

Seafood workers and respiratory disease: an update

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Purpose of review

This review focuses on seafood workers engaged in harvesting, processing and food preparation. These groups are increasingly at risk of developing occupational allergy and respiratory disease as a result of seafood handling and processing activities. This review provides an update of a previous review conducted a decade ago.

Recent findings

Exposure characterization studies have demonstrated that aerosolization of seafood (muscle, visceral organs, skin/mucin) during canning and fishmeal operations result in highly variable levels of airborne particulate (0.001–11.293 mg/m³) and allergens (0.001–75.748 µg/m³). Occupational asthma is more commonly associated with shellfish (4–36%) than with bony fish (2–8%). Other seafood-associated biological (*Anisakis*) and chemical agents (protease enzymes, toxins and preservatives) have also been implicated. Atopy, smoking and level of exposure to allergens are significant risk factors for sensitization and the development of occupational asthma. Molecular studies of the allergens suggest that aside from tropomyosin and parvalbumin, other as yet uncharacterized allergens are important.

Summary

Future research needs to focus on detailed characterization of allergens in order to standardize exposure assessment techniques, which are key to assessing the impact of interventions. The clinical relevance of agents such as serine proteases and endotoxins in causing asthma through nonallergic mechanisms needs further epidemiological investigation.

Keywords

allergy, asthma, occupational, risk factors, seafood

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Introduction

Recent years have seen a growing demand for seafood, which has led to increased production. Increased levels of production and consumption of seafood have led and continue to lead to more frequent reporting of work-related respiratory allergy and asthma. This review focuses on work-related respiratory disease associated with seafood (fish and shellfish) harvesting, processing and food preparation, as an update to an extensive review on this subject published previously [1]. To identify relevant manuscripts, MEDLINE searches were undertaken for studies on occupational seafood allergy and respiratory disease during the period 2000–2009.

Seafood working population

Occupational exposure to seafood allergens occurs mainly in the food and fishing industry. The Food and Agriculture Organization (FAO) estimated that in 2006, fishery and aquaculture production activities provided direct employment and revenue for 43 million people world-

wide, largely from developing countries, harvesting 110 million tonnes of food fish [2]. The number of fishers and fish farmers has been growing at an average rate of 3.5% per year since 1990. It is estimated that approximately 52% of this population work aboard fishing trawlers, 32% in aquaculture production (marine and freshwater), and 16% work inland as capture fishers or in other land-based activities such as processing [3]. More than 30% of fish for human consumption derives from aquaculture [4]. In many countries, labour in the fishing industry is divided along sex lines with men almost exclusively involved in harvesting the seafood at sea and women doing most of the processing ashore [5]. Most of the workforce are seasonal and often migrant working populations and are vulnerable to various workplace organizational factors which, in addition to the gendered distribution of work, may mediate hazardous occupational exposures [6].

Workers in several of these industries are exposed to seafood, especially those involved in either manual or automated processing of crabs, prawns, mussels, fish, and fishmeal in factories. Other occupations associated with

exposure to seafood include harvesting activities (fishermen, aquaculture, oyster shuckers, fishmongers, truck drivers, maintenance), food preparation activities (restaurant chefs and waiters), laboratory technicians and researchers, pet food production and value added (shell grinders, jewellery polishers) [1,7]. Recently, a worker developed fatal asthma following inhalation of dust produced from grinding shark cartilage intended for use as a natural remedy [8].

Seafood work environment and sources of airborne exposures

There is great variation in work activities for the different types of seafood. Seafood plants vary in the levels of technology, with some of the smaller workplaces relying entirely on manual handling of the seafood and larger companies using modern highly automated processes. Whereas these highly automated processes reduce direct contact with seafood, they have the potential for greater bioaerosol production. For some seafood, processing also occurs on board vessels, commonly characterized by confined spaces and inadequate ventilation systems [9]. Adverse respiratory reactions are mainly the result of biological and chemical agents associated with these work processes during the processing, preserving, storage or transport of the seafood. Recent studies suggest that high concentrations (0.2–10 µg/g) of pyroglyphid dust mites generally found in domestic environments may also pose an occupational risk to fishermen spending long periods of time aboard fishing vessels [10]. There are also physical exposure factors other than those of seafood origin, for example, hypertonic saline aerosols from wet environments, cold air, strenuous physical activity may also trigger respiratory symptoms [11].

