Seafood Allergy In South Africa – Studies in the Domestic and Occupational Setting

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Background: Increased consumption of seafood due to the promotion of a healthy diet and increased processing of seafood to meet these domestic consumption needs, has lead to more frequent reporting of allergic reactions. The spectrum of seafood allergy associated with domestic and occupational exposure in the South African setting was investigated.

Methods/data base: In vitro studies were conducted on sera of 80 subjects reporting allergic symptoms associated with ingesting seafood. The distribution of positive immunoglobulin E (IgE) responses was evaluated (by UniCAP-RAST) as well as patterns of concurrent reactivity and cross-reactivity (by Western-blotting) to different seafood groups, commonly encountered in South Africa. The contribution of occupational factors was investigated through a postal survey of 68 seafood-processing workplaces.

Results: Patterns of IgE sensitization indicate that the majority of subjects (50%) were positive to crustaceans, 30% to molluscs, and 20% to fish species. More than half of the individuals reacted to one seafood group, 36% to two seafood groups, and 11% to all three seafood groups. The complexity of immune responses to finfish and mollusc species was evident in the different allergen profiles obtained for fresh and cooked seafood. The strongest immune response among the four tested fish species was to hake – the most common seafood processed in workplaces and therefore likely to pose an allergenic hazard to workers in the seafood processing industry. Among seafood processing factories the prevalence of work-related skin symptoms per workplace was substantially higher (0%-100%) than that for asthmatic (0%-5%) and other allergic symptoms (0%-37%).

Conclusions: Our preliminary investigations into the spectrum of seafood allergy in South Africa indicate that the potential of local seafood species in causing sensitization, either through ingestion, skin contact or inhalation are important considerations when investigating seafood allergy in the domestic or occupational setting.

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Humans have eaten seafood since prehistoric times, when fish was caught by hand and shellfish opened by beating them against the rocks. In Southern Africa, there are over 10,000 species of marine plants and animals, representing about 15% of all coastal marine species known worldwide [1]. Increased consumption due to the high nutritive value of seafood and the promotion of a healthy diet and increased processing of seafood to meet these domestic consumption needs has led to the more frequent reporting of adverse reactions, including immunologically mediated reactions.

Seafood Allergy

The major edible seafood that induce allergic reactions belong to three phyla (see Table 1). The phylum Pisces include the bony fish species that constitute most of the common edible fish. The group of molluscs (Mollusca) includes three major classes of seafood, namely the Gastropoda, Bivalvia, and Cephalopoda. Crustaceans also have among them important species that cause allergies such as crabs, lobsters, and shrimps [2]. The latter two groups are commonly referred to as shellfish. Allergy to seafood is common among populations that commonly consume or process seafood. Many of the published studies assessing the prevalence of fish allergy have been performed in Scandinavian countries and Spain [3–5], whereas studies from North America have more frequently reported sensitization to crustaceans such as crab and shrimp [6, 7]. Among the few studies providing accurate population-based estimates, such as Norway, the prevalence of fish allergy approaches 1/1,000 in the general population [8].

Seafood Allergy in the Domestic Setting

In recent years, there has been an increase in the number of subjects being seen by the Allergology Unit of Groote Schuur

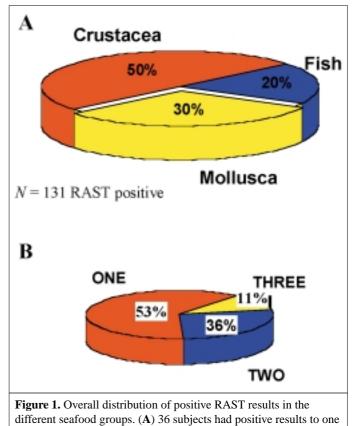
Table 1 Classification of Seafood Groups Causing Allergies				
Phylum	Class	Family (Common Name)		
Arthropoda	Crustacea	Crabs, lobsters, rock-lobsters, prawns, shrimp		
Mollusca	Gastropoda Bivalvia Cephalopoda	Abalone, snails Clams, oysters, mussels Cuttlefish (squid), octopus		
Pisces (sub-phylum Chordata)	Osteichthyes (bony fish)	Salmon, plaice, tuna, hake, cod, herring, sardine, trout, anchovy, mackerel		

Hospital, who have reported adverse reactions to indigenous fish and shellfish. Little is known about the prevalence of allergy to seafood in South Africa. We, therefore, embarked on a study of patients with a history of adverse reactions to local seafood species in order to investigate the spectrum of allergies associated with ingestion of seafood in this setting [9]. There were 105 volunteers who were recruited through print media advertisements in the Western Cape. Evaluation of the questionnaire responses implicated 26 seafood species in adverse reactions associated with seafood. The five most common seafood species reported by subjects to cause adverse reactions were prawns (47%), rock lobster (44%), abalone (35%), black mussel (33%), and oyster (24%). The most common bony fish species to cause reactions were reported to be hake (25%), yellowtail (22%), salmon and mackerel (15%), kingklip (13%), and snoek (11%).

