Fish Allergy: Fish and Products Thereof

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ABSTRACT: Allergy to fish is a common cause of IgE-mediated food allergic reactions especially in geographic regions where fish is an important dietacycompo.nent. Fish allergy is estimated to affect 0.4% of the total population in the United States. All species of fish are believed to be allergenic, but allergic reactions to fish reported in the medical literature are most commonly caused by cod and salmon. The major allergen In fish is a naturally occurring muscle protein called parvalbumln. Some evidence exists of allergic reactions to other fish proteins including collagen. This review addresses fish allergy and fish-derived ingredients, namely gelatin, isinglass, fish maws, ice-structuring protein, fish all, and Worcestershire sauce.

Keywords: food allergy, fish, parvalbumin, gelatin, collagen, isinglass, fish maws, ice-structuring protein, fish 011,Worcestershire sauce

Introduction

Ingredients derived from commonly allergenic foods, including fish, play important roles in processed foods. Although regulatory approaches vary from one country to another, some of these ingredients and their sources are not currently identified on the ingredient statements of packaged foods, especially in circumstances in which the ingredients function as processing aids having no functional effect in the finished product. In 1999, the Codex Alimentarius Commission adopted a list of commonly allergenic foods, including milk, eggs, fish, crustacean shellfish, peanut, soybeans, tree nuts, and wheat (CAC 1999). Codex recommended that member countries adopt this list and ensure that ingredient statements on packaged foods declare the presence of these commonly allergenic foods and of ingredients derived from these foods. Several countries, including Australia and New Zealand, have moved to adopt a list that would require labeling of ingredients sourced from commonly allergenic foods including fish. This review article is intended to address ingredients derived from fish and to examine whether all ingredients derived from fish are potentially hazardous to fish-allergic consumers.

Several widely used food ingredients are derived from fish. Adoption of the Codex guidelines would mandate that the fish origin of these ingredients be declared on the ingredient statement of any packaged food product in which these ingredients were used. For example, fish gelatin may be used to encapsulate certain vitamins and isinglass may be used as a fining agent in ales, wines, and champagnes. Currently, these ingredients are not identified on product labels in most countries because they are considered processing aids. Adoption of the Codex guidelines will mandate declaration of these ingredients and their fish origin. Because fish-allergic individuals avoid all products containing fish, these products must then also be avoided. Will this situation benefit fish-allergic individuals? Are all ingredients derived from fish allergenic to fish-allergic consumers?

Fish allergy

Allergy to fish is a common cause of IgE-mediated food-allergy reactions, especially in geographic regions where fish is an important dietary component. Symptoms of fish allergy, similar to other IgE-mediated food allergies, usually appear immediately (minutes to an hour) after exposure and range from mild to life-threatening. Fatal reactions have occurred as a result of allergic reactions to fish (Yunginger and others 1988; Bock and others 2001). The prevalence of adverse reactions to fish could be expected to increase because of worldwide increases in seafood consumption and technological advances in fish processing (O'Neil and Lehrer 1995).

Numerous studies have attempted to estimate the prevalence of fish allergy. A recent random digit–dial telephone survey in the United Stated estimated the prevalence of fish allergy in the United States at 0.4% in the overall population (Muñoz-Furlong and others 2004). Studies from Finland have estimated that 3% of 3-y-old Finnish children were fish-allergic (Saarinen and Kajosaari 1980); in an extrapolation study in Italy, 0.4% to 0.5% of children in the general population were allergic to codfish (de Martino and others 1993). Radioallergosorbent testing (RAST) revealed that 0.3% of an adult population in Sweden were fish-allergic (Bjornsson and others 1996). Although the exact prevalence of fish-allergic individuals is not firmly established, it is listed among the most common of allergenic foods (Bousquet and others 1998).

Although not specifically confirmed by clinical investigations, fish-allergic individuals are believed to be potentially reactive to all species of fish. Clinical studies of fish allergies have most commonly involved allergic reactions to cod and salmon. Table 1 presents an overview of numerous fish species implicated in allergenic reactions.

