Clinical Management of Seafood Allergy

Carla M. Davis, MD[a], Ruchi S. Gupta, MD, MPH[b], Ozge N. Aktas, MD[c], Veronica Diaz, MD[a], Sandip D. Kamath, PhD[d], and Andreas L. Lopata, PhD[d] *Houston, Texas; Chicago, Ill; and Townsville, QLD, Australia*

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1. To distinguish characteristics of shellfish allergy, fish allergy, and seafood poisoning
2. To recognize aspects of cross-reactivity regarding seafood
3. To order appropriate laboratory tests to distinguish shellfish from fish allergy

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Seafood plays an important role in human nutrition and health. A good patient workup and sensitive diagnostic analysis of IgE antibody reactivity can distinguish between a true seafood allergy and other adverse reactions generated by toxins or parasites contaminating ingested seafood. The 2 most important seafood groupings include the fish and shellfish. Shellfish, in the context of seafood consumption, constitutes a diverse group of species subdivided into crustaceans and mollusks. The prevalence of

[a]Texas Children's Hospital Food Allergy Program, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas
[b]Center for Food Allergy and Asthma Research, Northwestern University Feinberg School of Medicine and Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Ill
[c]Department of Pediatrics, University of Illinois College of Medicine at Chicago, Chicago, Ill
[d]College of Public Health, Medical and Veterinary Sciences, Australian Institute of Tropical Health and Medicine, Molecular Allergy Research Laboratory, James Cook University, Townsville, QLD, Australia

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Corresponding author: Carla M. Davis, MD, 1102 Bates Ave, MC 330.01, Houston TX, 77030. E-mail: carlad@bcm.edu.

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Abbreviations used
OFC- oral food challenge
PPT- prick-to-prick testing
SPT- skin prick test

shellfish allergy seems to be higher than that of fish allergy, with an estimate of up to 3% in the adult population and fin fish allergy prevalence of approximately 1%. Clinical evaluation of the seafood-allergic patient involves obtaining a detailed history and obtaining *in vivo* and/or *in vitro* testing with careful interpretation of results with consideration of cross-reactivity features of the major allergens. Oral food challenge is useful not only for the diagnosis but also for avoiding unnecessary dietary restrictions. In this review, we highlight some of the recent reports to provide solid clinical and laboratory tools for the differentiation of fish allergy from shellfish allergy, enabling best treatment and management of these patients. **(J Allergy Clin Immunol Pract 2020;8:37-44)**

Key words: *Fish allergy; Shellfish allergy; Crustacean; Mollusk; Diagnosis of fish allergy; Skin prick test; Oral food challenge*

INTRODUCTION

Seafood plays an important role in human nutrition and health. The growing international trade in seafood species and products has added to the popularity and frequency of consumption of various seafood products across many countries. However, seafood can also provoke serious adverse reactions in susceptible individuals.[1,2]

Adverse reactions to seafood can be classified into 3 categories, on the basis of underlying mechanisms: (1) immunologic reactions, including IgE and non-IgE allergic reactions such as food protein−induced enterocolitis syndrome[3]; (2) toxic reactions, including marine biotoxins[4]; and (3) food intolerance.[5] Adverse reactions due to toxins and/or food intolerance often resemble clinical symptoms of seafood allergy. A good patient workup and sensitive diagnostic analysis of IgE antibody reactivity can distinguish between a true seafood allergy and other adverse reactions.

Allergic symptoms after ingestion can occur within minutes and range from nausea, vomiting, urticaria to asthma exacerbation and anaphylaxis. Respiratory reactions along with oral allergy syndrome are very often reported in seafood allergy, but frequency might vary with geography and study population.[6,7] Reactions are usually reported within 2 hours; however, late-phase reactions are described particularly among people allergic to snow crab, cuttlefish, limpet, and abalone.[8] Crustacean and fish, similar to nuts, are among the most common causes of anaphylaxis and death from food allergy.[9-12]

Sensitization and subsequent reactions occur most frequently upon ingestion; however, they can also occur because of skin contact or inhalation of aerosolized proteins generated during cooking or processing in factories and domestic environment.[13]