Table 2

Frequency of Reported Symptoms in Subjects with Perceived Sensitivity After Ingestion of Seafood Species in the Western Cape Province of South Africa

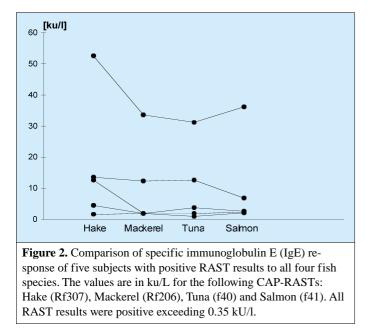
Symptom Prevalence of Symptoms per Seafood Group (%)				
	Finfish (<i>N</i> =38)	Crustacea (N=40)	Mollusc (N=61)	
Oropharyngeal itching/swelling	66	100	53	
Nausea/vomiting/ abdominal pain	53	78	61	
Urticaria/eczema	53	44	39	
Asthma/wheezing	42	61	41	
Flushing	40	22	34	
Headache	29	9	23	
Anxiety	26	48	49	
Diarrhoea	18	17	43	
Dizziness	13	13	26	



different seafood groups. (A) 36 subjects had positive results in the or more seafood species in the different groups (N=131). (B) Distribution of positive RAST results of subjects to species in one, two or all three seafood groups.

The spectrum of commonly experienced symptoms reported included oropharyngeal and cutaneous (51%), gastro-intestinal (54%), and respiratory reactions (36%). The pattern of immediate allergic reactions following the ingestion of seafood was generally similar to symptoms from allergy due to other foods reported in the literature [10]. However, in analyzing the data according to the three major seafood groupings, certain symptoms appeared more frequently than others (see Table 2). Flushing and urticaria were more frequent among fish-sensitive subjects, whereas itching/swelling of the throat and diarrhea were more frequently encountered in the crustacea- and mollusk-sensitive group.

In vitro studies were conducted on blood samples obtained from 80 subjects who consented to these tests to assess the distribution of positive immunoglobulin E (IgE) responses to seafood allergens, the prevalence of concurrent reactivity, and cross-reactivity among different seafood groups. The frequency of specific IgE responses to 12 seafood species as determined by radioimmunoassays (CAP-radioallergosorbent tests, CAP-RASTs) and in-house RASTs (for local seafood species such as abalone and yellowtail) is presented in Figure 1A. There were 36 subjects (N=131) who demonstrated positive RAST results to one or more seafood species. The majority of RAST results (50%) were positive to crustacean species (langoustine, crayfish, lobster, crab, shrimp), followed by molluscs (abalone, snail, blue mussel, oyster, squid) and fish (hake, salmon, mack-

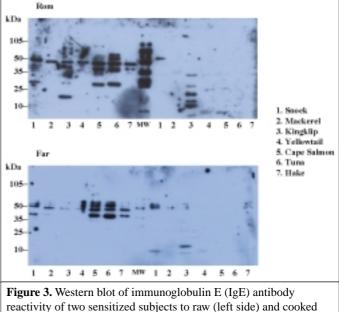


erel, tuna). A large proportion (53%) had positive RAST response to species in only one of the three seafood groups (see Figure 1B). These results clearly indicate that a general seafood avoidance regimen is not indicated for subjects with sensitivity to a particular species and that a clear identification of the offending species is of great importance when counseling patients. A closer look at the group of subjects with multiple sensitivity to species in all three seafood groups revealed that all 11% of subjects were positive to all the fish species tested.

In contrast to multiple sensitivity among the seafood groups, concurrent sensitivity to all tested species in a seafood group was high (56%) in the fish group (N=9) and 42% in the crustacean group (N=24). Figure 2 displays the RAST-positive response of five subjects with concurrent sensitivity to all four fish species analyzed (hake, mackerel, tuna, salmon). All concordant RAST results were highly significantly correlated in the fish and crustacean group, whereas the mollusk group demonstrated only 13% of concurrent sensitivity. These results support the view that the different fish and crustacean species, in contrast to the mollusk group, share common allergenic determinants. It would appear that the different molluscs, divided into three different classes, have species-specific allergens, which make the subject's immune response very species-specific. However, we have also demonstrated using RAST-inhibition studies that some cross-reactivity also exists between local mollusk and crustacean species, which is supported by data of other researchers [11, 12].

