

generalized urticaria, hypotension, and bronchospasm.

Patient 3. After administration of cisatracurium, fentanyl, thiopental, and succinylcholine, a 57-year-old woman developed erythematous rash, hypotension, and sinus bradycardia.

Patient 4. Shortly after cisatracurium administration, a 51-year-old woman with multiple previous general anesthetics developed bradycardia and a drop in blood pressure from 180/90 to 90/50. Three weeks later, under the same anesthetic protocol, the patient developed massive bronchospasm, respiratory insufficiency, and shock.

Patient 5. After induction with propofol and atracurium, a 54-year-old woman with known history of asthma and arterial hypertension developed generalized urticaria. Four months later, after administration of cisatracurium, thiopental, isofluran, and remifentanyl, generalized urticaria and bronchospasm appeared despite premedication.

Cisatracurium, a 1*R*-cis 1'*R*-cis isomer of atracurium, has been introduced as an agent practically devoid of unspecific histamine liberation and cardiovascular side-effects

(1, 2). A recent study reports one patient developing bradycardia and truncal flushing 2 min after administration of cisatracurium (4). Our report summarizes five patients with symptoms ranging from urticaria, bronchospasm, and bradycardia to severe hypotension, revealing in all patients positive skin testing to cisatracurium. Cross-sensitization to atracurium was found in all patients. This finding is of clinical relevance, as, in one patient (case 5), a reaction to atracurium was followed by a severe reaction to cisatracurium despite pretreatment with antihistamines. In our patients, no skin reaction was observed when other muscle relaxants were tested, a finding which is consistent with previous reports indicating different rates of cross-reactivity between neuromuscular blocking agents of different chemical background (5, 6).

Our study suggests that although cisatracurium may have only very little if any unspecific histamine-releasing activity, it retains considerable potential for the induction of anaphylactic reactions.

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Accepted for publication 5 August 1999
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ISSN 0105-4538

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True monosensitivity to a tropical sole

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Key words: fish allergy; food allergy.

● FISH is one of the most frequent causes of food allergy. All fish species investigated so far contain a 12-kDa parvalbumin analogous to Gad c 1, the major cod allergen (1–3); as a consequence, most allergic patients report clinical reactivity to several fishes, and those who are clinically sensitive only to specific fishes (4, 5) are generally positive on both skin prick test (SPT) and RAST with tolerated species. Since parvalbumin is both heat-stable and resistant to proteolytic digestion, symptoms of fish allergy are generally systemic. We report an unusual case of immediate contact allergy induced by a single fish species.

I.C., a 28-year-old man, experienced an episode of severe oral itching associated with

Table 1. Clinical characteristics and results of skin testing in patients investigated

Patient no.	Age (years)	Sex	IgE (kU/ml)	Type of anaphylactic reaction	Cisatracurium skin testing	Atracurium skin testing
1	25	F	79.2	Hypotension	1 mg/ml prick	1 mg/ml prick
2	60	M	12.8	Urticaria, bronchospasm, hypotension	10 µg/ml i.c.	10 µg/ml i.c.
3	57	F	255.3	Flush, bradycardia, hypotension	10 µg/ml i.c.	10 µg/ml i.c.
4	51	F	28.0	Bronchospasm, hypotension, bradycardia	100 µg/ml i.c.	10 µg/ml i.c.
5	54	F	509.0	Urticaria, bronchospasm	10 µg/ml i.c.	10 µg/ml i.c.

laryngeal edema immediately after eating a small piece of (cooked) tropical sole (*Solea senegalensis*), which had been purchased as frozen filets at a local store. He was not eating other varieties of fish. The patient reported regular fish intake (including the tropical sole) without any problem

in the past.

Since both SPT with commercial extracts of cod, salmon, and tuna (Dome/Hollister-Stier 1:20 w/v) and RAST for *Anisakis*

simplex were negative, SPT with different fresh raw fishes were carried out. The offending tropical sole induced an extremely strong skin reaction (20×20 mm wheal with pseudopods), whereas no reactivity was observed to fresh cod and fresh lemon sole (*Limanda limanda*).

