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Fish Allergy: Is It a Real Problem with Surimi-Based Products?

Key Words
Fish allergy
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Pollack
Surimi
Pizza topping
Hidden food allergens

Abstract
IgE-mediated reactions to fish are among the most commonly encountered food allergies in adults. This study was undertaken to assess fish-sensitive subjects' allergic reactivity to pizza toppings produced from Alaskan pollack derived surimi. Our results demonstrated that a significant proportion of fish-sensitive individuals react to pizza toppings by skin test and radioallergabsorbent test. Radioallergabsorbent test inhibitions also demonstrated that some cross-reactivity of pizza toppings with fish species exists, particularly with members of the Gadiforme family which includes Alaskan pollack. We believe that caution is advisable for fish-allergic subjects ingesting fish-based surimi products.

Introduction

Immediate reactions to seafood, particularly fish and crustacea, are among the most commonly encountered food allergies in adults [1, 2]. The prevalence of sensitivities to specific seafoods often depends on the eating habits of a particular region [3]. Current health concerns in North America about the fat and cholesterol levels of beef and pork products have caused fish to becoming increasingly more important as a food source. New food products, resembling beef or pork meat, are being developed. With fish in the form of surimi as a basis [4, 5], these foods are conceived as healthier, having reduced fat and cholesterol levels.

The Alaskan pollack, belonging to the Gadiforme family which includes cod, haddock, and hackes, is the major species of fish used for United States surimi production [5]. Since foodstuff, such as pizza toppings and hot dogs, can be made from surimi, consumers may not be aware that fish is a major ingredient. This could be a very serious dilemma for allergic subjects who develop profound reactions to fish and fish products. Our objective was to investigate the IgE reactivity of fish-allergic subjects to a pollack-based surimi imitation pork sausage pizza topping.

Materials ad Methods

Seafood Extracts

Pollack fillet, surimi, and uncooked and cooked (15 min at 180°C) pizza toppings were obtained from Seafest/JAC Creative Foods (Motley, Minn., USA). Extracts were prepared by homogenization of 500 g in 1 liter 0.1 *M* phosphate-buffered (pH 7.2) saline and a Waring blender (New Hartford, Conn., USA). Homogenates were extracted overnight at 4 °C under constant stirring. Extracts were centrifuged (70,000 g), supernatants concentrated on an Amicon YM1 filter (Amicon; Danvers, Mass., USA; molecular weight <1 kD, and recentrifuged (180,000 g). Aliquots were stored at –20°C. For radioallergabsorbent tests (RAST), uncooked salmon and tuna fillet were extracted in the same manner. Commercial extracts of codfish, flounder, and haddock were dialyzed against phosphate buffered saline, concen-

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trated by dialysis against Ficoll 400 (Pharmacia, Uppsala, Sweden), and stored at −20°C. The protein concentration was measured by applying the phenol reagent method (Sigma Diagnostics, St. Louis, Mo., USA). For preparation of skin test reagents, extracts were sterile filtered, checked for sterility, and aseptically added to skin test dropper vials (20 mg/ml of extract to an equal volume of sterile glycerol). The final extract concentration was 10 mg/ml in 50% glycerol.

Study Population

Thirty adults (19 females, 11 males, mean age 36.3 years, range 19–66 years) out of 38 potential subjects responding to local newspaper advertisement for fish-allergic patients were chosen for study based on responses to questionnaires. The subjects were skin prick tested with 16 commercial fish extracts – channel catfish, sardine/herring, black bass (Greer Laboratories), anchovy (Allergy Laboratories of Ohio), cod, flounder, halibut, salmon, tuna (Center Laboratories), haddock, mackerel, lake perch, snapper, sole, trout, and whitefish (Hollister-Stier) – and local common inhalant allergens – ragweed mix, Johnson and Bermuda grass, oak, house dust mite (*Dermatophagoides farinae*), cockroach mix, cat and dog epithelia, *Alternaria alternata*, and *Cladosporiuim herbarum* (Greer, Laboratories). A positive response was a mean wheal diameter of 2 mm or greater to the test antigen in subjects who were positive to the histamine control (1 mg/ml histamine diphosphate) and negative to the diluent (50% glycerol in phosphate-buffered saline). Results were recorded 15 min after testing.