Cross-reactivity among various fish species is believed to result from the presence of the major fish allergen, parvalbumin, in the muscle tissue of all fish species (Bernhisel-Broadbent and others 1992). Some studies have shown serological cross-reactivity in some fish species that did not elicit clinical reactivity in oral challenges, whereas other studies have shown serological and clinical cross-reactivity among various fish species (Bernhisel-Broadbent and others 1992; Hansen and others 1997; Bugajska-Schretter and others 2000). These results suggest that parvalbumin (Gad c 1) is a pan-allergen present in most, if not all, fish species, whereas some fish species may contain additional species-specific allergens.

Hansen and others (1997) demonstrated IgE cross-reactivity in all 8 adult codfish-allergic individuals tested using double-blind placebo-controlled food challenge (DBPCFC), skin-prick tests, his-

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Table 1—Overview of fish varieties implicated in allergenic reactions[a]

Fish	Symptoms	nr	Age of subjects (y)	Oral challenge	Skin test	RAST	Other	Reference
Salmon, flounder, shad (bony fish), cod, mackerel, bluefish, bass, carp, tuna, sturgeon	Urticaria, asthma, angioedema	6	unknown		+		In vitro neutralization	Tuft and others 1946
Cod, salmon	Urticaria, asthma, rhinitis, nausea, eczema, vomiting, cough, laryngeal reaction	89	0 to 13 y	Single blind	+			Aas 1966b
Halibut	Dyspnea, urticaria, hypotension, angioedema, diarrhea, nausea, emesis	1?	27-y-old male		+		Histamine release	Golbert and others 1969
Cod	History of anaphylaxis	26	16 mo to 19 y	DBPCFC	+			Sampson 1983
Unknown	History of anaphylaxis, laryngeal edema, death due to fish	1	31-y-old male				Stomach contents examined	Yunginger and others 1988
Bass, eel, dentex (dog's teeth), cod, sole, tuna, carp, dogfish, mackerel, anchovy, sardine, red gilthead (bream), perch, tench (doctor fish), trout mullet, salmon	Urticaria, angioedema, vomiting, asthma, AD	20 cod allergic	2 to 8 y		+	+	RAST inhibition	de Martino and others 1990
Catfish, bass, perch[b], mackerel, tuna, salmon[b] trout, cod[b], flounder[b], sardine, snapper[b], mahi mahi[b]	Oral pruritus, urticaria, nausea, vomiting, diarrhea, angioedema, urticaria	11	6 to 20 y	DBPCFC	+		Open challenge, immunoblotting	Bernhisel-Broadbent and others 1992
Cod	Itching, diarrhea, angioedema, rhino-conjunctivitis, vomiting, pruritus	10	21 to 31 y	DBPCFC (7 +)	+	+		Hansen and Bindslev-Jensen 1992
Bass, dentex, sole, tuna	Asthma, urticaria, rhinitis, conjunctivitis, angioedema, AD	68 cod allergic	6 to 19 mo		+	+		de Martino 1993
Flounder	Respiratory and GI symptoms	320 (29 fish allergic)	6 mo to 30 y	DBPCFC			Pulmonary function tests	James and others 1994
Cod, mackerel, herring, plaice		8 cod allergic	21 to 31 y		+	+	SDS-PAGE, immunoblotting, histamine release, RAST inhibition	Hansen and others 1997
Catfish, cod, snapper, tuna	History of anaphylaxis, angioedema,	10 fish allergic	2 to 56 y	DBPCFC	+	+	Open challenge	James and others 1997
Yellowtail, hake	Oropharyngeal itching, swelling	(105 fish allergic); 9 given food challenge	7 to 74 y	DBPCFC	+	+	Western blot	Zinn and others 1997
Cod, tuna, salmon, perch, carp, eel	History of clinical symptoms	30 fish allergic				+	Immunoblotting, RAST inhibition	Bugajska-Schretter and others 1998
Catfish, cod, snapper	Urticaria, conjunctivitis, rhinitis, emesis, flushing, oral allergy syndrome, pruritus, dyspnea	22	17 to 39 y	DBPCFC	+	+		Helbling and others 1999