The commercially important seafood causing occupational respiratory allergy is presented in Table 1. Among the arthropods, the crustacean class includes some of the most allergenic species of seafood. In addition to the high molecular weight seafood proteins (>10 kDa), 'fish juice' produced during seafood processing has been shown to contain microbes, biogenic

amines, degradation compounds due to post mortem changes, as well as digestive enzymes (pepsin and trypsin) emanating from the seafood [1]. The nonseafood associated agents with the potential to cause respiratory disease include various contaminants such as parasites [*Anisakis simplex* [11–18], protochordates – sea squirt (*Hoya*) [19], marine toxins (histamines) [20], bacterial toxins (endotoxin), chemical additives (sodium disulphite, formaldehyde) [21,22] and spices (paprika, flour additives, garlic)]. Gases produced by anaerobic decomposition of fish (hydrogen sulphide) have also been reported to cause acute respiratory disease [23].

Exposure to seafood has been shown to occur primarily through inhalation of dust, steam, vapours and seafood proteins generated during cutting, scrubbing or cleaning, cooking or boiling, and drying activities. Aerosolized seafood particulate (muscle, exoskeleton, visceral contents, skin slime/mucin, collagen) produced during processing and fishmeal operations as well as seafood allergens present in the steam and vapours has been identified as the potential route for sensitization and the development of asthma. Recently there have been an increasing number of studies that have attempted to characterize exposures in more detail using newly developed immunoassays [24]; however, the major challenge lies in the standardization of these assays. Furthermore, there is also a considerable degree of cross-reactivity between taxonomically related inhalant allergens of seafood origin as the fish exposure assessment studies have demonstrated [25].

Studies of environmental exposure assessments in seafood processing environments are summarized in Table 2. These studies demonstrate a wide range of total inhalable airborne particulate (0.001–11.293 mg/m³), protein (0.001–6.4 mg/m³) and allergen (0.001–75.748 µg/m³) levels. Particulate and allergen levels reach very high levels in the processing operations aboard vessels at sea in the case of crab processing and during fishmeal operations. Work processes causing aerosol production include butchering or grinding; degilling, 'cracking' and boiling of crabs; cleaning and brushing of crab; 'tailing' of lobster; 'blowing' of prawns; washing or scrub-

Table 1 Seafood and nonseafood associated agents causing occupational allergy and asthma

Phylum	Class	Family species (common name)
Arthropoda	Crustacea	Crabs, lobsters, prawns, shrimp, scampi, shrimpmeal
Mollusca	Gastropoda	Abalone [12]
	Bivalvia	Clams, oysters, mussels, scallops [13]
	Cephalopoda	Cuttlefish (and bone), octopus [14], squid [15]
Pisces (sub-phylum Chordata)	Osteichthyes (bony fish)	Salmon, plaice, tuna, hake, cod, herring, pilchard, anchovy, trout, swordfish, sole, pomfret, yellowfin, shark (cartilage) [8], fishmeal (flour)
Other nonseafood associated biological agents		Hoya (sea-squirt), <i>Anisakis</i> , red soft coral, daphnia, marine sponge, algae

Updated with permission from [1].

Table 2 Exposure assessment studies of seafood processing workers on land and aboard vessels

Seafood category	Particle fraction measured	Particulate concentration (mg/m ³) range	Protein concentration (mg/m ³) range	Allergen concentration (µg/m ³) range
Crustaceans				
Crabs (snow, Tanner, common, King)	Total inhalable	0.001–0.680	0.001–6.400	0.001–5.061
Crabs (snow) ^a [26]	Total inhalable	ND	ND	0.079–21.093
Prawns	Total inhalable	0.100–3.300	ND	ND
Shrimp [27]	Total inhalable	ND	ND	1.500–6.260
Rock lobster [25]	Thoracic	LOD-0.661	LOD-0.002	ND
Scampi [28]	Total inhalable	ND	ND	0.047–1.042
Finfish				
Salmon	Respirable	0.040–3.570	ND	0.100–1.00
Pollock	Total inhalable	0.004	ND	ND
Whiff megrim/hake	Total inhalable	ND	ND	0.002–0.025
Pilchard [24]	Thoracic	LOD-2.954	LOD-0.006	0.010–0.898
Cod [27]	Total inhalable	ND	ND	3.800–5.100
Salmon [27]	Total inhalable	ND	ND	LOD-1.600
Herring [27]	Total inhalable	ND	ND	0.300–1.900
Fishmeal (anchovy) [25]	Thoracic	LOD-11.293	LOD-0.004	0.069–75.748
Shark cartilage [8] ^b	Respirable	0.920–5.140	ND	ND
	Total inhalable	26.400–44.700	ND	ND

ND, not done; LOD, limit of detection. Modified and updated with permission from [1].