The prevalence of shellfish allergy seems to be higher than that of fish allergy, with an estimate of up to 3% in the adult population.[2,12] Fin fish allergy occurs in approximately 1% of adults. Shellfish allergy is of particular importance in the Asia-Pacific region, with self-reported rates of shellfish allergy ranging from 0.9% to 1.19% in children younger than 7 years to 5.12% to 7.71% in adolescents and adults in Hong Kong, Philippines, and Singapore.[14,15] Similarly, a cross-sectional study on doctor-diagnosed seafood allergy in Vietnam confirmed the high prevalence among children up to age 6 years. Crustacean was the predominant allergy-inducing food (3.8%), followed by fin fish (1.2%) and mollusk (1.0%) in a study population of more than 8600 participants.[16] Unlike most other food allergies, seafood allergy is thought to persist for life in up to 90% of patients, with a similar trend also observed in peanut allergy.[17]

The 2 most important seafood groupings include the fish and shellfish (see Figure 1). Within the large group of fish, most reported allergies are to bony fish, whereas cartilaginous fish (rays and sharks) seem to be of lower allergenicity.[18] Shellfish, in the context of seafood consumption, constitutes a diverse group of species subdivided into crustaceans and mollusks. Crustaceans, including shrimp, crab, and lobster, are classified as arthropods together with mites, spiders, and insects.[19,20] This might provide an explanation of the observed molecular and clinical cross-reactivity. The term "shrimp" and "prawn" are often used interchangeably in the commercial as well as scientific sector, with the latter term used more in the United Kingdom and Australia.[21] However, there are anatomical differences between the 2 animals. In general, prawns are bigger in size than shrimp. The most prominent difference is in the carapace. In shrimp, the second segment of the shell overlays the first and the third, thereby giving them the typical bend in their body. However, in prawns, the segments of the shell overlap each other front to back, thereby imparting a lesser bend to the body.

Patients with seafood allergy may fail to identify the offending seafood species, often as a result of confusion regarding the diversity of seafood consumed and the different common names used to describe seafood. In addition, fraudulent substitution and/or mislabeling of produce have been demonstrated for various seafood species, most frequently for fish.[22] Because there is specificity to seafood allergy, with some patients allergic to only fish and not shellfish and some patients allergic to crustaceans and not mollusks, identification of the specific allergy is important for further management of the disease.

The group of mollusks is a large and diverse cluster, further subdivided into the classes bivalve, gastropod, and cephalopod, including several important consumed species such as mussels, oysters, abalone, snails, and squid (calamari). The mollusks and crustaceans seem to include similar but also different allergens important in distinguishing allergic sensitization to one or the other group. Several panallergens are characterized in detail, including tropomyosin and arginine kinase, responsible for clinical cross-reactivity with other frequent invertebrate allergen sources, comprising mites, insects, and parasites[1] (see Figure 1). However, additional shellfish allergens have been characterized,[23] making component-resolved diagnosis possible in the near future.[24,25] Most shellfish allergens, including the major allergen tropomyosin, are known to be heat-stable. Current *in vitro* diagnostic tools for shellfish allergy include a mix of raw or heated shellfish extracts to account for sensitization and allergy to heat-labile as well as heat-stable shellfish allergens.[24,25]

