

The Sea of Change in Fish Allergy: Navigating Toward a Personalized Approach



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The term “seafood” has been used to describe a wide array of edible organisms living in the water, spanning diverse species from distant evolutionary phyla—vertebrates such as bony and cartilaginous fish, crustaceans such as shrimp, lobsters, and prawns, and mollusks including oysters, clams, squid, and cuttlefish among others (Figure 1). The broad categorization under a single term, seafood, often leads to confusion and unnecessary dietary restrictions among patients with fish allergies, who may avoid all forms of seafood without a real need. This confusion is compounded by the lack of public knowledge of allergen cross-reactivity patterns among these diverse groups as well as mislabeling and the misidentification of seafood.¹

Previous studies show allergen cross-reactivity rates of more than 50% among different fish species and more than 75% for crustaceans, yet significant subgroup clinical cross-reactivity allows for selective tolerance in some cases. There is very little cross-reactivity between fish and shellfish, although co-allergy is present in a minority of patients.² However, in routine clinical practice, one often encounters situations in which patients avoid all seafood, including fish and shellfish, voluntarily after an original reaction to either fish or shellfish.

Previous studies looking into clinical cross-reactivity between fish species have largely been surveys. These surveys indicated allergy to multiple fish species at rates ranging from 33% to 48%.^{3–5} The current study by Leung et al⁶ more rigorously assessed the rate of multiple fish allergy through oral food challenges to multiple fish in 75 of the 249 recruited subjects. Not surprisingly, the current study found that although 75% of participants reported allergies to multiple fish species, only 37% exhibited reactions to more than 1 species on OFC, consistent with previously mentioned surveys. This discrepancy suggests that many fish-allergic individuals might be avoiding certain fish unnecessarily. In addition, the likelihood of a reaction was found to correlate with the β -parvalbumin levels in the fish, prompting

the suggestion of a β -parvalbumin ladder for guiding oral challenges, starting with fish species having lower β -parvalbumin levels. The study also showed that tolerance patterns to fish were not directly related to societal eating patterns, with salmon being the most consumed and tolerated fish for the subjects and carp being the next most consumed but being one of the least tolerated fish in the cohort.

Moreover, the study delved into the co-occurrence of shellfish allergies in individuals with fish allergies. Although the results of the shellfish challenge data are difficult to incorporate into clinical practice because just 18 of 249 individuals underwent a shrimp OFC, it raises an important clinical point that echoes the previously mentioned point: fish-allergic individuals are likely unnecessarily avoiding shellfish. Previous surveys have indicated a co-allergy rate between 6% and 10%.^{3,4} In addition, the co-occurrence of fish and shellfish allergies was thought to stem from concurrent allergies in the context of underlying atopy, rather than from cross-reactivity. This hypothesis was reinforced by the observation of a higher incidence of co-allergies to peanut and egg than to fish and shellfish.⁷ The concept of a co-allergy, as opposed to cross-reactivity, is further supported by the distinct nature of the primary allergens involved: parvalbumin in fish and tropomyosin in shellfish. Furthermore, cross-reactivity generally necessitates a homology of at least 70% in the primary amino acid sequence.⁸ Given that fish tropomyosin exhibits only about 55% homology with that of crustaceans, this points to a reduced likelihood of cross-reactivity.⁹

These insights call for a more personalized approach in managing fish allergies. The diverse evolutionary paths of seafood species necessitate a nuanced understanding of potential cross-reactivities as well as knowledge about the available diagnostic extracts for skin prick testing and serum IgE testing. With the numerous types of dietary fish and shellfish associated with potential reactions, the clinician not only must know phylogenetic associations within fish and shellfish families, but must also have appropriate extracts for diagnostic testing, use prick to prick testing, or have access to appropriate serum IgE testing for a complete diagnostic evaluation. In absence of such knowledge or diagnostic accuracy, both the clinician and the patient might feel safer to institute broad avoidance measures.