The presence of cross-reacting and also species-specific allergens could be demonstrated in seven local fish species using IgE immunoblot analysis (see Figure 3). A more detailed study of food allergy to an indigenous mollusk species identified a novel allergen in abalone, *Haliotis midae* [13].

Not all subjects with a convincing history of adverse reactions to seafood had positive RAST results. We therefore



reactivity of two sensitized subjects to raw (left side) and cooked fish species, respectively. The species names are labeled from 1 to 7 and the molecular weights (MW) are indicated on the left side in kilodalton (kDa).

conducted skin prick tests (SPT) with in-house produced extracts, to provide additional information on the immune response of subjects with negative RAST results. It was shown that one third of the tested RAST-negative subjects were SPT positive to one or more species. This demonstrated the sensitivity of this *in vivo* test, which used extracts of local seafood species. However, the most reliable method for diagnosis of food allergy due to ingestion is still the double-blind placebo-controlled food challenge (DBPCFC) to confirm the fish allergy and to identify putative species [14].

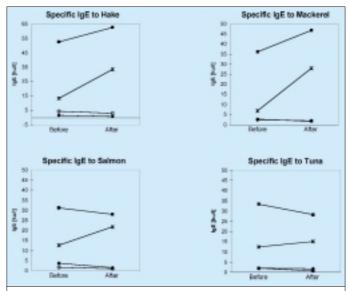


Figure 4. Specific immunoglobulin E (IgE) reactivity of four fishsensitive subjects prior to and 3–4 years after attending our clinic, as measured by CAP-RAST in kU/l. One subject (*) demonstrated an increase in IgE reactivity to all analyzed fish species. Note the different scale of the y-axis for hake. All RAST results were positive exceeding 0.35 kU/l.

In our previous study on nine subjects with convincing sensitivity to fish and negative RAST and/or SPT results, we were able to identify one subject sensitized to yellowtail using DBPCFC [9].

Sensitivity to various seafood species can persist for a prolonged time, despite allergen avoidance, as was demonstrated in a small cohort of patients: 3-4 years after their initial consultation at our clinic and avoidance of fish ingestion, all four subjects maintained a raised specific IgE titer (see Figure 4). The strongest immune response among the four tested fish species was to hake. The reason for the persistence of specific IgE could be the occurrence of cross-reacting allergens in other food ingested by the patient or inhalation of seafood aerosols. It has been suggested that accidental exposures to cooking aerosols at home or in the workplace could elicit clinical symptoms, which could result in delaying the development of tolerance [15, 16]. Dominguez and coworkers also came to a similar conclusion for patients who displayed allergic symptoms only by handling and touching fish [17]. We, therefore, decided to investigate the contribution of occupational factors towards the development of seafood allergy in more detail.

Seafood Allergy in the Workplace Setting

In our study on the spectrum of allergy due to seafood ingestion almost 30% reported respiratory and/or cutaneous symptoms after handling seafood or inhaling aerosols from the cooking process [9]. The high prevalence of symptoms with these exposures, which were usually domestic rather than occupational, along with the likelihood that similar workplace exposures would be more intense and prolonged, prompted us to investigate the health effects of these occupational exposures among workers.

Various studies indicate that allergy to fish is common in fish-processing communities as well as in fish-eating populations. Workers in the fishing and seafood processing industries are commonly exposed to seafood, especially those involved in either manual or automated processing of crabs, prawns, mussels, fish, and fishmeal. Other occupations associated with potential high-risk exposure to seafood include oyster shuckers; laboratory technicians and researchers; jewelry polishers; restaurant chefs and waiters; fishmongers and fishermen [18, 19].

The respiratory tract is often the primary route of occupational exposure as a result of inhalation of aerosols generated during seafood processing [18]. However, reactions can also occur via the dermal route as a result of direct handling of the seafood itself [19]. These reactions are due to chemical substances added to or associated with seafood which act as irritants or due to contact with high molecular weight proteins present in the seafood which result in an IgE-mediated response [20].