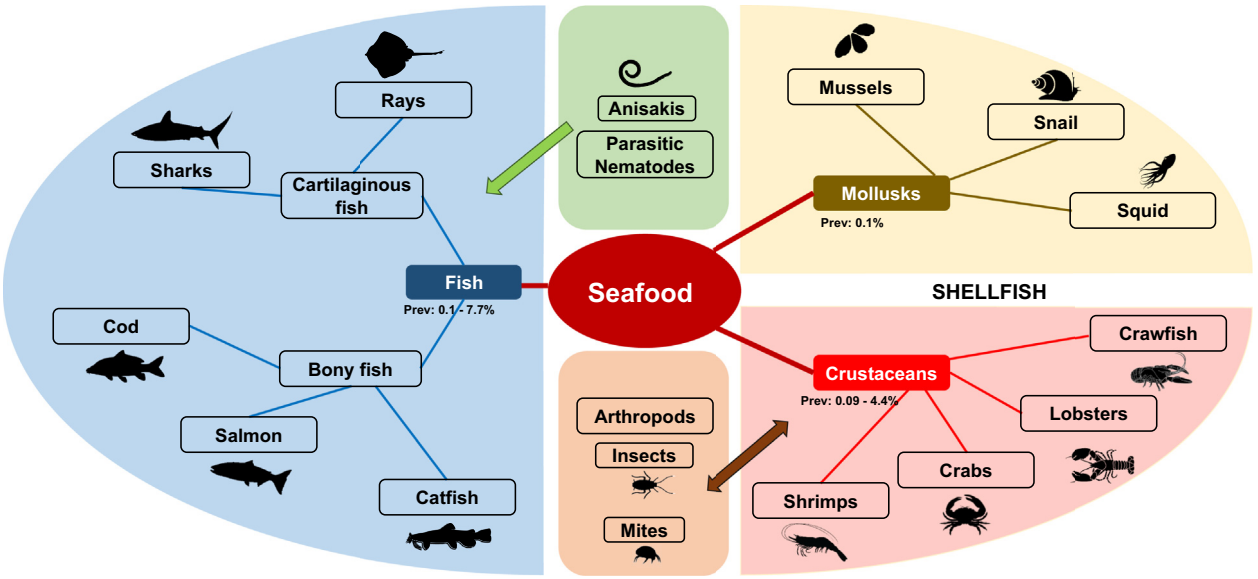

FIGURE 1. Edible seafood can be broadly categorized as vertebrates (fish) and invertebrates (shellfish). Edible fish species are mainly grouped as cartilaginous fish and bony fish. The term shellfish includes species from the phylum molluska and subphylum crustacea. Closely related arthropods such as insects and mites (brown arrow) can contain cross-reactive allergens. Nematodes such as Anisakis are commonly found in edible fish (green arrow); however, they have shared allergens with crustaceans. Allergy prevalence values (%) stated for bony fish, crustaceans, and mollusks are derived from self-reported, doctor-diagnosed, or challenge-proven studies.

In contrast, the major fish allergen parvalbumin seems to be very different between many fish species, reflected in "mono-sensitization" to specific groups, such as salmon and trout.[26-29] Additional allergens seem to be present only in raw fish (enolase and aldolase),[29] whereas some other allergens are highly concentrated in the skin (collagen and gelatin).[1,30] A study among 9 fish species identified codfish, salmon, pollock, and herring as the most allergenic and cross-reacting species, whereas halibut, flounder, tuna, and mackerel seem to be less allergenic.[27] In addition, the marine roundworm Anisakis, contaminating marine fish, can cause allergic sensitization, resulting often in misdiagnosis as allergy to the fish.[31,32]

In this review, we will highlight some of the recent reports to provide solid clinical and laboratory tools for the differentiation of fish allergy from shellfish allergy, enabling best treatment and management of these patients.

CASE PRESENTATION: PEDIATRIC SHELLFISH ALLERGY

A 16-year-old female presented with allergic rhinitis to dust mite and cat. She had several severe episodes of anaphylaxis to shellfish. The first documented reaction involved tongue and lip swelling with pruritus 20 minutes after eating shrimp, which self-resolved in 24 hours. The second reaction was a more severe episode, with periorbital, lip, and tongue swelling along with hives 30 minutes after eating rice with shrimp. Epinephrine and diphenhydramine were given at home by emergency medical services. She did not go to the emergency department despite mild persistent facial swelling, because of severe inclement weather. Her facial swelling worsened and she developed new-onset shortness of breath, which prompted her to seek medical care after several days.

Because of concerns for late-phase anaphylaxis and airway obstruction, she was admitted to the pediatric intensive care unit where she was treated with solumedrol, ranitidine, and diphenhydramine. The Allergy and Immunology service was consulted because of severe late-phase anaphylaxis. The workup was significant for a total IgE level of 1060 kU/L, with levels of specific IgE of 15.6 kU/L for crayfish, of 13.8 kU/L for shrimp, of 1.44 kU/L for sea crawfish/langust (spiny lobster), of 7.93 kU/L for lobster, of 0.56 kU/L for crab, and of 0.47 kU/L for anchovy. All other fish and all mollusk test results were negative (<0.35 kU/L). She had normal C1 esterase nonfunction level of 38 mg/dL and function inhibitor (80%, >60% is normal), ruling out hereditary angioedema.