[a]AD = atopic dermatitis; DBPCFC = double-blind placebo-controlled food challenge; GI = gastrointestinal; RAST = radioallergosorbent testing; SDS-PAGE = sodium dodecyl sulfate-polyacrylamide gel electrophoresis.
[b]Showed +.

tamine release tests, specific IgE, sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), immunoblotting, and RAST to 4 species of fish: cod, mackerel, herring, and plaice.

In a prospective study by Bernhisel-Broadbent and others (1992), 11 fish-allergic individuals were tested with DBPCFC and open challenges to 4 to 6 fish species. All of the patients were able to consume at least 1 or more other fish species without any adverse reactions. Thus, individuals with reactivity to parvalbumin likely need to avoid all species of fish, whereas individuals who appear to be reactive to more species-specific allergens seem able to tolerate some species of fish. de Martino and others (1990) examined whether codfish-allergic children had an increased frequency of positive skin tests to other species of fish. Of 60 children, 20 were cod-allergic, whereas 40 were not but did have a food allergy to 1 or more of 17 other fish species that were investigated. The cod-allergic children showed a higher frequency of skin tests to eel, bass, dentex, sole, and tuna; cod-negative children exhibited negative skin tests for all species except sole, tuna, and dentex.

More research is needed to investigate the clinical reactivity of various fish species. However, fish-allergic individuals would be advised to avoid all species of fish, although some fish-derived ingredients may be safe if they do not contain parvalbumin or other fish allergens. Research is needed to allow diagnostic evaluation of individual fish-allergic patients to determine whether certain species of fish might be safe to consume.

Diagnostically, fish allergy must be distinguished from scombroid fish poisoning. Scombroid fish poisoning is an allergy-like intoxication with symptoms that mimic IgE-mediated food allergy that is caused by ingestion of fish that are contaminated with elevated levels of histamine as a result of bacterial spoilage (Stratton and Taylor 1991). Certain fish species including tuna, mackerel, bluefish, mahi-mahi, and sardines are more commonly implicated than other species (Lehane and Olley 2000).

Fish allergens

The major allergen in codfish, namely Gad c 1, is the most studied and well-known fish allergen. The protein has been identified, purified, and characterized by a series of studies by Aas and later Aas and Elsayed in the 1960s and 1970s (Aas 1987). Gad c 1 is a member of the parvalbumin family found in muscle tissue of amphibians, fish, and other animals. Parvalbumins are acidic proteins with molecular weights in the range of 11000 to 12000 Da that control the flow of Ca^{2+} in and out of cells. Once believed to occur only in white muscle of lower invertebrates, parvalbumin has been isolated from skeletal muscle in higher vertebrates (Gazzaz and Rasco 1993). Gad c 1 is a stable protein, resistant to denaturation as defined by loss of IgE binding at extremes in pH, temperature or random folding of the molecule when exposed to dissociating agents (Aas and Elsayed 1975). Gad c 1 is also comparatively resistant to pepsin digestion (Bindslev-Jensen and others 2003).

All cod-allergic patients react to Gad c 1 (Elsayed and Aas 1971; Hansen and others 1997). The IgE-binding epitopes (regions) of Gad c 1 appear to be linear sequences of amino acids and not conformational (3-dimensional) epitopes (Elsayed and Aas 1971). Serological and clinical cross-reactivity exists between fish species, implying that parvalbumins are the major allergens of most fish species. Gad c 1 shares amino acid sequence homologies in the 34% range with parvalbumins from carp, hake, and whiting (Elsayed and Bennich 1975; Lindstrom and others 1996). The allergens from other fish species are also parvalbumins including salmon (Sal s 1), horse mackerel (Tra j 1), and bigeye tuna (Thu o 1) (Shiomi and others 1998, 1999; Van Do and others 1999).

