linked immunosorbent assay and DOT-blott to lispro, lispro with protamine and regular insulin was positive. A single 6-kDa allergen was detected by IgE-immunoblott. Both tests were performed in two control subjects, and one of them, an insulin-dependent diabetic male, resulted negative.

Insulin again became necessary and a desensitization protocol to regular human insulin was conducted. The initial dose of 0.001 IU was progressively increased to 5 IU in 3 days (9 IU cumulative dose) without pre treatment. The patient did not experience adverse reactions. He later received 8 IU t.i.d. of lispro insulin with good tolerance.

When lispro was increased to 15 IU t.i.d. he occasionally suffered local immediate reactions. As he received 34 IU, local reactions appeared daily and he developed hives two times in every place after injection of the insulin. Urticaria was resolved with cetirizine 10 mg and for the following 10 days no local reaction appeared.

Six months after the desensitization protocol was performed, a new allergologic study was performed. SPT to regular and lispro insulin remained positive and s-IgE to human insulin decreased to 6.04 kU/l. Local reactions were successfully avoided with daily cetirizine administration since then.

As human insulin is being used, severe allergic reactions are rare (1), with the analog lispro which is considered an alternative treatment for local reactions to human insulin (2). As its molecular form has a rapid subcutaneous absorption the reduced exposure time to cutaneous mast cells may decrease its allergenicity (3, 4). Yet, cross-reactivity between lispro and human insulin has been reported (3).

After the desensitization protocol, our patient remained asymptomatic for several weeks, being able to received lispro to control the diabetes and in 6 months a marked decrease (60%) of sIgE insulin levels was observed. The insulin desensitization was a success. Although cutaneous reactions reappeared, as it has been already reported (5), the use of antihistamines was enough to continue treatment with insulin.

We present an IgE-mediated anaphylaxis by a human insulin analog in a patient who had only received insulin lispro and had never interrupted it. A clinical cross-reactivity between human insulin and lispro, in our patient, was observed. A successful desensitization protocol was carried out. Although mild local reactions were resumed, it was successfully avoided with daily administration of antihistamines.

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Type-I hypersensitivity to ceftriaxone and cross-reactivity with cefalexin and ampicillin

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Key words: adverse reaction; ampicillin; cephalexin; ceftriaxone; hypersensitivity.

Anaphylactic shock to ceftriaxone.

Besides penicillins, cephalosporins represent the most commonly prescribed beta-lactams, capable of inducing IgE-mediated reactions. Ceftriaxone is a third-generation cephalosporin used for treating serious infections. There are three documented reports of IgE-mediated reaction to ceftriaxone, two with selective immediate hypersensitivity to ceftriaxone (1, 2), and one with cross-reactivity between ceftriaxone and cefotaxime (3).

A 3-year-old girl who had an anaphylactic reaction within 10 min after i.v. administration of the second dose of ceftriaxone (750 mg) for urinary infection is reported here. Symptoms included generalized urticaria, angioedema, rhinitis, dyspnea, shortness of breath, wheezing, tachycardia and hypotension. After treatment with anti-shock therapy, her symptoms were considerably reduced within 1 h and completely resolved after 12 h. She had no previous history of drug allergy or atopy and no family history of allergic disease. Six months later, the child was referred to this department in order to study the drug reactions and to determine safe alternative drugs for the future.

The child underwent prick and intradermal skin tests with standard concentration of penicilloyl-polylysine (Torlak, Yugoslavia), minor determinant mixture, penicillin G, penicillin V, ampicillin, amoxicillin, cephalexin, cefaclor, cefotaxime and ceftabuten diluted in 0.9% sodium chloride and administered at increasing concentrations, as previously described (3). Tests were considered positive when wheals larger than 3 mm in diameter for prick tests or greater than 5 mm in diameter for intradermal tests appeared 20 min later.

Commercially available assays for specific IgE (UniCAP System; Pharmacia, Uppsala, Sweden) were performed for penicilloyl G and penicilloyl V. Levels of specific IgE >0.35 kU/l were considered positive.