RAST and RAST Inhibition

RASTs were performed by the method of Ceska and Lundkvist [6], using paper disks coated with 1 mg dry weight/disk. Duplicate antigen-coated disks were incubated overnight with 100 µl undiluted serum. After washing with saline (0.9%), 100 µl of ^{125}I-labelled anti-IgE (15,000 cpm/disk; Kallestad, Chaska, Minn.) was added and the disks incubated overnight. The disks were washed and bound ^{125}I (cpm) measured in a gamma counter (Gamma 5500; Beckman, Irvine, Calif., USA). The results were expressed as mean percent binding of total radioactivity added. RAST inhibition was based on the method of Gleich et al. [7], using pollack, surimi, uncooked and cooked pizza toppings, haddock, cod, flounder, tuna, or salmon. The concentration of inhibiting antigens, based on the protein concentration of each extract, ranged from 5 to 0.0005 mg/ml (10-fold dilutions).

Statistical Analysis

RAST inhibition dose-response curves were analyzed by multiple linear regression. Slopes and intercepts of heterologous inhibiting antigens were compared to those of autologous pizza topping inhibition by Dunnett's multiple-comparison test. Chi-square analysis was used to compare pizza topping skin test reactivity with that to other fish species.

Results

Skin Test and RAST

Twenty-seven of 30 (90%) fish-allergic subjects reacted by skin test to at least one fish, and 7 (23%) responded to all fish extracts. Twenty-five subjects (83%) had a positive skin test to at least two common inhalant allergens. Skin test and RAST reactivity to pollack, surimi, and pizza toppings are shown in table 1. Half of the fish-allergic subjects reacted to the pollack and surimi extracts. Fish-sensitive subjects' reactivity to the uncooked and cooked topping extract was 47 and 43%, respectively. RAST results of skin test positive and negative subjects demonstrated that subjects reacted more frequently to uncooked and cooked pizza topping than to pollack and surimi. Although 30% of the fish-allergic subjects had positive RAST to pollack and surimi, the least RAST reactivity was observed to surimi.

Table 1. Skin test and RAST reactivity of 30 fish-sensitive subjects to pollack and surimi extracts

	Positive skin test		Positive RAST[a]		Mean RAST, %	
	n	%	n	%	skin test positive	skin test negative
Pollack	15/30	50	9/30	30	9.8	1.3
Surimi	15/30	50	9/30	30	6.4	1.4
Topping	14/30	47	13/30	43	11.6	1.4
Topping[b]	13/30	43	10/30	33	10.4	1.3

[a] Percent bound >3.
[b] Cooked.

RAST Inhibition

RAST inhibition results are shown in figures 1 and 2. In figure 1, uncooked pizza topping RAST was inhibited by all extracts, although to varying degrees. Pizza topping extract demonstrated less inhibition when cooked than uncooked, suggesting that some allergens in the topping were destroyed by the cooking process. The least effective inhibitor of the pizza topping RAST was surimi. Figure 2 shows that different fish extracts inhibit the pizza topping RAST to varying degrees. The most significant inhibition was obtained with haddock, the least with cod.

Comparison between Skin Test and RAST

Skin test reactivities of uncooked and cooked pizza toppings were compared to each fish extract. In general, as significant correlation existed between skin prick test reactivity to pizza topping extract and commercial fish extracts. A highly significant correlation ($p>0.001$) was shown between skin test reactivity of uncooked and

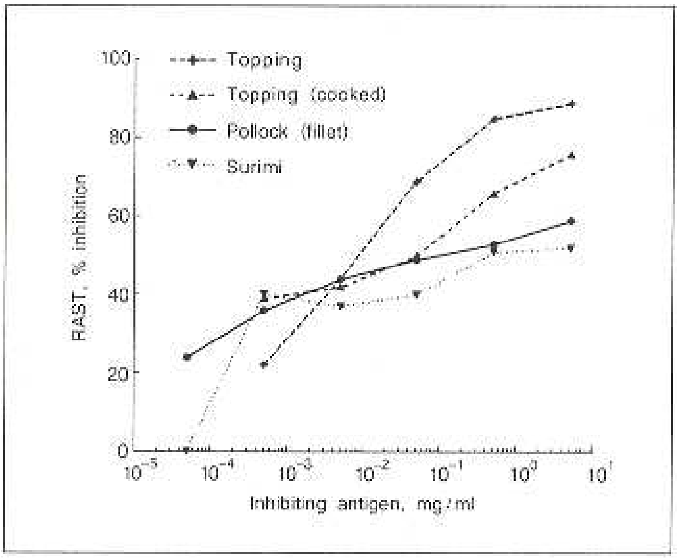

Fig. 1. Inhibition of uncooked pizza topping RAST which is maximally inhibited 89% by homologous extract, 76 by cooked pizza topping, 59 by pollack, and 52 by surimi.