Occupational allergic reactions due to seafood commonly manifest as rhinitis, conjunctivitis, urticaria, asthma, and protein contact dermatitis [21]. Both occupational asthma and protein

Table 3 Common Processing Techniques Employed for the Major Seafood Groupings and Sources of Potential High-Risk Exposure to Seafood Product/s Processed in the Western Cape Province of South Africa				
Seafood Category	Processing Techniques	Sources of Potential High-Risk Exposure to Seafood Product/s		
Crustacea				
Lobsters	Cooking (boiling or steaming), "tailing" lobsters, scrubbing and washing, cooling	 Inhalation of wet aerosols from lobster "tailing," boiling, washing, cooling, cleaning processing lines/ tanks with pressurized water 		
Molluscs				
Mussels, squid	Washing, mussel opening, cooking (boiling or steaming) Chopping, dicing, slicing squid	– Inhalation of wet aerosols from mussel opening, washing		
		 Dermal contact from unprotected handling of molluscs 		
Finfish				
Various species (e.g., hake, kingklip, snoek, pilchard, anchovy, red eye)	Heading, degutting, skinning, mincing, filleting, trimming, cooking (boiling or steaming), spice/batter application, frying, milling, bagging	 Inhalation of wet aerosols from fish heading, degutting, boiling 		
		 Inhalation of dry aerosols from fishmeal bagging 		
		 Dermal contact from unprotected handlng of various fish types 		







Figure 5. (A) Rock-lobster processing (water-jet scrubbing).(B) Fish canning (degutting and heading). (C) Fishmeal processing (bagging).

contact dermatitis (PCD) have been associated with occupational exposure to all three major seafood groupings. The commercially important seafood causing occupational allergies (except for snails) is presented in Table 1. The prevalence of occupational asthma reported in studies (outside Africa) using direct investigator assessment of disease status varies from 7%–36% for asthma and 3%–11% for occupational protein contact dermatitis [20, 22–25].

The fishing and seafood processing industry in South Africa employs approximately 28,000 workers in more than

100 workplaces [26]. These workers are directly dependent on the industry, supplying food for the whole of the Southern African subregion. Labor in the industry tends to be divided along gender lines, with men almost exclusively going out to sea to catch the fish and women doing the majority of on-land seafood processing. The degree of exposure to seafood is likely to be highest during the harvest season (which varies dependent on the seafood type) when most of the processing occurs.

Comprehensive data on working conditions and specific health outcomes associated with occupational allergy in the seafood processing industry in South Africa is lacking. In 1998, of 5679 cases reported under South African workers' compensation law, there were, in total, 180 cases of occupational asthma (3.2%) and 678 cases of dermatitis of an allergic or irritant nature (11.9%). However, the current reporting format of the data does not allow us to ascertain the proportion of occupational asthma and dermatitis due to seafood processing. A separate surveillance system, the Surveillance for Occupational Respiratory Diseases in South Africa (SORD-SA), operating for the past 3 years has, to date, not received any reports from participating physicians of asthma due to seafood allergy. These data suggested that there appears to be a considerable degree of under-reporting due to the lack of occupational health services in the country and the low index of suspicion among occupational health practitioners in identifying such cases.

In the first phase of our investigations, we investigated the work practices, occupational health services, and allergic health problems among seafood processing workplaces in the Western Cape province of South Africa [27, 28]. A cross-sectional study was conducted among 68 workplaces that were sent a selfadministered postal survey questionnaire. Workplaces that reported a high prevalence of work-related symptoms associated with seafood exposure were also inspected to identify highrisk exposure processes. Forty-one (60%) workplaces responded to the questionnaire. The study found that the workforce in the industry comprised mainly women (62%), and a considerable proportion (31%) were seasonal workers. The most common seafoods processed by these workplaces were bony fish (76%) and rock lobster (34%), followed by squid (21%), mussel (16%), abalone (13%), and prawn (3%). Among the bony fish, hake (47%) and pilchard (26%) were by far the most commonly processed seafood. The former was primarily used for filleting purposes and the latter for canning. More than half the workplaces used freezing (71%), cutting (63%), and degutting (58%) procedures during processing. The latter two processes are known to be associated with increased generation of aerosols.

There was substantial variation in processing methods for various seafood in these workplaces. Descriptions of commonly observed work processes and sources of potential high-risk exposure to seafood product/s are outlined in Table 3. Aerosolization of the seafood during processing was identified as a potential high-risk activity for sensitization through the respiratory route. Identified processes with high potential for aerosol exposure included scrubbing and tailing of rock lobster (see Figure 5A); degutting and heading of fish (see Figure 5B); and bagging of fishmeal (see Figure 5C). Workers employed in highly automated facilities were also at high risk for sensitization due to inadequate and poorly designed local exhaust ventilation systems in these plants. High-risk dermal exposure occurred as a result of unprotected handling of rock lobster or various fish types, the latter generally occurring under wet and low temperature conditions.