When both *in vivo* and *in vitro* tests were negative, single-blind, placebo-controlled challenges with progressively increasing amounts (0.01, 0.1 and 1.0) of the respective therapeutic doses of drugs

were performed as previously described (3).

The patient responded positively to prick testing with ceftriaxone (wheal 20 × 25 mm) at a concentration of 2 mg/ml, 10 min after application. Urticarial rash appeared on her arm, face and neck, which required immediate administration of an antihistamine. She also responded positively to skin testing with ampicillin at a concentration of 20 mg/ml (wheal 8 × 10 mm). Prick and intradermal histamine test produced wheals with maximum diameters of 5 and 10 mm respectively. Intradermal test with the above cephalosporins and semisyntetic penicillins were negative in 10 healthy control subjects, who had previously tolerated those drugs. All assays for specific IgE were negative.

Challenges were positive only to cephalexin. Within 20 min of receiving the second dose of the drug, she began to experience facial flush with intensive itching in the throat and eyes, swelling of the lip, and urticarial rash on her trunk. She was immediately treated with anti-shock therapy.

Clinical findings and positive skin tests with ceftriaxone and ampicillin, as well as positive challenges with cephalexin imply that the child developed type-I hypersensitivity. The observed cross-reactivity among drugs suggested presence of antigenic determinants unrelated to β-lactam ring but at the same time not completely side-chain specific. The patient reacted to cefalexin and ampicillin but not to cefaclor, the drugs with the identical side-chain. In fact, the difference between cephalexin and cefaclor is in only one functional group (methyl group instead of chlorine at R2 position of the thiazolidine ring).

To our knowledge, this is the first case of immediate hypersensitivity to ceftriaxone and cross-reactivity with cefalexin and ampicillin demonstrated in children.

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CD63 expression by flow cytometry in the *in vitro* diagnosis of allergy to omeprazole

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Key words: CD63; Drug allergy; FAST; *in vitro* diagnosis; omeprazole.

To date, six cases of anaphylactic reactions to protein-pump inhibitors have been reported in the literature (1–4). The presence of *in vitro* specific IgE against these drugs could not be proven in any of those cases. The usefulness of the basophil activation test in the *in vitro* diagnosis of allergic reactions to drugs has been described here.

Usefulness of the basophil activation test in the diagnosis of IgE-mediated allergic reactions to omeprazole.

A 75-year-old man received a prescription for omeprazole (Losec®) from his general practitioner. Fifteen minutes after the administration of the first tablet, he had scalp pruritus, lip angioedema and disseminated wheals. These symptoms decreased with i.v. dexchlorpheniramine and methylprednisolone, and s.c. adrenaline.

The patient had no personal or family background of atopy. He had had no food or drug allergy, or previous urticaria episodes. The patient had tolerated previous treatments with omeprazole.

One month after the reaction, prick test was performed with inhalant and food allergens with negative results. Prick test with omeprazole (4 mg/ml) resulted in a wheal and erythema similar to the histamine prick test (10 mg/ml). Omeprazole prick test in 20 atopic patients and 10 control health subjects caused no reactions.

Flow-cytometric cellular allergen stimulation test (FAST) was performed as previously described (5). The patient presented a positive response to both omeprazole concentrations tested (Table 1). FAST was performed in seven

Table 1. Percentage of basophil activation in FAST in controls and patient

	Basal (negative control) (% Act basoph)	Anti IgE (positive control) (% Act basoph)	Omeprazole (5 μg/ml) (% Act basoph/SI)	Omeprazole (1.25 μg/ml) (% Act basoph/SI)
Control 1	0.4	13.0	0.81/2	0.44/1
Control 2	0.4	6.7	4.18/9	1.35/3
Control 3	0.2	20.7	0.56/2	0.37/1.7
Control 4	0.1	14.8	0.23/2.3	1.53/15
Control 5	0.4	23.6	0.19/0.38	0.37/0.7
Control 6	1.4	97.4	1.34/0.95	2.22/1.5
Control 7	0.1	64.2	1.65/15	0.25/2.2
Patient	0.3	36.8	54.8/182	43.4/144

% Act basoph: percentage activated basophils.
SI (stimulation index): antigen-specific divided by basal response.