^a Processing aboard vessels.

^b Non food-handling environment.

bing of shellfish; degutting, heading, and cooking/boiling of fish; mincing of seafood; and cleaning of the processing line or storage tanks with high pressured water hoses [1]. Since water is a major feature of this work environment, it may also influence the size, lifetime, or other dynamics of small protein particles. Processes that generate dry aerosols such as prawn blowing operations using compressed air and fishmeal loading/bagging appear to generate higher concentrations of particulate than wet processes (prawn blowing with water jets).

Aside from allergen exposures, endotoxin levels during seafood operations have also been investigated. Whereas surveys among crab processing workers reported mean concentrations of airborne endotoxin to be 32.6 EU/m³ (total fraction) and 15.6 EU/m³ (respirable fraction), recent studies of shrimp processors have demonstrated mean levels between 5.8 and 29.9 EU/m³ (total fraction) [27,29]. Fish processing operations have reported highly variable mean airborne endotoxin levels for pilchard canning operations (49 EU/m³); filleting/slaughtering of cod (8.6–23.9 EU/m³), salmon (6.8–7.9 EU/m³) and herring (103.7 EU/m³); and anchovy fishmeal (136 EU/m³) [5,25]. It would appear that gutting and fishmeal operations demonstrate consistently elevated endotoxin exposures. More detailed endotoxin exposure characterization and dose–response studies are needed to assess the relative contribution of this exposure to symptoms experienced by workers.

Pathophysiological mechanisms and occupational respiratory disease

Adverse respiratory reactions in the seafood processing environment can be mediated by immune (allergic) and

nonimmune-mediated mechanisms. Although seafood contains a wide variety of proteins, only a few are known allergens. Most studies have identified proteins causing typical IgE-mediated symptoms in individuals who have been sensitized through ingestion. A number of seafood allergens have been isolated, purified, and characterized in the past 2 years and is the subject of a recent review [30•]. By contrast, inhalation of seafood proteins present in aerosols responsible for asthmatic reactions encountered predominantly in occupational environments have not yet been fully described. Table 3 outlines the allergenic proteins identified on immunoblotting of sera in individuals with work-related allergy and asthma. The molecular weights of crustacean allergens originating from ‘meat’ (muscle) and waste water during processing range between 4.4 and 97 kDa. It has been suggested that some of these allergens in the 30–39-kDa range may be similar to the major cross-reactive crustacean allergen, muscle protein tropomyosin (38–40 kDa). Other minor allergens (e.g. 97 kDa paramyosin) similar to the allergen found in patients with allergy to *Anisakis* have also been identified [31]. Allergens from mollusks (meat and viscera) have lower molecular weights ranging from 19 to 43 kDa, with some studies implicating tropomyosin and its dimers due to the close taxonomical relationships shared with crustaceans. Studies of sera of workers involved in bony fish processing have demonstrated IgE reactive proteins in fresh, frozen and canned pilchard ranging from 12 to 250 kDa, suggesting that a component of the immune response is directed to oligomeric (36, 48 and 60 kDa) rather than the monomeric (12 kDa) forms of parvalbumin (Lopata AL, Jeebhay MF, unpublished observation). Furthermore, there remains additional high molecular weight allergens identified in immunoblotting of sera of symptomatic workers that have yet to be

Table 3 Allergenic proteins identified following occupational inhalation of seafood

Seafood category	Family species and common name	Source of allergen	Molecular weight (kDa) of protein identified on immunoblot	Reference
Crustacean	Snow crab (<i>C. opilio</i>)	Crab meat, crab water	34, 25, 18.5, 4.4	[32 ^a]
	Freshwater shrimp (<i>Gammarus</i> sp.)	Dried whole shrimp	80	[33]
	Shrimp/scallops ^a	Raw shrimp/scallop and water	35–39	[34]
	Brine shrimp (<i>Artemia</i> sp.)	Cysts	97	[31]
	Scampi (<i>N. norvegicus</i>)	Scampi meat, scampi waste water	97	[28]
Molluscs	Scallops (<i>C. opeccularis</i> , <i>P. maximus</i>)	Scampi meat	30.2	[35]
		Scallop meat and viscera	19–42	[13]
	Octopus ^a	Octopus meat	32, 43	[14]
Finfish	Pilchard (<i>S. sagax</i>)	Whole pilchard	36, 48, 60	^b

^aSpecies not identified.^bLopata and Jeebhay (manuscript in preparation).

characterized. Future studies need to focus on identifying and characterizing the specific seafood protein allergens present in aerosols generated during processing activities that are responsible for allergic respiratory disease.

