

therapeutic alternatives, we decided to carry out a desensitization protocol (Table 1). Mesalazine solutions were prepared by the pharmacy at two concentrations (10 and 100 mg/ml) for easy dispensing. As the usual initial adult dose of mesalazine is 3 g daily in divided doses, it was the highest dose tested. The patient had no recurrence of the fever either during or after the mesalazine desensitization schedule (his current mesalazine daily regimen is 500 mg/8 h).

Drug fever is pyrexia that develops coincidentally with the administration of a drug and disappears with discontinuation, for which no other cause can be established by a careful examination and laboratory investigation. The pathogenesis of fever by drugs remains unknown in most cases. To our knowledge, this is the first case described in the literature of a patient with fever induced by mesalazine who was successfully desensitized. Although there are some cases reported of mesalazine causing fever associated with other symptoms – hypotension (1); vasculitic rash, arthritis, pericarditis, and pericardial effusion (2); and watery stools and vomiting (3) – in our case, all symptoms could be explained by fever alone.

Tolerance induction through exposure to graded doses has been proposed as a safe means to suppress the allergic response, although the mechanism by which tolerance is induced is unclear. Regarding our results, we think that desensitization is an important therapeutic strategy in cases similar to ours.

Although Nakajima et al. suggest that mesalazine is effective for the treatment of patients who are intolerant of sulfasalazine (4), other authors report allergic reactions to 5-ASA in patients who had previously experienced similar reactions to sulfasalazine, a fact which suggests that 5-ASA is responsible for these reactions rather than sulfapyridine (3, 5, 6).

In conclusion, mesalazine treatment can induce fever in some patients, but desensitization is possible.

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IgE response to *Anisakis* compared to seafood

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Key words: allergen; *Anisakis*; fish allergy; IgE; RAST; seafood.

● ANISAKIASIS is a human gastrointestinal disease caused by ingestion of larvae of the nematode family Anisakidae (especially *Anisakis simplex*) in raw or undercooked fish or squid. Typical symptoms are sharp epigastric pain or diffuse abdominal pain; anisakiasis is often misdiagnosed as appendicitis. On the other hand, acute allergic symptoms such as urticaria or angioedema, associated with the ingestion of mackerel or other fish, may be caused by type I allergic reaction. Kasuya et al.

(1) observed that *Anisakis* larvae were the real causative agent in some cases of urticaria following seafood ingestion. Montoro et al. (2) reported that recidivous acute urticaria in 16 patients was caused by allergic reaction to *A. simplex*, not to fish. Eosinophilic gastroenteritis was correlated with presence of *Anisakis* in a study by Gomez et al. (3).

Serologic diagnosis of *Anisakis* and seafood allergy is often based on quantification of specific IgE antibodies. In a study of normal (nonallergic) subjects, the incidence of IgE antibodies to *Anisakis* was 47/1008 cases (4.7%) (Garcia-Palacios et al. [4]).

However, there have been no studies on the comparative incidence of IgE responses to seafood and *Anisakis* in a large sample of allergic patients. Here we describe the incidence of serum IgE specific to *A. simplex*, various fish species, and squid in a Japanese population.

Sera from patients throughout Japan were collected from Mitsubishi Kagaku Bio-Clinical Laboratories during 1994–7. Initial diagnoses were urticaria or food allergy. Serum levels for antigen-specific IgE against *A. simplex*, mackerel, sardine, saurel (horse mackerel), salmon, cod, tuna, and squid were assayed with the Pharmacia CAP System FEIA (Pharmacia & Upjohn, Uppsala, Sweden). Results greater than 0.70 UA/ml (score 2) were considered positive, to avoid false positives, according to the manufacturer's instructions. The total number of single assays was 34 400, including 2022 combined assays on *Anisakis* and seafood allergens. The chi-square test was used for statistical analyses.

