

## Brief communications

### Recurrent anaphylaxis caused by *Anisakis simplex* parasitizing fish

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Hypersensitivity reactions to ingested material can produce a wide spectrum of symptoms, ranging from digestive and cutaneous manifestations to anaphylactic shock.<sup>1</sup> Such reactions can be caused by allergens present in the food itself (e.g., fish, eggs, or milk) or in contaminating substances, such as spices, preservatives, bacteria, and fungi. Another potential source is parasites in meat and fish.

Human anisakiasis is caused by infection with the larval forms of *Anisakis simplex*, which is a parasite of many species of fish (Fig. 1). The disease was first reported in the Netherlands<sup>2</sup> and has since been frequently reported in Japan.<sup>3,4</sup> Although the frequency of infection in Europe is apparently lower than that in Asian countries, the number of reported cases has been increasing during recent years, particularly in France.<sup>5</sup>

In 1990, Kasuya et al.<sup>6</sup> pointed out the allergenic potential of *A. simplex* and emphasized the need to consider it as an etiologic factor in urticaria related to the consumption of fish. The development of serologic tests for antibodies to *A. simplex* are useful tools for the study of allergic reactions to this parasite.<sup>7</sup>

#### CASE REPORT

A 52-year-old woman was referred to us because of periodic anaphylactic episodes. The patient has had four anaphylactic episodes, two in June 1990 and others in May and August of 1993. These began with intense itching in the axillary and groin foldings, eyes, and vulva, which spread with generalized urticaria and facial angioedema. These were accompanied by intense hypogastric pain with lumbar bilateral irradiation, rectal tenesmus, and abdominal cramps; the episode ended with

vomiting and diarrhea. All of these episodes occurred within 30 minutes after eating hake (*Merluccius merluccius* L), with the exception of the last, which occurred after the patient prepared fish for cooking. The possibility of ingestion of a small piece cannot be excluded. No further problems have occurred in the last 4 years, and the patient has tolerated consumption of hake and other kinds of fish and drugs.

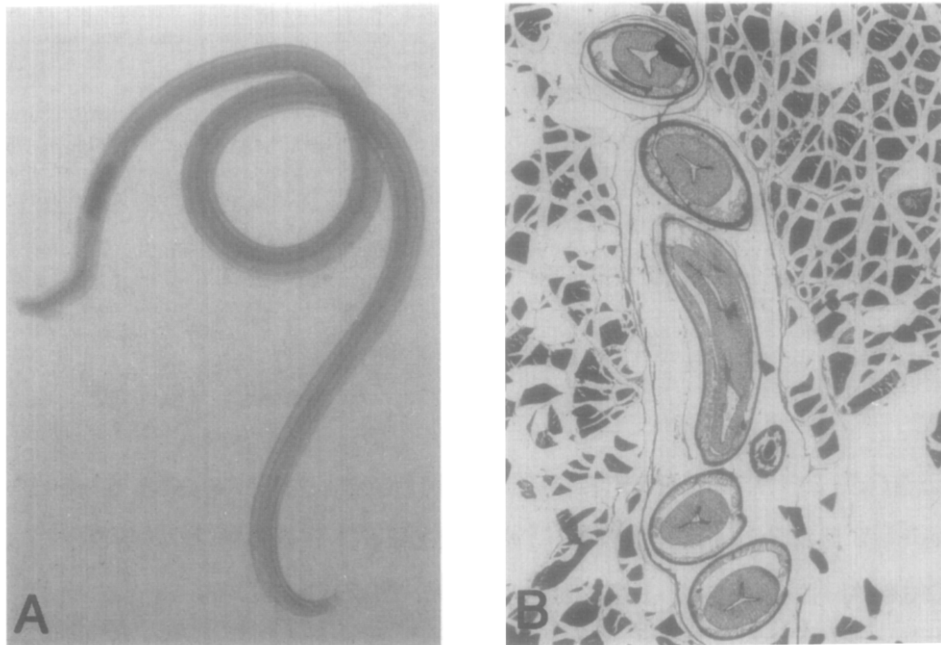
Physical examination revealed no signs of any abdominal conditions, but abdominal palpation induced pain on the left iliac fossa. Results of radiologic and laboratory tests, including serologic tests for hydatidosis were negative. The symptoms subsided within 2 to 3 hours after treatment with epinephrine, corticosteroids, and antihistamines.

Results of skin prick testing with foods (including hake, tuna, and sardines), drugs, and preservatives were also negative; and a diagnosis of idiopathic relapsing anaphylaxis was made. High levels (816 and 1051 kU/L) of total serum IgE were found on two occasions and therefore parasitologic examinations were initiated. Five fecal examinations revealed no infection, but specific IgE for *Ascaris lumbricoides* was detected in serum (4.01 kU/L, class 3) with the CAP System (Pharmacia, Uppsala, Sweden).

