

an elimination-challenge procedure. The patient fulfilled all the diagnostic criteria of FIE (1, 5): vomiting and/or diarrhea occurring within 24 h of the challenge, stool containing blood and leukocytes, and a rise in PNL of $>3500/\text{mm}^3$. We also observed a rise in the eosinophil count.

Although the clinical picture in our patient seems to be clear, the mechanism remains obscure. As the target organ was the gastrointestinal tract, we think that the cow's milk antigens probably present in the amniotic fluid might have been responsible.

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Advantage of insulin lispro in suspected insulin allergy

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● RECENTLY, Lluch-Bernal et al. discussed insulin lispro as an alternative therapy in type 1 diabetes mellitus with insulin hypersensitivity (1). Here we report on the treatment by insulin lispro of a 54-year-old woman with type 2 diabetes mellitus, and insulin and protamine hypersensitivity.

Our patient developed gestational diabetes mellitus, which was treated by diet alone, during her first pregnancy at 23 years of age in 1968. After the delivery, her diabetes mellitus was classified as type 2 diabetes. Her good metabolic control was achieved by diet only. In 1978, oral antidiabetic agent therapy

Successful treatment of type 2 diabetes mellitus with allergy to human insulin.

became necessary. She had adverse reactions to chromium, pollen, dust, penicillin, acarbose, and metformin. Since she had an adverse reaction to metformin, therapy with sulfonylurea (glibenclamid) was introduced.

In 1998, the metabolic control maintained by diet and sulfonylurea treatment weakened (HbA1c level of 9.1%), and a commonly used combined therapy with daytime administration of sulfonylurea and bedtime administration of insulin was initiated. The administration of Humulin N insulin (Lilly) had to be discontinued because of allergic skin reaction. The patient developed local painless, nonitching, urticariform erythema with a wheal diameter of 15 mm immediately after the injection on the injection site. This lesion cleared up in a few hours. However, by 2–3 h after the injection, painful itching and induration appeared at the injection site, lasting for a few days.

We performed intradermal tests with human, bovine, and porcine insulin, as well as with various additives of insulin preparations (protamine, paraben, phenol, metacresol, zinc, and isophane), using the Novo Insulin Allergy Kit (Novo Nordisk). We also did an intradermal test with the new insulin analog, insulin lispro (Humalog, Lilly). We tested for the presence of the human insulin-specific IgE and IgG antibodies in the patient's plasma, using the indirect avidin-biotin and indirect immunofluorescence methods, respectively.

The intradermal tests were positive for all types of regular insulin tested and for protamine, but the reactions were different. There was an immediate reaction (urticariform erythema) to insulins and a delayed-type one to protamine (induration). These two types of reactions were similar to the adverse reactions previously described and produced by Humulin N insulin containing human insulin and protamine. The intradermal test was negative for insulin lispro. No circulating insulin-specific IgE or IgG antibodies were found in the patient's plasma.

Since the intradermal test with insulin lispro was negative, we chose it for the patient's therapy. Because of the delayed adverse reaction to protamine, bedtime sulfonylurea treatment was chosen instead of NPH insulin therapy for nighttime metabolic control. Good metabolic control was achieved with this combination (HbA1c level of 5.48%). Insulin lispro therapy was well tolerated in our patient with insulin and protamine hypersensitivity.

Insulin lispro is a rapid-acting insulin analog identical to human insulin except at positions B28 and B29. This structural modification of human insulin greatly reduced its self-association characteristic, causing very rapid absorption. There have been only a few immunologic studies on insulin lispro (1–7). In view of the published reports, we suggest that the

reduced immunogenicity of insulin lispro is related more to its faster absorption rate than to any changes in the immunogenic epitopes.

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Allergy to cypress pollen

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Key words: asthma; children; Cupressaceae; cypress.

● CUPRESSACEAE pollen allergy, which has been reported to cause winter conjunctivitis, rhinitis, and asthma in various parts of the world, is on the increase in the Mediterranean area (1-3). This study was conducted to determine the frequency of cypress sensitivity in children with asthma in southeast France.

Between October 1995 and October 1998, skin prick tests with the major aeroallergens (dust mites, cat and dog danders, *Blatella germanica*, *Alternaria*, and mixed grass pollen) and *Cupressus sempervirens* pollen were performed in 759 children with asthma living in Marseille and the surrounding area. Cypress extracts were 1:20 w/v, while the other extracts were standardized

In our region, 7.1% of children with asthma are allergic to cypress.

(Laboratoires Stallergènes, France). Atopy, defined by at least one positive skin response to allergens, was found in 469 children (61.8%). Among them, 54 children (39 boys), aged 26-184 months (95.4 ± 40.8), were sensitive to cypress extracts; i.e., 7.1% of all the children with asthma and 11.5% of the atopics. These 54 patients completed a questionnaire concerning asthma, symptoms suggestive of cypress allergy, and place of residence.

Except for two children with persistent asthma, the 52 remaining subjects suffered from frequent episodic asthma. They were all treated with inhaled corticosteroids, plus long-acting β_2 -agonists in 12 cases (22.2%). Asthma was mainly perennial but most of the symptoms were noted in winter, during which colds were described as exclusive triggers of acute episodes in the youngest. Antihistamines were prescribed in 18 children (33.3%) with allergic rhinitis. Two children reported spring conjunctivitis. Thirty-five children (64.8%) lived in apartments in the town center. Frequencies of responses to allergens in the 54 children are shown Fig. 1. Multiple skin sensitivities were found in 48 children (88.9%). The six children with isolated sensitivity to cypress were younger than the multiple-sensitive

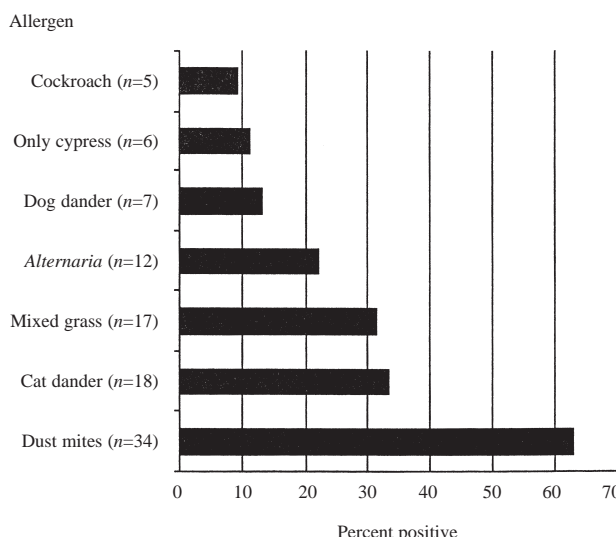


Figure 1. Frequencies of responses to allergens in cypress (*Cupressus sempervirens*)-sensitive children with asthma living in southeast France (n=54).