In addition to the major allergen, Gad c 1, evidence suggests that minor allergens may exist in codfish that may be recognized by certain cod-allergic individuals (Aas 1966a; Aukrust and others 1978). A study of minor codfish allergens identified 3 additional allergens of 28, 41, and 49 kDa with a pool of sera from cod-allergic patients and anti-parvalbumin monoclonal antibody. The 28-kDa and 49-kDa proteins were not further evaluated; however, the 41-kDa protein was dissimilar to Gad c 1 with respect to molecular weight (11 to 12 kDA compared with 41 kDa), isoelectric point (pI 4.75 compared with pI 5.8), and a higher proportion of hydrophobic amino acids (45% compared with 59%), and cod-allergic sera demonstrated IgE binding to this protein (Galland and others 1998).

Hamada and others (2000) identified a high-molecular-weight allergen recognized by 1 fish-allergic serum sample in surimi made from walleye pollack. SDS-PAGE, immunoblotting, and amino acid analysis identified the allergen as collagen. In a separate study, a high-molecular-weight allergen was detected after 5 protein fractions were prepared from bigeye tuna muscle (Hamada and others 2001). SDS-PAGE, immunoblotting, and amino acid analysis identified the myostromal protein fraction as collagen. Five of 8 sera samples obtained from individuals known to be fish-allergic reacted in a dose-dependent manner to bigeye tuna collagen in amounts of 0.01 μg to 10 μg using ELISA analysis (Hamada and others 2001). Previously, Yamada and others (1999) analyzed allergens from albacore and yellowfin tuna by immunoblotting and identified 2 IgE reactive proteins of 120 and 240 kDa. Although not further investigated, this suggests collagen as the likely allergen.

Minimal eliciting dose

Exposure to small quantities of an allergenic food can elicit an adverse reaction in individuals with an IgE-mediated food allergy (Taylor and others 2002). The threshold dose is defined as the lowest amount of offending food needed to elicit mild, objective symptoms in the most sensitive individuals (Taylor and others 2002). Precise threshold doses of allergenic foods have not been fully investigated and may vary from individual to individual. Hansen and Bindslev-Jensen (1992) examined 10 adults with immediate allergic reaction to cod. Doses eliciting symptoms varied between 6 mg and 6.7 g of fresh cod determined by DBPCFC. On the basis of this study, the minimal eliciting doses for fish are finite and appear to be in the milligram range for the most sensitive patients (Hansen and Bindslev-Jensen 1992). Other studies indicate that threshold doses for allergenic foods are finite although examination of additional subjects is warranted before threshold doses can be selected for common allergenic foods (Taylor and others 2002; Morisset and others 2003).

Ingredients derived from fish

Several food ingredients are derived from fish. These ingredients include fish gelatin, isinglass, fish maws, ice-structuring protein, fish oil, and Worcestershire sauce. The Codex Alimentarius Commission has recommended the labeling of fish and products thereof because of the notion that fish-allergic individuals are allergic to ingredients derived from fish (CAC 1999). However, it is important to note that the allergenicity of ingredients derived from fish has not been proven by clinical research in most cases.

Fish Gelatin. Fish gelatin is derived from collagen obtained from fish skins and bones. Collagen is a large extracellular rod-like protein composed of 3 hydroxyproline-rich polypeptide chains that wrap around each other creating a very stable triple helix known as tropocollagen. Collagen is an intercellular component of connective tissue that provides strength and durability, supports soft tissues, and provides reinforcement during compression. At least 20 different forms of collagen have been isolated and identified from both animal and human tissues with variations in the primary amino acid sequence (Bailey and Light 1989; Lee and others 2001). Collagen and products derived from collagen also serve a variety of useful functions in numerous industries including medicine, pharmacy, cosmetics, photography, and the food industry. Globally, the largest user of gelatin is the food and food-processing industry (Dinker 2004). More than 110-million pounds of gelatin is produced in the United States annually (GMIA 2004).

