.

In spite of the fact that further studies are needed to analyze the nature and the origin of proteins causing honey allergy, the results reported here, and a review of the relatively scarce literature, suggest that bee products are the main cause of food allergy to honey.

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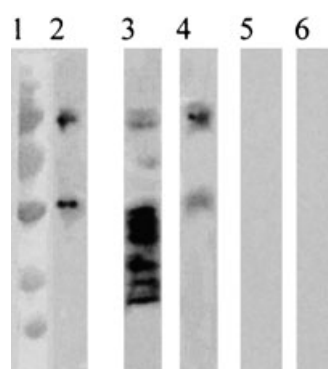


Figure 1. SDS-PAGE IgE-immunoblot. Lane 1: MW marker. Lane 2: honey extract and serum from a patient allergic to honey. Lane 3: Whole-body bee extract and serum from a patient allergic to honey. Lane 4: honey extract and serum from a pollinic patient not allergic to honey. Lane 5: whole-body bee extract and serum from a pollinic patient not allergic to honey. Lane 6: honey extract and serum from a patient allergic to honey inhibited with whole-body extract.

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Anaphylaxis to Pepto-Bismol

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Key words: anaphylaxis; bismuth subsalicylate; Pepto-Bismol.

● SALICYLATES ARE frequently used medications, and reactions to these medications and other nonsteroidal anti-inflammatory drugs (NSAIDs) are common, involving both allergic and nonallergic mechanisms (1,2). These reactions can be due to drug-specific IgE, or may be related to the nonspecific depletion of prostaglandin E_2 via inhibition of the cyclooxygenase enzyme (1).

First case of presumed allergy.

Bismuth subsalicylate, the active compound in Pepto-Bismol (Proctor and Gamble, Cincinnati, OH), is frequently used in the US for the prevention of traveller's diarrhoea and in the treatment of dyspepsia (3). Reactions known to be caused by bismuth-containing compounds include encephalopathy, erythroderma, and other skin reactions (3,4). To date, anaphylaxis to Pepto-Bismol has not been described. We present a case of anaphylaxis to Pepto-Bismol and demonstrate positive, reproducible skin prick testing (SPT) to this drug.

A 25-year-old man presented to our emergency department with acute urticaria. He had symptoms of acute gastroenteritis on the day before presentation, including nausea, vomiting and diarrhoea. He self-medicated with Pepto-Bismol, taking a total of eight caplets over the next 6 h. Approximately 30 min after the final dose, he experienced generalized urticaria for which he sought medical care. He denied symptoms of shortness of breath, wheezing, syncope, rhinorrhea, metallic taste or sensation of

impending doom. The patient had tolerated Pepto-Bismol in the past, as well as other NSAIDs, denied the use of other medications, and had not taken anything else by mouth (except water) for at least 12 h before the onset of urticaria.

Physical examination was notable only for generalized urticaria. The patient was admitted and treated with intravenous fluids and H_1 -blockers. Total serum tryptase at admission was elevated to 17 ng/ml (normal = 2–10 ng/ml).

The patient returned to our allergy clinic one month later for SPT to Pepto-Bismol. The skin test material was prepared in the following manner: two Pepto-Bismol caplets, each containing 262 mg of bismuth subsalicylate, were crushed and added to 10 ml of phosphate-buffered saline. After obtaining informed consent, SPT were performed using a prick and wipe method on the volar surface of the patient's forearm, using histamine sulfate 1 mg/ml and normal saline as positive and negative controls, respectively. SPT to the Pepto-Bismol solution caused a 9×12 mm wheal, surrounded by 20×25 mm erythema, along with appropriate responses to positive and negative controls. Five control subjects tolerant to Pepto-Bismol had negative SPT to the same solution. SPT were repeated two weeks later, showing a 6×8 mm wheal and a surrounding 14×18 mm erythema. A dot blot assay, as described previously (5), was unsuccessful in demonstrating *in vitro* IgE to Pepto-Bismol in the patient's serum.

It was concluded that our patient had allergic anaphylaxis to Pepto-Bismol based on the result of the serum tryptase as well as positive reproducible SPT (2). Our inability to demonstrate *in vitro* IgE is not surprising, given the inconsistent and difficult nature of measuring IgE antibodies against NSAIDs (6). Based on the proposed classification of reactions to cyclooxygenase inhibitors by Stevenson (6), our patient's reaction would be categorized as "single-drug anaphylaxis". In this type of reaction, previous sensitization has occurred, with the formation of drug-specific IgE, and cross-reactivity with other NSAIDs is unlikely (6).

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Post-streptococcal nonallergic urticaria?

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Key words: amoxicillin; antigen M; nonallergic urticaria; *Streptococcus pyogenes*.

● URTICARIA is apparently triggered by many causes, and the term chronic idiopathic urticaria has been used when no triggering factor can be identified (1). The term nonallergic urticaria is now preferred when evidence for an immunologic mechanism is lacking (2). Common antiallergic drugs are routinely used to treat the disease, but they have only a symptomatic effect. IgG autoantibodies directed against the IgE high-affinity receptor $Fc\epsilon RI$ (3) have been detected in 25–60% of subjects with urticaria, and several forms of autoimmunity have been associated with it. Infections from *Helicobacter pylori*