A second episode of anaphylaxis happened 1 hour after eating prepackaged BBQ chicken wings and was significant for hives, lip, tongue, throat, and hand swelling. She required intramuscular epinephrine twice and diphenhydramine and was admitted for observation given the severity of the reaction. Despite intravenous steroids, diphenhydramine, and ranitidine, facial and throat swelling worsened 5 to 6 hours later. She required a third dose of intramuscular epinephrine and transfer to the pediatric intensive care unit for an epinephrine drip to control the swelling. There were no reported episodes of hypotension. She improved within 24 hours and had mild residual lip swelling on discharge. It was later noted that the BBQ wing sauce contained shellfish, fish, artichoke, and anchovies. Repeat testing showed a total IgE level of 647 IU/mL, with levels of specific IgE of 0.44 kU/L for artichoke, of 0.49 kU/L for anchovy, and of less than 0.35 kU/L for both salmon and codfish.

Her third episode of anaphylaxis occurred 30 minutes after eating a cheese and sausage pastry from the school cafeteria where fish and shellfish were being prepared. Despite receiving intramuscular epinephrine and diphenhydramine in school, the swelling and hives worsened when she reached the emergency department. A second dose of epinephrine was given along with solumedrol, pantoprazole, and a normal saline bonus. Tryptase level on admission was 3.1 μg/L. Specific IgE level for wheat, beef, pork, chicken, and milk were all less than 0.35 ku/L. Her

symptoms improved and she was discharged home the next day without any late-phase reactions documented.

Shellfish allergy although more common in adults than in children is an important food allergen to be aware of in the pediatric population.[10,33-35] In a pediatric US prevalence study by Gupta et al,[35] 8% of children had food allergies, 38.7% with severe reactions, of which shellfish was the third most common.[35] In a prevalence study among children in Vietnam, up to 7% reported diagnosed food allergy, with crustacean, fish, and mollusk being the 3 most common food allergens.[16] Shellfish allergy tends to present with anaphylaxis and episodes can be life-threatening.[1,34] Data from the National Electronic Injury Surveillance System in the United States showed that 24% of emergency department visits for anaphylaxis were seen in children 6 years or older, with shellfish being the most common culprit.[11] Furthermore, shellfish allergy is now the leading cause of death from food anaphylaxis in Australia, derived from the Australian Bureau of Statistics.[36]

This case highlights the importance of creating awareness of potential cross-contamination and how small doses of aerosolized allergen can be enough to cause symptoms of an allergic reaction and even anaphylaxis.[37-40] In fact, sensitization to food allergens via inhalation is suggested to be a distinct form of food allergy.[39,41,42] Traditionally, sensitization to ingested food is termed class 1 food allergy, while class 2 food allergy is commonly observed following allergic sensitization to pollen aeroallergens, due to cross-reactive allergens. However, over recent years what has become evident is that many food allergens can act as a primary sensitizer through inhalation at the workplace, causing occupational allergies. Affected individuals experience mainly respiratory symptoms, usually without associated symptoms after ingestion of the offending food, and the term class 3 food allergy is proposed.[43]

Although there is not much data on crustacean and mollusk allergy cross-reactivity, many physicians recommend avoidance of both because of the risk of cross-contamination.[33] Although cross-reactivity is common in shellfish-allergic patients (75%), studies have shown that crustacean-allergic patients are not always allergic to mollusks, which could be a potential source of protein for a child's diet.[12,33] Of note, she was also allergic to house-dust mites, known to cause clinical cross-sensitivity due in most part to Pen a 1 IgE-binding regions of the tropomyosin protein.[44] In addition, her uncontrolled allergic rhinitis potentially contributed to her symptoms.[33,37] Her case also features recurrent late-phase anaphylaxis, which, although rare, is potentially fatal if not recognized promptly.[8-11]

CASE PRESENTATION: ADULT FISH ALLERGY

A 25-year-old man with no significant past medical history presented to the emergency room because of progressive rash and facial swelling concerning for a food-related adverse reaction. Three days ago, at dinner he developed an itchy rash on the face, quickly progressing to his neck, as well as some swelling on the lips and face. Upon detailed history taking, he stated eating a meal containing fish in the restaurant 3 hours before presentation, and denied having associated symptoms including gastrointestinal (eg, nausea, vomiting, diarrhea, and abdominal pain), respiratory (eg, cough, shortness of breath, and wheezing), and cardiovascular (tachycardia and hypotension). He had never experienced similar symptoms in the past. Past medical history was remarkable only for a diagnosis of eczema in childhood. He did not use any medications and did not have any known allergies. He had a younger cousin with multiple seafood allergies including fish and crustacean allergy as well as peanut allergy. He stated he did not usually eat fish or other types of seafood and that it had been 6 months since he had last been to a seafood restaurant.