Gelatin is produced by controlled hydrolysis using an acidic or alkaline extraction process with hot water from collagen from various animal sources including bovine, porcine, and fish skin and bones (Norland 1990; Leuenberger 1991). All gelatins are composed of the same 20 amino acids, but there is variation in the proline and hydroxyproline concentration, which determines gelation (Norland 1990). Fish gelatin possesses a different chemical structure from mammalian gelatins, with varying amounts of the imino acids, proline and hydroxyproline, and may prove useful in numerous applications (Leuenberger 1991). Gelatin from cold-water fishes has lower melting and gelling temperatures than gelatin from bovine or porcine because of a lower imino acid content. The colder the water environment, the lower the imino acid content of fish gelatin (Gudmundsson 2002).

Acting as a stabilizer, gelatin is widely used as an additive to live vaccines and food products. Whereas collagen forms fibrils and precipitates from solution, gelatin remains soluble. Beef and pork constitute the major sources of gelatin but, because of religious restrictions, a need was created for alternatives. Fish gelatin is acceptable in both Islam and Judaism (Regenstein and others 1996). In addition, fish skins and bones are plentiful from several species of commercially harvested fish. Primary sources of fish gelatin include cod, pollack, haddock, hake, tilapia, and tuna (Norland 1990; André and others 2003).

Allergic reactions to ingested gelatin are infrequently reported. However, numerous reports exist of allergic reactions to injected gelatin in the form of measles-mumps-rubella vaccines (Kelso and others 1993; Sakaguchi and others 1997; Nakayama and others 1999), encephalitis vaccine (Sakaguchi and others 2001), as well as intravenous (Sakaguchi and others 1999) and surgical products (Purello-D'Ambrosio and others 2000; Sakaguchi and Inouye 2001) containing primarily beef and pork gelatin.

Few reports indicate allergy from ingesting gelatin-containing foods, even in those individuals who reacted upon injection. Sakaguchi and others (1996) identified 7 of 24 children with anti-gelatin IgE who reacted to gelatin-containing foods. Symptoms included systemic urticaria, vomiting, wheezing, and angioedema. Laryngeal edema with obstruction occurred in 1 child. Kawahara and others (1998) identified 11 of 525 atopic children with gelatin-specific IgE and high titer IgG with adverse reactions to gelatin; 5 of 11 experienced anaphylaxis: 2 of 5 to gelatin-containing vaccine and 3 of 5 to gelatin fruit gums. Wahl and Kleinhaus (1989) reported a case of oral allergy and urticaria after a woman ingested fruit gum candy. RAST inhibition determined IgE to gelatin as well as cross-reactivity between gelatin-containing products and modified gelatin used in plasma substitutes.

Although reports of adverse reactions because of fish gelatin do not exist, recent interest in the possible allergenicity of fish-derived ingredients has prompted investigation. Fish gelatin–specific IgE antibodies have been identified in fish-allergic patients. Sakaguchi and others (2000) demonstrated IgE antibody to fish gelatin in 3 subject groups: 10 patients with fish allergy and specific IgE to fish meat, 2 patients with fish meat allergy and bovine gelatin allergy as well as specific IgE to fish meat and bovine gelatin, and 15 patients with atopic dermatitis and specific IgE to fish meat. Specific IgE to fish gelatin was found in 3 of 10 patients with fish allergy and specific IgE to fish meat, 2 of 2 patients with fish and bovine gelatin allergy and specific IgE to fish and specific IgE to bovine gelatin, and 5 of 15 patients with atopic dermatitis and specific IgE to fish meat. Patients with allergy to injected gelatin may have IgE that cross-reacts with fish gelatin, but this does not necessarily imply that they would react adversely upon ingestion of fish gelatin. It is possible to have specific IgE to a particular food but not necessarily exhibit allergic symptoms upon ingestion (Sampson and Ho 1997). Also, the source of the fish gelatin used by Sakaguchi and others (2000) was not a commercial product. The possibility exists that the gelatin was contaminated by other fish allergens resulting in the positive IgE-binding responses occurring with individuals with documented fish allergy.