In view of the clinical findings, both RAST and immunoblot analysis with self-prepared extracts of the offending tropical sole as well as of control fishes were carried out. Lemon sole, tropical sole, and cod meats were homogenized and extracted 10% w/v by overnight incubation with 0.15 M phosphate-buffered saline (PBS), pH 7.2. Particulate material was removed by centrifugation at 18 000 g for 30 min; the supernatant was exhaustively dialyzed against PBS. Protein contents were 3.1, 3.5, and 2.1 mg/ml for the three fishes, respectively. Immunoblot analysis was carried out by conventional methods; the resolved proteins, transferred onto a nitrocellulose membrane, were incubated with patient's serum 1:2 in saturation buffer. Bound specific IgE were detected by peroxidase-conjugated anti-human IgE antibodies (1:1000 in saturation buffer) with an ECL blotting kit as substrate.

RAST showed a strong IgE reactivity to the tropical sole extract, but no reactivity to cod. Immunoblot analysis revealed marked IgE reactivity to a 6–7-kDa protein and weaker reactivity to a 40-kDa protein in tropical sole only (Fig. 1A); notably, both lemon sole and cod extracts contained a 6–7-kDa protein on

SDS–PAGE, but the patient's serum did not show reactivity to such proteins (Fig. 1A). As expected, a positive control serum from a cod-allergic patient reacted to a 12-kDa protein as well as to several other proteins with higher molecular mass in cod, lemon sole, and (more weakly) tropical sole as well (Fig. 1B). Two negative controls did not show fish reactivity (Fig. 1C and D).

In view of SPT and serologic findings, open oral provocations with cod, lemon sole, and swordfish were carried out on distinct days. After a negative SPT with the boiled fish under investigation, the patient was asked to chew about 10 g of fish for 1 min and then spit it out. In the absence of adverse effects, after 15 min, the patient was asked to eat 10 g of fish and was kept under observation for 1 h. The patient tolerated all three fishes without any problem.

This is one of the first cases of fish allergy characterized by clinical as well as immunologic monosensitivity. SPT and serologic methods did not detect any reactivity to cod, tuna, salmon, lemon sole, and swordfish; moreover, the ingestion of cod, lemon sole, and swordfish did not cause any adverse reaction. The clinical presentation (immediate oral itching and laryngeal angioedema, in the absence of both gastrointestinal symptoms and delayed skin reactions), suggests that the relevant allergen is heat-stable but pepsin-sensitive. Our

investigations revealed a strong IgE reactivity to a 6–7-kDa protein and a slightly weaker reactivity to a 40-kDa protein present in tropical sole; these proteins are clearly distinct from the major cross-reacting cod allergen Gad c 1 and seem to represent novel fish allergens.

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Accepted for publication 5 August 1999
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ISSN 0105-4538

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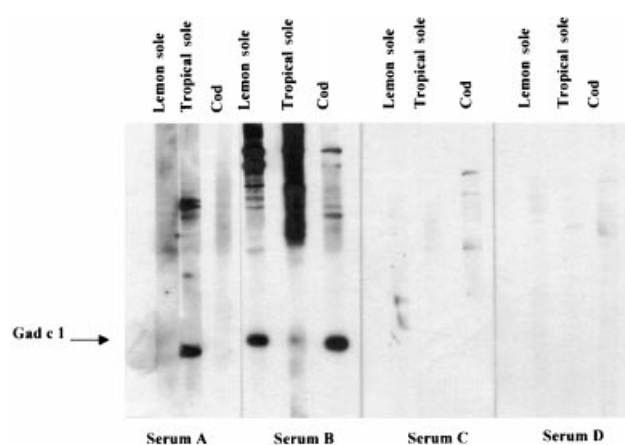


Figure 1. Immunoblotting profile of different fish extracts using sera from following: A) patient monosensitive to tropical sole; B) patient allergic to several fishes; C) allergic subject without fish allergy; D) normal subject.