Studies estimate that, at most, only 50% of asthma cases are attributable to eosinophilic allergic airway inflammation, suggesting a possible role of neutrophil-mediated asthma triggered by endotoxins and other nonspecific irritant factors causing asthma symptoms [36]. Concomitant exposures to toxins (e.g. histamine, endotoxin) in seafood bioaerosols and chemicals (e.g. formaldehyde in fishmeal production; sulphite preservatives in canning and shellfish harvesting activities, amines and other antimicrobial agents used to soak gloves, forklift exhaust emissions) and other biological contaminants in seafood bioaerosols have also been known to cause mucous membrane irritation and/or asthma on an inflammatory nonallergic basis [1,27,37^{••}]. One such study assessed cytokine release (IL-8 and IL-1 β) in sera of herring processors and identified substances in the work environment with a pro-inflammatory potential comparable to that of endotoxin, suggesting a priming effect of the work exposure [38]. More recent studies have focused on the role of non-muscle proteins from visceral contents and the outer mucous layer of fish as potential causative agents for the symptoms observed. One such candidate is the group of serine protease enzymes such as salmon trypsin, which has been shown to cause airway inflammation through stimulating IL-8 in cultured airway epithelial cells mediated by protease activator receptor (PAR)-2 in in-vitro studies [39]. These enzymes were compared to endotoxin, which was not found to stimulate IL-8 in an in-vitro airway epithelial cell model [40[•]]. Future studies need to address the clinical relevance of serine proteases by direct airborne measurement of these enzymes through detailed exposure characterization and relate this to adverse respiratory health outcomes observed in epidemiological studies.

Respiratory health effects associated with seafood: epidemiology and clinical manifestations

Occupational asthma is the most frequent work-related respiratory disease reported in the seafood industry, with the prevalence varying from 2 to 36%. Differences in prevalence are partly due to varying definitions of occupational asthma, most studies relying on questionnaires and assessment of specific sensitization; the allergenic potential of the seafood proteins involved; and the type of work process resulting in excessive exposure (e.g. steam, organic dust, air blowing, water jets). Table 4 summarizes the findings of published studies reporting occupational asthma cases and surveys, updated since the review of Jeebhay *et al.* [1].

A higher prevalence of occupational asthma is associated with exposure to aerosols arising from arthropods (crab and shrimp) than to molluscs and bony fish. Symptoms of asthma may develop after only a few weeks or months or after several years [46]. Symptoms are worse at work, improving on weekends or holidays and often awaken affected patients at night. Rhinitis, conjunctivitis (and less frequently skin rashes on exposed parts of the body) are often associated and may precede the development of chest symptoms [47]. It is estimated that 7% of workers with ingestion-related seafood allergy also have asthma symptoms associated with inhalational exposure to seafood [37^{••}]. There have also been isolated case reports of workers (fishmonger handling shrimp and lobster, fish smoking factory worker handling trout, anchovy, salmon and sardines) with work-related asthma symptoms who subsequently developed ingestion-related allergic symptoms [1]. However, prospective studies are needed to explore this in detail so as to quantify the risk of pre-existing seafood allergy predisposing to respiratory allergy. Furthermore, the risk of workers with initial work-related respiratory sensitization subsequently developing ingestion-related symptoms also merits further investigation.

Table 4 Epidemiological studies and case reports of occupational asthma due to seafood