However, to limit unnecessary food avoidance, as was shown in this publication, because avoidance of all fish is unlikely to be necessary for most fish-allergic patients, the use of improved diagnostic tools is important. Component-resolved diagnostics for fish parvalbumins, rGad c 1 and rCyp c1, or for shrimp tropomyosin, rPen a 1, can be helpful in predicting cross-sensitization with the fish and shellfish family, respectively.¹⁰ Although this might not obviate the need for OFC, those with a desire to include individual fish or shellfish in their diet should consider OFCs to explore selective tolerance. Future potential

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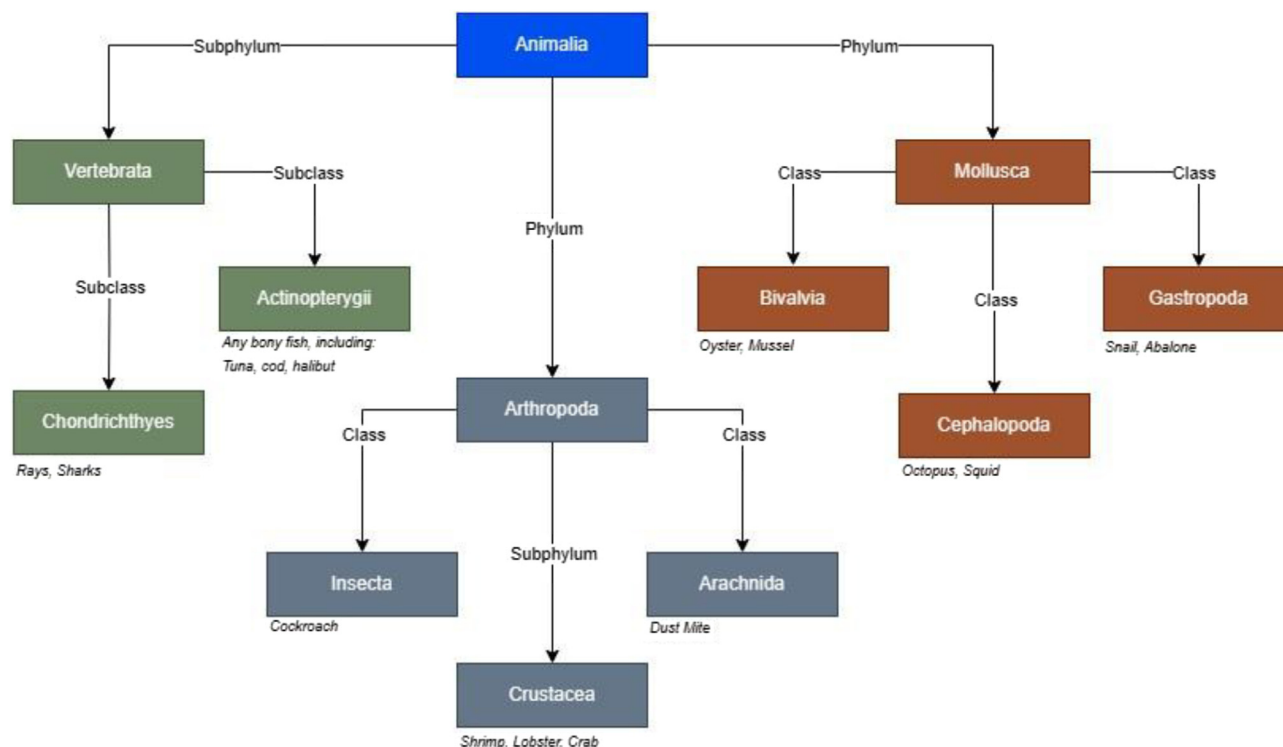


FIGURE 1. An abridged phylogenetic overview of seafood, encompassing both fish and shellfish (comprising crustaceans and mollusks), is presented. In addition, insects and arachnids are included to emphasize their close evolutionary connection with crustaceans.

assays that include epitope mapping and functional assays such as basophil histamine release also show promise as we underscore the need for precision medicine in the realm of seafood allergies. A better understanding of individual sensitization profiles can lead to more tailored and effective dietary recommendations, enhancing the quality of life for those affected by seafood allergies.

In summary, this “Sea of Change in Fish Allergy” advances our understanding and management of seafood allergies. As we navigate these complex waters, it becomes increasingly clear that a one-size-fits-all approach is often not appropriate. Clinicians must know about differences in dietary fish and shellfish cross-reactivity, and have appropriate diagnostic tools to chart individualized routes for each patient. The insights from this study highlight the need for more tailored avoidance recommendations to support the cultural and personal preferences of patients with fish or shellfish allergies. This journey, though challenging, promises a horizon where unnecessary dietary restrictions are minimized, and personal health is maximized, steering us toward a future of personalized allergy care.

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