André and others (2003) analyzed serum samples of 100 children and adults with IgE reactivity to various species of fish and tested for IgE antibodies to tuna skin–derived gelatin, tuna flesh, tuna skin, and bovine and porcine gelatins. SDS-PAGE and immunoblotting showed only 3 of 100 serum samples with evidence of reactivity to tuna skin–derived gelatin, and there was no evidence of cross-reactivity between fish, bovine, and porcine gelatin. In further testing of the 3 subjects that showed reactivity to gelatin derived from tuna, skin prick tests for tuna skin gelatin were negative and a food challenge test using 5 g of tuna gelatin was also negative.

In a DBPCFC study, 30 codfish-allergic patients were given a cumulative dose of 3.61 g of codfish-derived fish gelatin with no adverse reactions (Hansen and others 2004). From this study, it can be concluded with 95% certainty that 90% of fish-allergic individuals do not react to the ingestion of 3.61 g of fish gelatin. One mild, subjective reaction was observed to ingestion of a cumulative dose of 7.61 g of codfish-derived fish gelatin among these 30 patients (Hansen and others 2004).

Commercially, fish gelatin is derived from several fish species. Arguably, fish gelatin from different species is probably similar because the starting material in all cases would be fish-derived collagen, and similar processes are used to derive functional fish gelatin from the collagen. For that reason, information on adverse reactions to fish gelatin can be considered collectively because fish gelatin from all fish species should be comparable. This presumes that differences in proprietary processes for deriving fish gelatin used by different manufacturers do not have any influence on the potential allergenicity of fish gelatin.

Based on the totality of evidence, fish gelatin derived from fish skin and bones by existing commercial practices does not appear to be allergenic to fish-allergic individuals. Fish gelatin is a collagen-derived ingredient derived from fish skin, whereas the major allergens in fish are parvalbumin proteins from edible muscle tissues. Edible fish gelatin has been produced since at least 1981. No evidence exists to indicate that fish gelatin is contaminated with allergens from fish muscle, which should be evident in the studies of Andre and others (2003) and Hansen and others (2004). Some preliminary evidence exists to suggest that fish collagen may be a minor fish allergen (Hamada and others 2001); however, the clinical importance of fish collagen as an allergen has not been well documented, and the reactivity of any such patients to ingestion of fish gelatin has not been proven.

Isinglass. Another product derived from fish collagen is isinglass. Isinglass finings, composed mainly of collagen, are protein solutions extracted from swim bladders of certain species of tropical marine fish, sturgeon, hake, and cod. Isinglass serves several functions in the brewing and wine industries to produce clarification, to enhance physical stabilization of cask-conditioned ales, and improve filtration performance (Leather 1994; Leiper and others 2002). Because the molecule is amphoteric, the negative charge is able to bind yeast cells, and the positive charge attracts proteins in solution. Isinglass is quite insoluble when added to beverages, and virtually all of the isinglass is removed during the process. Thus, isinglass has been considered as a processing aid and has not been labeled.

Despite being used since the 18th century, no reports exist of allergic reactions to isinglass. Isinglass may be used as a fining agent in the beer, wine, and champagne industries. For example, isinglass is added to beer at levels of 0.001% to 0.002%, and 15 billion liters of isinglass-treated beer is consumed annually (BBPA and BFBi 2000). Because isinglass is mostly removed during the filtration and maturation process (Leiper and others 2002), little if any isinglass would be present in the beverage as consumed. Thus, the likelihood of allergic sensitization to isinglass is low. Isinglass residues in filtered beer ranged from 0.02 ppm to 0.16 ppm in recent tests (BBPA and BFBi 2000).