Physical examination was remarkable for urticarial rash on the face, neck, and anterior chest and mild periorbital and perioral angioedema. The patient was given a dose of cetirizine and discharged home after resolution of the symptoms and a 6-hour observation period in the emergency room with a follow-up appointment with the primary care physician who then referred the patient to the Allergy-Immunology Clinic for further evaluation of food allergy.

Following a detailed review of clinical history and complete physical examination in the Allergy-Immunology Clinic, specific IgE levels to fish including codfish, halibut, mackerel, walleye pike, salmon, trout, and tuna, and shellfish including clam, crab, lobster, oyster, scallop, and shrimp, were tested and resulted positive for codfish (2.36 kU/L), halibut (0.7 kU/L), and salmon (1.98 kU/L). To confirm the diagnosis, an oral food challenge (OFC) was performed with all 3 fish and resulted in urticaria, perioral angioedema, and mild abdominal discomfort with codfish and salmon, but not with halibut. After confirmation of salmon and codfish allergy, intramuscular epinephrine injection was prescribed to the patient with instructions to avoid salmon and codfish in his diet.

Evaluation of the seafood-allergic patient *in vivo*

History. A detailed history including time and duration of the reaction, type of foods/medications consumed 6 to 8 hours before the reaction including specific fish/shellfish species, location of the event, symptom characteristics involving skin/mucosa, gastrointestinal, cardiovascular, respiratory, and neurologic system, medical care given and treatment administered, timing of resolution of symptoms, recurrence of symptoms after initial resolution, prior history of a similar reaction, past medical history of allergic conditions including dust mite or cockroach allergy, and family history of allergic diseases is essential to diagnose seafood allergies. It allows clinicians to understand and better characterize the etiology and characteristics of the reaction and help inform further confirmatory allergy testing. Cross-reactivity between and among fish and shellfish is also crucial to consider because at least one-third of seafood-allergic patients report multiple seafood allergies.[2,45] Cross-reactivity is shown to be more common among shellfish allergies (75%)[46-49] than among fish allergies (29%-67%).[45,46,49-53] Therefore, it is essential to obtain a thorough history regarding complaints and symptoms with all other types of seafood that might serve as a clue to understand clinical cross-reactivity between and among fish and/or shellfish species (see Figure 2).

Skin prick testing and prick-to-prick testing. Skin prick test (SPT) is a common *in vivo* procedure to help understand sensitivity to food allergens including fish and shellfish. The procedure involves applying drops of allergen extracts as well as the positive (histamine) and negative (usually 0.9% saline or 50% glycerol saline) control solutions to the forearm or back, usually with the help of a lancet. Following 15 to 30 minutes of allergen application to the skin, wheal sizes are measured, with the mean of the longest diameter of the wheal and the longest perpendicular diameter. Another type of skin testing is prick-to-