In single assays, specific IgE against *Anisakis* was detected in 629 out of 2108 patients (29.8%), an incidence significantly higher than that for any other allergen tested ($P < 0.001$ in all comparisons). For mackerel, CAP-positive specific IgE was observed in only 343 out of 8539 patients (4.0%). For sardine,

Among 34 400 cases, IgE positivity was 29.8% for *Anisakis*, significantly higher than for mackerel (4.0%) or other seafood species.

Table 1. Serum IgE levels against *Anisakis* and seafood allergens in combined assays

	<i>Anisakis</i> (+)	<i>Anisakis</i> (–)	Total
Mackerel (+)	27	14	41
Mackerel (–)	394	1209	1603
Total	421	1223	1644
Other seafood* (+)	6	8	14
Other seafood (–)	111	253	364
Total	117	261	378

*Sardine (n=88), salmon (83), tuna (54), saurel (100), and squid (53).

saurel, salmon, cod, tuna, and squid, 2355, 3635, 5117, 3211, 6311, and 4124 sera were tested, giving positive incidences of 7.0, 6.6, 7.4, 8.5, 6.2, and 10.0%, respectively. Table 1 shows comparison of IgE titers against *Anisakis* with those against various seafood species in the same patients. For example, 1644 cases were assayed simultaneously for *Anisakis*- and mackerel-specific IgE. Among these, 394 cases were *Anisakis* positive and mackerel negative, 14 cases were *Anisakis* negative and mackerel positive, 27 cases were positive for both antibodies, and 1209 cases were negative for both antibodies. For other seafood species tested, the IgE response against *Anisakis* was significantly higher than that against the seafood per se. *A. simplex* infestation is common in mackerel and other edible fish such as those listed in Table 1. For example, Murata (5) reported *Anisakis* infestation in 94–100% of mackerel samples from Tokyo Central Market in 1985–90. In view of our results, human sensitization to *Anisakis* allergen is considered to be more common than sensitization to fish allergens. Gomez et al. (3) reported that eosinophilic gastroenteritis is caused by *Anisakis*. Recurrent anaphylaxis is also caused by *Anisakis* in fish [Teresa Audicana et al. (6)].

The results of this and previous studies indicate that acute recidivous type I allergic symptoms following ingestion of *Anisakis*-containing seafood usually represent reaction to *Anisakis*-specific allergen, and that the patients are not sensitized to allergens of the seafood per se.

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Tetrazepam allergy

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Key words: allergy; benzodiazepines; diazepam; tetrazepam; type IV hypersensitivity.

● THE most frequent side-effects of benzodiazepines are neurologic and digestive. Although cutaneous disorders due to these drugs are rare, cases of contact dermatitis (1–4) and fixed eruption (5) have been described, and tetrazepam is frequently implicated in this kind of reaction.

Up to now, data on cross-reactivity reactions to different benzodiazepines have been lacking. However, in clinical practice, we frequently must

Patients diagnosed with tetrazepam allergy tolerated oral administration of diazepam.

offer an alternative medication to the patient after an allergic reaction to a benzodiazepine.

Patient 1. A 59-year-old man was treated daily with one capsule of Myolastan® (tetrazepam) for lumbar arthralgia. Eight days after beginning this treatment, he developed a pruritic maculopapular eruption that disappeared 1 week after the withdrawal of the medication.

Patient 2. An 80-year-old woman developed a maculopapular eruption with facial edema and fever after 3 months of treatment with tetrazepam and diclofenac.

Patient 3. A 68-year-old man with arthralgia presented a generalized pruritic micropapular rash 24 h after the ingestion of one tablet of tetrazepam. The rash cleared within 8 days.

Patient 4. A 65-year-old woman developed a widespread, pruritic, maculopapular eruption, with fever of 40°C, 15 days after beginning treatment with tetrazepam and nabumetone for severe lumbar arthralgia. The patient was hospitalized and treated with systemic corticosteroids, antihistamines, and antibiotics. Cutaneous lesions disappeared after 2 weeks with scaling.