At least one case of work-related allergy had been reported by 50% of workplaces in the past year. Common work-related allergic symptoms/ailments included skin rashes (78%), asthma (7%), and other nonspecific allergic symptoms, namely conjunctivitis, rhinitis, and angioedema (15%). The annual prevalence of work-related skin symptoms per workplace was substantially higher (0%-100%) than that for asthmatic (0%-5%) and other allergic symptoms (0%-37%). The relatively low prevalence of employer-reported asthmatic symptoms (81% reported near-zero prevalences) when compared to epidemiological studies using direct investigator assessment of individual health status suggests that there may be under-detection. This is due to the fact that only 45% of workplaces provided an on-site occupational health service that conducted specifically targeted medical surveillance programs. This was more apparent among small workplaces (employing less than 200 workers). Furthermore, the lack of specific statutory guidelines for the evaluation and control of bioaerosols in South African workplaces has also contributed to the lack of awareness and reporting of occupational seafood allergies by employers. We have recently made a detailed submission to the Department of Labor in South Africa to ensure that occupational seafood allergy is included within the scope of application for its proposed Regulations for Hazardous Biological Substances under the Occupational Health and Safety Act.

Another factor that may explain the low prevalence of health outcomes relates to the "healthy worker" effect in which susceptible workers either avoid "high-risk" jobs or leave their jobs soon after working for only a short period of time ("healthy hire" effect). Alternatively, the most affected workers may have already left the workplace or moved to low-exposure jobs at the time of the study and, therefore, did not appear on current company records as ill ("survivor" effect). Both these factors tend to result in an underestimate of the true prevalence of disease in cross-sectional studies of workers in high-risk jobs [29].

Future Directions

This is the first African study that has investigated the allergic symptoms associated with ingestion of seafood. We identified common as well as novel allergens in species from the fish, crustacean, and the mollusk groups. In our future work we intend identifying and characterizing the specific allergens found in indigenous seafood species that have not been previously described in the literature. In addition the immune responses to novel allergens associated with *Anisakis*, a fish-derived parasite, will be studied in greater detail. Furthermore, studies using specific monoclonal antibodies, developed for the novel allergens of abalone, will characterize the cross-reacting allergens found in species of the three major seafood groups. In addition, these monoclonal antibodies will advance the technology for the sensitive detection of environmental allergens found in the domestic and occupational setting.

Our study on occupational factors is also the first African study to document (employer-acknowledged) work-related symptoms and allergic health problems among workers in the seafood processing industry. In our future work we intend embarking on further epidemiological studies that will focus on quantifying the disease burden attributed to seafood exposure and identifying environmental and host-associated risk factors that result in allergic sensitization to occupational seafood allergens. This would necessitate the development of appropriate industrial hygiene monitoring techniques for exposure characterization of at-risk workers and health outcome assessment protocols that utilize more sensitive immunological markers for early diagnosis. In this manner the pattern of occupational seafood allergy among seafood processing factories in Africa and the Southern African subregion will be better characterized. This will also result in more reliable information being available to guide the timely implementation of appropriate interventions to minimize inhalation and dermal exposure to seafood agents commonly processed in this region. These initiatives will also contribute to the development of occupational exposure limits (OEL) for seafood aerosols, since none currently exist, either locally or internationally, to protect the health of workers in the seafoodprocessing industry.

Summary

The spectrum of allergy associated with domestic and occupational exposure in the South African setting has been described. The immunological findings using different patientspecific sera and the monoclonal antibodies generated have provided important information and new insights into the concordant and multiple sensitivity to species belonging to the major seafood groupings, namely finfish, crustacea, and molluscs. The complexity and stability of immune responses to finfish and mollusk allergens was also demonstrated in allergic subjects. Furthermore, this study has also shown that the strongest immune response among the four tested fish species was to hake, the most common seafood processed in workplaces and, therefore, likely to pose an allergenic hazard to workers in the seafood processing industry. Our preliminary investigations into the seafood industry indicate that the prevalence of employer-reported symptoms is much lower than epidemiological studies using direct investigator assessment of individual health status. This suggests likely underreporting of work-related allergic symptoms, more especially for asthma symptoms. This under-detection is probably due to the under-provision of occupational health services among small workplaces and the presence of poorly designed medical surveillance programs to detect seafood allergy. The absence of a legal framework to prevent the development of occupationally-related seafood allergy is also a contributory factor. Future directions of our research are described in greater detail.

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