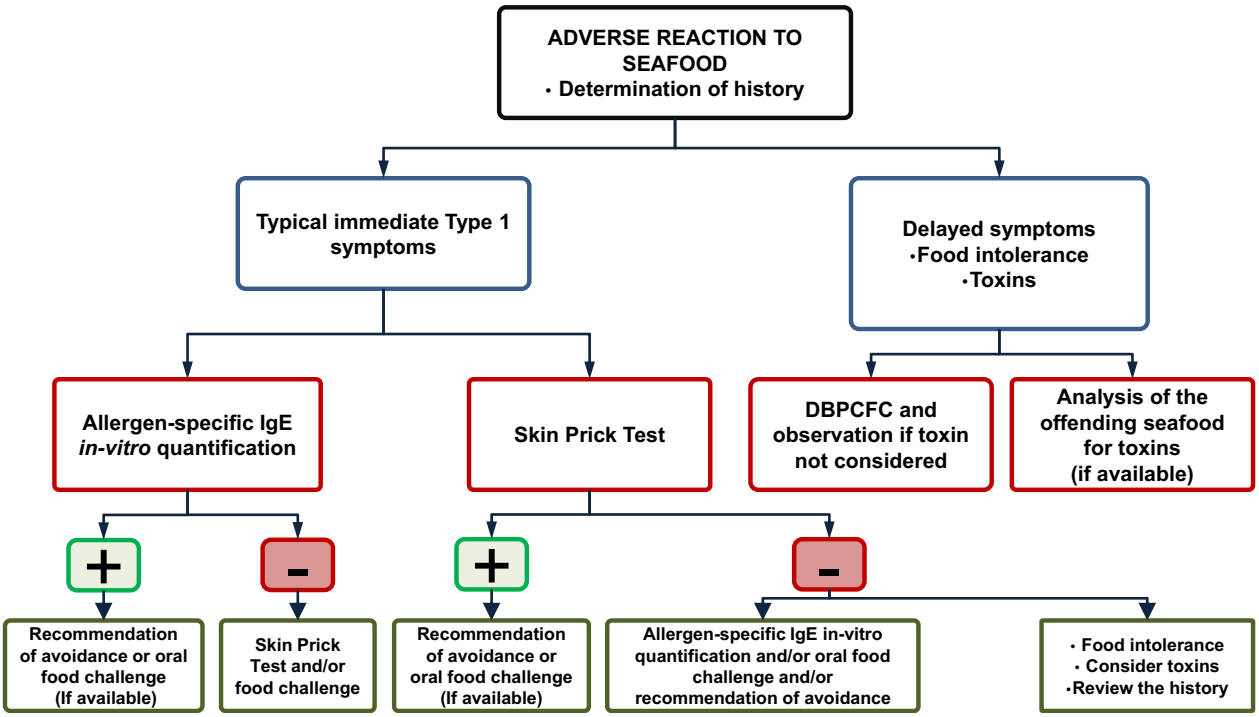

FIGURE 2. Diagnostic algorithm to distinguish and diagnose IgE-mediated allergy, food intolerance, and toxic adverse reactions to seafood. *DBPCFC*, Double-blind placebo-controlled food challenge.

prick testing (PPT), where the tester first pricks the fresh food and then pricks the skin for allergen exposure. PPT is not a standardized method of testing. Medications such as antihistamines, beta-blockers, phenothiazine, and antidepressants may lead to false-negative results, and thus should be avoided before skin testing.[54]

Previous studies show low risk of severe allergic reaction during SPT or PPT.[52-54] There are few case studies reporting anaphylaxis during these tests that mostly presented with testing 4 or more fish allergens simultaneously.[55-61] Young age,[55,56,60] active eczema,[56,60] previous history of anaphylaxis,[55] and PPT with fresh foods[55,56,62] were risk factors for developing a generalized reaction or anaphylaxis during the test and should be considered while performing skin testing in daily practice. Overall, skin testing is safe to perform under surveillance of a certified provider; thus, the low risk of anaphylaxis reported in the literature should not create hesitation regarding the decision of performing a skin test. In addition, SPT has been widely used to aid the diagnosis of food allergies, but clinicians should keep in mind that clinical reactivity does not correlate directly with the level of reactivity or wheal size.[63-66] Furthermore, it has been demonstrated for fish SPTs that some commercial preparations lack some of the important fish allergens, potentially leading to false-negative outcomes.[21]

Allergen specific IgE *in vitro* testing. Serum specific IgE testing is also a commonly used *in vitro* method of determining the presence of seafood specific IgE (sensitization) and the potential for clinical reactivity to specific fish or shellfish. The combination of a characteristic clinical history of an allergic reaction with a level of allergen specific IgE or SPT is a foundation of food allergy diagnosis (see Figure 2). Studies of the clinical value of seafood specific IgE testing are limited.[67] Studies have shown that the efficacy for confirming crustacean allergy varies, with in-house measurements of IgE to the major shrimp allergen tropomyosin being superior to commercial IgE testing using whole shrimp protein and skin prick testing (88.5%, 74.2%, and 65.7%, respectively).[68] Positive predictive values were low for SPTs (33.3%) and measurement of IgE to shrimp (41.6%) compared with positive predictive values for IgE to shrimp tropomyosin (71.4%).[68] The specificity and clinical predictive value of ImmunoCAP specific IgE testing for shrimp is best in patients without dust mite allergy.[68,69] In one study, a shrimp specific IgE level of more than 3.55 kU_A/L showed 100% sensitivity for the diagnosis of shrimp allergy in patients not allergic to dust mite.[69] This is evidence that component-resolved diagnosis could improve the diagnostic capability of serum specific IgE testing in shellfish allergy.[70]

A study of codfish specific IgE levels in challenge-proven codfish-allergic patients determined that 20 kU/L is highly predictive of clinical allergy.[71] In addition, patients anaphylactic to pilchard or anchovy have been described to have specific IgE levels as low as 1 kU/L,[71] and most patients allergic to bony fish tolerate ray, a cartilaginous fish, because of the low allergenicity of its α-parvalbumin.[18] Studies are needed to determine the specific IgE values predictive of clinical allergy for commonly ingested fish species.