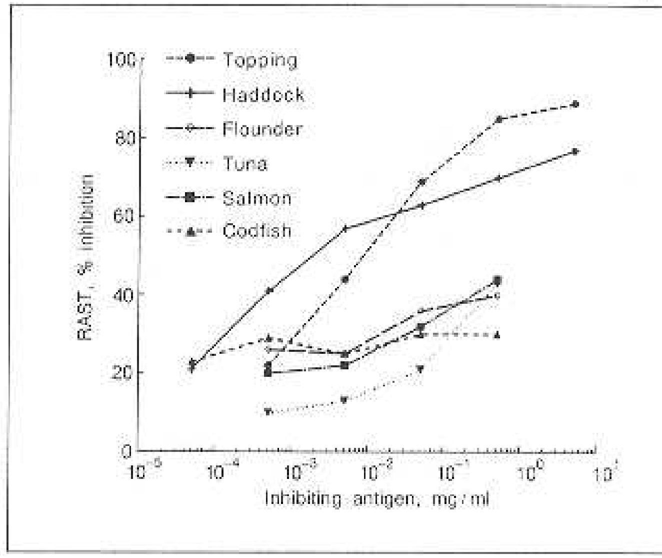

Fig. 2. Inhibition of uncooked pizza topping RAST which is maximally inhibited 89% by homologous extract, 77 by haddock, 44 by salmon, 43 by tuna, 40 by flounder, and 30 by cod.

cooked pizza toppings with surimi, pollack, haddock, mackerel, sole, and trout extracts. There was a correlation between both uncooked and cooked pizza toppings. No correlation existed with anchovy, catfish, cod, herring/sardine, perch, or tuna.

Discussion

Fish is commonly reported as an important cause of immediate food allergy [1–3]. Allergenic reactivity in fish-hypersensitive subjects is of increasing concern, since processed fish meat/surimi is used more frequently as a beef or pork substitute in processed foods [4, 5].

Our study demonstrated that the majority of fish-sensitive individuals, especially those with strong skin test reactivity to multiple fish species, have significant skin test reactions to Alaskan pollack, surimi, and pizza toppings. Although most of the subjects who were skin test positive to pizza topping reacted to species of the Gadiforme family, they also responded to a variety of other commonly consumed fish, such as perch, whitefish, snapper, trout, or bass. This suggests that fish-allergic individuals have the potential to react to pizza toppings.

In spite of the correlation of skin test reactivity, the relationship of pizza topping and fish allergens is not clear-cut. Several study subjects with little reactivity to fish extracts reacted strongly to pizza topping extracts, indicating that other non-fish-allergic components, such as seasonning, might be present in the pizza toppings. Interestingly, skin test/RAST reactivity to uncooked pizza topping did not always correlate with cooked. These observations suggest that allergenic activity in uncooked pizza topping may be destroyed by the cooking process. Still, allergenic activity remained in cooked pizza topping extract, as indicated by the RAST reactivity found.

Pizza topping skin tests, like other food or inhalant skin tests used to detect the presence of IgE antibodies, do not by themselves confirm a diagnosis. However, RASTs also demonstrated IgE antibody reactivity of the pizza toppings. Also, RAST reactivity correlated well with the skin test reactivity of most fish extracts. These results support the notion that fish-sensitive subjects may have positive IgE antibody responses to the surimi-based pizza toppings.

RAST inhibition results suggest that some cross-reactivity exists of pizza topping allergen and those of other fish species. The most significant cross-reactivity occurred between pizza topping and haddock and Alaskan pollack, both members of the Gadiforme family. Surprisingly, the least potent inhibitor was cod, also a member of the Gadiforme family. It is possible that cod proteins were less reactive than other fish proteins, since the extract was commercially prepared and not fresh.

Food allergy is a very complex process, and we still do not known the exact pathomechanism leading to a food-induced allergic response. The only method to definitely confirm that pizza toppings induce an immediate allergic reaction in sensitive individuals is to perform an oral, double-blind, placebo-controlled challenge [8]. Since almost one half of the fish-sensitive subjects reacted by skin test and one third by RAST to surimi-based pizza toppings, the potential for allergic reactions to them appears to be high. Although no challenges have been performed, we believe it advisable to caution fish-allergic subjects concerning the potential threat from ingestion of surimi-based products.

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