

You can have fish allergy and eat it too!

Sami L. Bahna, MD, DrPH Shreveport, La

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Seafood (finfish and shellfish) is one of the most potent common food allergens. It can cause severe reactions, even after trivial exposures, such as hidden contamination of another food, indirect exposure, skin contact, or inhalation.¹⁻⁵ Because of its popular palatability and increasing demonstration of its nutritional values, seafood consumption has been on the rise. As a consequence, an increase in the prevalence of seafood allergy would not be surprising.

In this issue of the Journal, Sicherer et al⁶ present the first epidemiologic data on seafood allergy in the United States. The data are based on a well-designed, nationwide, cross-sectional, random telephone survey. As the authors admit, telephone questionnaires and self-reported allergies have some limitations. Nevertheless, the study revealed several worthwhile findings. I chose to comment on 4 issues in particular, namely prevalence, cross-reactivity, tolerance, and the effect of processing.

First is the prevalence of seafood allergy. A strong history of allergy to seafood (fish or shellfish) was reported by 2.3% of individuals, to fish in 0.4%, to shellfish in 2%, and to both in 0.2%. Because the subjects were neither evaluated for IgE sensitization nor verified by means of challenge testing, the reported figures can be overestimates, particularly for the claimed allergy to shellfish (2%). Perhaps shellfish is more allergenic than fish, although the latter is more consumed. However, the reported figures might not be too far from the true prevalence considering the increasing trends of seafood popularity and of the prevalence of food allergy, as has been reported for peanut allergy.^{7,8} Modification of the gastrointestinal function might be one of the contributory factors. A recent experimental study demonstrated that the concomitant administration of antacids enhanced the IgE sensitization of mice to the major fish allergen parvalbumin.⁹ Several antacid preparations are being widely

promoted to the public and are available without a prescription. It is of interest that almost 10% of the subjects with seafood allergy reported more severe reactions caused by inhalation or skin contact than by ingestion. Such an observation, if validated, should underscore the role of the respiratory tract mucosa and of the skin as routes of exposure in certain subjects. It is not known whether those particular patients were initially sensitized or primed through inhalation or epicutaneous contact. This phenomenon could be analogous to the oral allergy syndrome, in which patients typically ingest the offending food with impunity. Also, in baker's asthma patients wheeze on inhalation of wheat flour but tolerate ingested wheat well.

Second, seafood allergy is not universal. In this survey individuals who reported reactions to multiple species of the family were two thirds for fish, one half for mollusks, and one third for crustacea. This suggests that not all IgE-binding epitopes are shared by all members of the seafood family. Using IgE-binding cluster analysis of 10 allergens, Tanaka et al¹⁰ could classify seafoods into 4 groups: (1) salmon, sardine, and mackerel; (2) cod and tuna; (3) octopus and squid; and (4) crab and shrimp. The incomplete cross-reactivity among fish species has been previously reported.^{11,12} Actually, some individuals' allergy might be limited to one particular type of fish¹³ or shrimp.¹⁴ For many years, crustacea was thought to have no or minimal cross-reactivity with mollusks. In this survey, however, 14% of crustacean-intolerant individuals were intolerant to mollusks as well. Laboratory studies have demonstrated that certain allergens are shared between these 2 shellfish families.^{15,16} These findings should encourage expanding the evaluation of subjects with seafood allergy to include testing for multiple species. Negative results of skin testing or in vitro testing must be cautiously verified with appropriately designed, titrated, blind challenge testing. Such an approach would allow many individuals to enjoy eating certain kinds of fish or shellfish. Self-injectable epinephrine should be constantly available, particularly when the food is prepared in commercial facilities, to guard against possible errors or contamination. This survey revealed that self-injectable epinephrine was prescribed to only 1 of every 12 patients. Reviewing a sample of charts of patients who presented with food allergy at 21 emergency departments in different regions of the United States revealed that self-injectable epinephrine was prescribed to only 16%, with a range of 0% to 39%.¹⁷ Although there is a wide spectrum of food allergy manifestations, the constant availability of self-injectable epinephrine can be life-saving for patients who had experienced severe reactions.

From the Allergy/Immunology Section, Department of Pediatrics, Louisiana State University Health Sciences Center.

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Reprint requests: Sami L. Bahna, MD, DrPH, Allergy/Immunology Section, Department of Pediatrics, Louisiana State University Health Sciences Center, 1501 Kings Highway, Shreveport, LA 71130-3932. E-mail: sbahna@lsuhsc.edu.

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Third, seafood allergy is not forever. In the surveyed sample 3.5% of the subjects with fish allergy and 4% of the subjects with shellfish allergy reported loss of that allergy. This is in line with allergies to other foods, including peanut.¹⁸⁻²⁰ The duration of seafood avoidance until the attainment of tolerance is unknown but probably varies widely.^{21,22} It probably depends on several factors, such as age of onset, degree of sensitization, type of symptoms, severity of reaction, multiplicity of causative foods, and degree of avoidance. It is worth noting, however, that recurrence of intolerance might occur,²³ just as in the case of peanut.²⁴

Fourth is the effect of processing. This survey apparently did not inquire about the effect of various methods of processing on seafood allergenicity. Patients often report reactions to seafood when prepared in a certain way but not in another. This phenomenon is often attributed, perhaps erroneously, to possible contamination with another food allergen or additive. Any of boiling, frying, grilling, salting, drying, or freezing might reduce or increase allergenicity. Peanut is a classic example; its allergenicity is markedly increased by roasting but not by boiling or frying.²⁵⁻²⁷ The allergenicity to certain fish proteins seem to be reduced by heat.²⁸ Additionally, the survey did not provide information about intolerance to fish oils. Investigation of these 2 issues is likely to reveal information that can have a substantial effect on the prevention and treatment of seafood allergy.

Lastly, I would like to address adverse reactions to fish that mimic fish protein allergy. A negative skin test result or in vitro test result should alert the physician to possible reactions to substances in fish other than fish protein allergens. Bacterial spoiling of certain fish can produce histamine and cause scombroid fish poisoning.²⁹ In rare cases the allergy might be to a roe protein rather than a fish muscle allergen.³⁰ Several studies have demonstrated that certain patients with fish-related allergic reactions were actually allergic to the fish parasite *Anisakis simplex*.^{31,32} The extent of this problem in the United States is unknown and is worth investigating.

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