Interpretation of serum IgE test results is highly dependent on the allergen content, potency, and stability of the allergen extracts. The current commercial SPT solutions and IgE quantification assays for shellfish and fish are produced from variable heat-treated or raw extracts. Recent comparative immunologic studies on different commercial SPTs confirmed the immense allergenic variability, resulting in false-negative patient evaluation.[68,69,71-73]

For instance, currently available IgE testing for prawns was shown to result in more than 25% of patients being missed.[68,69,71,72] Although the use of the major shrimp allergen tropomyosin has been shown to have clinical utility in diagnosis,[74] it is not currently commercially available. Therefore, food challenges are considered essential to the diagnosis of shellfish allergy, especially in cases in which clinical cross-reactivity with other allergens such as dust mites, cockroaches, and edible insects may account for positive serum IgE results.[74-76]

The interpretation of the results of specific IgE testing to seafood must incorporate the understanding that relevant seafood allergens may not be included in the extract used for the immunoassay. Twenty allergenic proteins groups within the 3 distinct seafood groups—crustacean, mollusks, and fish—have been characterized biomolecularly.[73,77] For instance, the major allergens of shrimp are tropomyosin, arginine kinase, myosin light chain, sarcoplasmic calcium-binding protein, hemocyanin, and troponin C.[26,74,75] The major allergens of fish are parvalbumin, tropomyosin, collagen, aldolase A, β-enolase, and vitellogenin.[21,27] Many allergen isoforms have been characterized in different species, with more than 72 seafood allergens now being registered with the International Union of Immunological Societies (WHO/IUIS Allergen Subcommittee; 41 in crustacean, 25 in fish, and only 6 in mollusk).[1] Although the immunologic cross-reactivity between fish and shellfish allergens has not been demonstrated conclusively, panallergens in seafood allergy, including parvalbumin and tropomyosin, have the potential to induce immunologic and clinical cross-reactivity.[73] The basophil activation test has not been studied extensively in seafood allergy, but it has been shown to correlate with severity of reactions in shellfish and fish challenge. However, it is currently not readily available for routine testing.[18]

Advances in immunoproteomics enable the comprehensive *in vitro* analysis of individual sensitization profiles with purified and recombinant allergens.[70,73] A recent study on the allergenicity of the Pacific oyster used a combined chemical, bioinformatic, and immunoproteomic analysis to identify more than 20 allergenic proteins, filling a gap in the current management of patients at high risk of concurrent reactivity to diverse allergen sources.[23] Development of component-resolved diagnosis reagents would allow the identification of diagnostic patterns, facilitating better management of prawn allergy. Component-resolved diagnosis is already applied in the ImmunoCAP assay range or the ISAC allergen microarray (Thermofisher, Waltham, MA), a multiplex assay.[67] Specific fish and shellfish allergen IgE assays would assist in the identification of children and/or adults at risk of severe clinical reactions and persistent seafood allergy.

Oral food challenge. OFC is a reliable *in vivo* test to confirm food allergies in which incremental amounts of a suspected allergenic food are introduced to the patient to evaluate its potential to cause an adverse reaction. OFCs can be open, single-blind, or double-blind placebo-controlled, the latter being the criterion standard for diagnosis. It can be performed for patients of any age and is especially useful when there is uncertainty regarding the type of food eliciting the adverse reaction. While performing OFC, fish and shellfish can be masked in another tolerated ground meat or fruit juice to avoid the smell or taste of the seafood ingested for blind procedures.[78-81] Exclusion criteria for an OFC are pregnancy, unstable asthma, medications that interfere with the treatment of a challenge-induced allergic reaction, such as beta-blockers, or confounding medical conditions that might interfere with the outcome including chronic urticaria, symptomatic allergic rhinitis, severe uncontrolled asthma, and acute infection.[78] OFC should not be performed if a patient is on prolonged systemic high-dose steroids, omalizumab, or other systemic immunosuppressants that might confound the interpretation of the test result.[78] Of note, nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, alcohol, and antacids can elicit a response with increased reactivity in susceptible patients.[79,80] Beta-blockers should be avoided because of safety concerns because epinephrine might be required to control the reaction during the OFC.[80]