Hake is commonly infected with larvae of a nematode parasite belonging to the Ascaridoidae family, of which *A. lumbricoides* is a member, and the possibility of reactivity to *A. simplex* was considered. Larvae collected from muscle tissue of hake obtained locally were kindly identified by Dr. David I. Gibson, of the Natural History Museum, London, as those of *A. simplex* (Rudolphi, 1809) third-stage larvae. An extract of a sample of these was prepared (8 mg/ml protein, Lowry method) according to the method of Desowitz et al.<sup>7</sup> and stored at -40° C until required. A 1:100 dilution in saline solution was used for a skin prick test on the patient and control subjects. Samples of the extract, heated at 40° C for 10 minutes and 100° C for 20 minutes, were also applied to the patient. Histamine, 10 mg/ml, and saline solution were used as controls.

Positive reactions were observed with the three extracts in the patient (8 × 8 mm wheal with crude, heated, and boiled extracts and a 7 × 8 mm wheal with histamine), whereas more than 100 controls did not elicit any reaction. High specific IgE values to *A. simplex* (90.8 kU/L) were detected by means of the commercially

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**FIG. 1.** **A,** *A. simplex*, third-stage larvae extracted from an infected hake. The size of the worm is about 15 mm in length. **B,** Circular and longitudinal sections of the worm appeared in the muscular tissue of the hake, but no inflammatory reaction was observed. (Masson trichromic stain;  $\times 40$ .)

available CAP System. No IgE could be found against hake or cod.

## DISCUSSION

We report a case in which occasional severe hypersensitivity reactions were associated with fish consumption by a patient who normally showed no reaction to any type of fish. No reactions were found to spices, preservatives, or antibiotics; but the detection of an IgE response to *A. lumbricoides* suggested responsiveness to allergens of this or related nematode parasites. *A. lumbricoides* is a member of the Ascaridoidae family, and it has antigens that are immunologically cross-reactive with *A. simplex*,<sup>8,9</sup> a common parasite contaminant of several species of fish, including hake. Therefore it is likely that the patient's reactions were caused by ingestion of fish containing this parasite. If this is the cause, then the severity of the reaction is unusual, because only simple urticaria has been reported until now.<sup>6</sup> Also, hake has not before been implicated in anisakiasis or anaphylaxis, despite the fact that this species of fish is the most commonly parasitized fish in the North Sea.

Deep-freezing and cooking at temperatures higher than 60°C for 10 minutes is important in protecting against infection with live parasites<sup>5</sup> but

may not protect against reactions to their allergens. For instance, *A. simplex* contains an antigen that is immunologically cross-reactive with the ABA-1 allergen of *A. lumbricoides*, and heat treatment of this protein does not destroy its allergenic activity.<sup>8</sup> Furthermore, our observations on skin testing with deep-frozen and heat-treated extracts from *A. simplex* demonstrated the resistance of allergen from this source. Therefore anaphylactic reactions may occur after either infection or exposure to allergen only.

In cases of hypersensitivity reactions accompanying the consumption of fish, it is important to consider exposure to *A. simplex* allergens.

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## Generalized urticaria caused by sesame seeds with negative prick test results and without demonstrable specific IgE antibodies

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Investigation of patients with suspected food allergy comprises a clinical history, skin tests, and determination of specific IgE antibodies to food. However, a definite diagnosis can only be established by adequately performed oral challenge tests with the suspected allergens.<sup>1</sup> This is demonstrated by the case of a patient with generalized urticaria provoked by sesame seeds in whom no evidence of an IgE-mediated mechanism could be found.

### CASE REPORT

A 58-year-old man reported that he had facial erythema and swelling, generalized wheals, and itching all over the body about 30 minutes after he had eaten a slice of crisp bread with sesame seeds and one small salami sausage in June 1993. About 2 months later, a similar reaction occurred after ingestion of a buttered slice of bread containing sesame seeds. On both occasions the patient had been successfully treated with clemastine intravenously. The patient was otherwise healthy and did not take any medi-

cations. He had no personal history of hay fever, asthma, or atopic eczema.

Skin prick tests, performed in October 1993 with a standard series of common aeroallergens and food allergens (including sesame), yielded a 1+ reaction to *Dermatophagoides pteronyssinus* and baker's yeast. Crushed sesame seeds were tested after suspension in a drop of physiologic saline solution by means of the prick test technique without a positive result.

Intracutaneous skin tests with a standard series of foods yielded a 3+ reaction to malt, 2+ reactions to baker's yeast and shredded wheat, and 1+ reactions to garlic, cocoa, and orange. A commercial intracutaneous skin test solution for sesame seeds was not available in Germany.

Specific IgE antibodies could not be detected against shredded sesame (tested twice), wheat flour, rye flour, barley flour, oatmeal, malt, buckwheat flour, or baker's yeast (Pharmacia CAP system; Pharmacia, Uppsala, Sweden).

Oral challenge tests were performed in the hospital under careful control. Challenges were performed with 200 mg, 1 gm, and 2 gm of sesame seeds (each 30 minutes apart). Twenty-five minutes after ingestion of 2 gm of sesame seeds, the patient experienced flushing of the head, generalized itching, and whealing. The eruption cleared rapidly after intravenous administration of 2 mg of clemastine and 200 mg of prednisolone.

Additional challenges were performed with 600 mg, 3 gm, and 6 gm of shredded wheat; with one tenth, one half, and one whole small salami sausage (as ingested by the patient before the previous reaction); and with

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