Fish Maws. Fish maws or swim bladders are the air bladder of fish that allows ascending and descending motions in water. The principal component of fish maws is collagen. Fish maws are removed during gutting, are processed, and used as food, generally to prepare thick soups, in countries such as mainland China, Taiwan, and Singapore (Dey 2003; Regenstein 2004). There are no documented cases of allergic reaction to fish maws. However, parvalbumin was purified, and the complete amino acid sequence was determined in the swim bladder muscle of the toadfish *(Opsanus tau)* (Gerday and others 1989). Ingestion of fish maws would represent a far higher exposure to parvalbumin as well as fish collagen than ingestion of isinglass in alcoholic beverages.

Ice-structuring Protein. Ice-structuring protein (ISP) is a novel protein ingredient recently approved for use in foods to control ice crystal size. ISPs are widely distributed in nature (Bindslev-Jensen and others 2003) but the ISP Type III approved for food use is structurally identical to an ISP from ocean pout fish (Bindslev-Jensen and others 2003). However, this ISP is actually derived by fermentation of genetically modified yeast that contains the identical amino acid sequence from ocean pout fish (Bindslev-Jensen and others 2003).

Bindslev-Jensen and others (2003) performed procedures proposed by the Food and Agriculture Organization/World Health Organization for investigation of novel food proteins to evaluate the potential allergenicity of this ISP. Sera from 20 cod-allergic individuals were used to test the novel protein, ISP Type III. None of the procedures performed indicated the novel protein would produce adverse effects if ingested by fish-allergic individuals.

Fish Oil. Fish oil is obtained from various species of fish including cod, salmon, and menhaden. Fish oil contains nutritionally desirable long-chain, polyunsaturated fatty acids. Alternatively, these fatty acids may also be produced by algal fermentations because fish derive these fatty acids by feeding on marine algae. Fish oil would contain only trace residues of fish protein and thus fish allergens. Data have not been published on the level of protein in fish oil, however. Allergic reactions to fish oil are not documented in the medical literature.

Worcestershire Sauce. Worcestershire sauce contains anchovies. Although no reports exist in the medical literature documenting allergic reactions to anchovies, the assumption must be made that ingestion of anchovies would be hazardous to fish-allergic individuals because anchovies likely contain parvalbumin, the pan-allergen of fish. Thus, the ingestion of Worcestershire sauce should also be considered potentially hazardous to fish-allergic individuals unless evidence is produced to the contrary. The U.S. Dept. of Agriculture has enforced the recall of several meat products in the United States that contained undeclared Worcestershire sauce.

Conclusions

Allergy to fish is a common cause of IgE-mediated food allergic reactions (CAC 1999). The major codfish allergen, Gad c 1, is the most extensively studied fish allergen. Gad c 1 is a naturally occurring muscle protein, parvalbumin. Parvalbumin is also the major allergen in other fish species. If parvalbumin is not present in fish-derived ingredients, then these ingredients may be considered safe for most fish-allergic individuals to consume. Fish-derived ingredients such as gelatin, isinglass, fish maws, ISP, fish oil, and Worcestershire sauce serve several functions in foods. Most allergic reactions to gelatin are associated with its use as a vaccine expander in injectable pharmaceutical products involving beef or pork gelatin. Very little evidence of fish-gelatin allergy exists. Fish gelatins from all fish species are likely equivalent, and it appears that this product is safe for fish-allergic individuals on the basis of challenge trials with codfish gelatin in codfish-allergic individuals. ISP has also been documented to be safe for fish-allergic individuals. Alternatively, Worcestershire sauce is considered potentially hazardous for fish-allergic consumers despite a lack of evidence of anchovy allergy. No evidence exists for allergic reactions to isinglass, and such reactions would not be anticipated on the basis of the extremely low exposure levels to isinglass. However, clinical experiments documenting the lack of IgE binding to isinglass in fish-allergic individuals would further serve to document its safety.

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