OFC is useful not only for the diagnosis but also for avoiding unnecessary dietary restrictions. Recent studies show that some patients with fish allergy may tolerate certain fish types.[18,81,82] For instance, in a small group of patients (N = 35) undergoing OFC with codfish, salmon, and mackerel, 54% of participants were partially tolerant, characterized by symptoms to 1 or 2 fish allergens although nearly all participants had sensitization to all 3 fish extracts.[81] Thus, complete avoidance of fish in patients with fish allergy may not be necessary in selected cases, and further research is needed to understand the risk factors of developing a reaction to multiple fish types as well as partial tolerance in fish allergy.

Nonimmunologic adverse reactions to seafood

Adverse clinical reactions to seafood can also be generated by toxins or parasites contaminating the ingested seafood. Seafood is responsible for at least 1 in 6 food poisoning outbreaks in the United States, and the proportion is even higher in Japan.[83] Seafood toxins are very stable, and different food preparation methods do not reduce toxicity.

The 2 most well-described fish-related adverse reactions are scombroid and ciguatera poisonings.[84,85] The former occurs after eating fish that has been improperly refrigerated. Bacteria convert the amino acid histidine into histamine, generating allergy-like clinical reactions. Symptoms commence within 30 minutes and include hives, flushing, nausea, and even anaphylaxis. Fish species commonly involved include mackerel, tuna, mahi mahi, and marlin.[84] Scombroid poisoning typically resolves within 12 to 48 hours with no long-term sequelae.[84]

In contrast, ciguatera poisoning is caused by algae-derived toxins, consumed by fish via the food chain. Ciguatera toxin causes symptoms that occur within 1 to 6 hours of ingesting fish with the toxin and can last for days, months, or years.[85-87] Clinical symptoms may include gastrointestinal, cardiovascular, and neurological reactions, affecting up to 50,000 individuals annually.[88] Neither scombroid nor ciguatera toxins are affected by heating or cooking the affected fish.[86,87] Marine fish are often contaminated with the parasite Anisakis and on ingestion can cause zoonotic infection (anisakiasis), reported worldwide. Infection with live Anisakis is associated with abdominal pain, nausea, and diarrhea and can lead to eosinophilia and formation of gastrointestinal granulomas. Reinfection can lead to systemic allergic reactions, making Anisakis an important source of hidden allergens in seafood.[89,90]

Shellfish can also cause food poisoning that can be generated by other toxins. A significant contributor is the so-called red tides, where large algae blooms of small dinoflagellates are taken up by filter-feeding shellfish. Most frequently, mussels and oysters are affected. Some neurotoxins derived from paralytic

shellfish poisoning, blocking cellular sodium channels, account for most human fatalities through algae-derived toxins.[85,88]

However, frequently the source of bacterial and viral contamination of shellfish is the harvest from polluted waters. Different vibrio strains as well as Listeria and Salmonella species have been implicated as well as small round-structured viruses and Norwalk virus. Although the clinical presentation often includes gastrointestinal symptoms, these can occur several hours after consumption, similar to allergic reactions.[91]

CONCLUSIONS

Seafood allergies include shellfish (crustaceans and mollusks) and fish, and can cause severe clinical reactions ranging from immunologic toxic to infectious etiologies. Adults are most commonly affected, but children can also present with seafood allergy. Clinical management requires a detailed history coupled with careful diagnostic testing through skin prick testing, serum specific IgE, and, in appropriate cases, an OFC. After diagnosis, the current treatment of seafood allergy is strict avoidance.

Nonimmunologic reactions to seafood should be determined in the clinical evaluation of seafood reactions and specific shellfish/fish species tested to avoid unnecessary diet restriction. Autoinjectable epinephrine should be prescribed, and counseling regarding cross- contamination is an important component to seafood allergy management. More investigations are needed in the future to improve diagnostic methods and best practices in the clinical management of fish and shellfish allergy.

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