Agent	Occupation	Subjects (n)	Occ. asthma prevalence (%)	Other symptoms	SPT or ID tests (n or % of positive)	Other immunological evidence (% positive)	SIC (% positive)	Other evidence
Epidemiological studies and case reports of occupational asthma due to arthropods								
Crab	King crab processors	186	13%	ND	60% (of random sample of 15)	Precipitins: + in 9/15 tested ND	ND	Across shift spirometry ND
	Snow crab processors	825 [41]	5.5% (incidence of 2%/month)	ND	ND	ND	ND	ND
		303 [42]	16%	Rh-C; skin rash	+: 22%, 54/110	sgE [43], Water: 31/110 tested, Meat: 39/111 tested RAST: 6–8%	33/46 tested	PEF + PC ₂₀ monitoring
		107	Incidence of 2%/6 weeks	Rh	ND		ND	Spirometry
Prawn		215 [44••]	15.8%	Rh-C; rash	+: 18.3% (30/164 tested)	SlgE: +14.3% (28/196 tested)	ND	PEF monitoring
	Rock crab processors	29	NA	Rh-C	+: 7/28 tested	sgE: + in 4/27 tested	4/14 tested	PC ₂₀
	Dungeness, king, snow and tanner	82 [26]	4% (28%: cough)	ND	ND	ND	ND	ND
	Prawn processors	50	36%	Rh-C; itchy hands	+: 13/50 (7/18 symptomatic workers)	sgE: + in 18/50 (7/18 symptomatic workers)	2/2 tested	Across shift spirometry
		135	26 patients with respiratory symptoms/52 workers tested	Rh-C; dermatitis	ND	sgE: + in 16/52 tested, sgG: not discriminative	ND	ND
		57	Shrimp: 2/57, clam: 1/57	Rh-C	+: 16%, +: 7%	sgE: + in 14%, slgE: + in 7%	1/3 tested, 2/3 tested	PC ₂₀
Shrimp or clam	Food processors (lyophilized powder)	1	NA	Rh	+: shrimp	sgE: + (shrimp, crab)	+	ND
Shrimp meal	Technician	1	NA	U; Rh	+: lobster, shrimp, crab	sgE: + (lobster, shrimp, crab)	+(lobster & shrimp)	ND
Lobster and shrimp	Fishmonger	1	NA	U	+: lobster, haddock, scallops, oyster, clam, cod	ND	+: lobster	PC ₂₀
Lobster	Chef	1	NA	U	+			
Shrimp	Seafood delivery	1 [7]	NA	U; anaphylaxis	+: herring, shrimp	sgE: + (herring, sardine, swordfish, shrimp)	ND	ND
	Processors	132 [11]	Up to 24% of workers reported WRAS	Rh	ND	sgE: + to shrimp in 20.3% of those tested	ND	Spirometry
Epidemiological studies and case reports of occupational asthma due to molluscs								
Cuttle fish	Deep sea fishermen	66	Incidence of 1%/year	Dermatitis, C	ND	ND	ND	ND
	Fishermen	50	ND	Rh; U; eczema	ND	ND	ND	Spirometry
	Mussel openers	224	32.3% with at least one WRAS	ND	ND	ND	ND	Across shift PEF
Mussel (?)		1	NA	ND	ND	ND	ND	ND
Mussel or crustaceans	Cook	1 [13]	NA	U	ND	sgE: + King & Queen scallop, scallop viscera	ND	PEF monitoring
King & Queen scallop	Processor	1	NA	ND	ND	ND	+	ND
Abalone	Fisherman	1	NA	ND	ND	sgE: + for octopus, squid, shrimp	+	PC ₂₀ , PEF monitoring
Octopus	Processor	1 [14]	NA	Rh-C	+: octopus (raw and cooked), raw squid, raw shrimp		+	

Epidemiological studies and case reports of occupational asthma due to Pisces (bony fish)								
Salmon	Fish processors	291	8,2%	Rh	ND	slgE: 9% +, precipitins: 33% o+	ND	PEF monitoring
Trout (?)	Fish processors	8	NA	Rh	ND	slgE: 100%, Antiendotoxin Ab: 13%	ND	PEF monitoring, PC ₂₀ , spirometry
Pilchard, Anchovy	Fish processors – fish canning (pilchard), fishmeal: (anchovy and pilchard offal)	594 [37••]	1.8% to fish with 16% of WRAS	Rh-C	+ in 6% for any fish	slgE: + anchovy (5/15); pilchard (4/15)	ND	Spirometry, PC ₂₀
Plaice, hake, salmon, tuna	Fish processors	2	NA	Rh-C	+ to all fish extracts	slgE: +	+	PEF monitoring
Various fish and seafood	Fishmongers	64 [45]	2/64 reporting WRAS (shrimp, mussel)	Rh	+ : shrimp (12.5%); spiny lobster (10.9%); mussels (7.8%); crab (3.1%); cod (3.1%); sardines, salmon and trout (1.6% each)	slgE: same as SPT	ND	PEF monitoring in one patient (shrimp)
Salmon	Processors	211 [11]	Up to 13.2% reporting WRAS	Rh	ND	slgE: + to cod in 2,7% of those tested	ND	ND
Haddock, cod, pollack	Processors	387 [11]	Up to 14.1% reporting WRAS	Rh	ND	slgE: - to salmon of those tested	ND	ND
Epidemiological studies of occupational asthma due to other nonseafood associated biological agents								
<i>Anisakis simplex</i> (AS)	Fish processing workers	578 [18]	Chest symptoms in 2% of workers	Rh-C, rash	AS: + in 8%, Fish + in 6%	ND	ND	Spirometry, PC ₂₀
Hoya (sea-squirt)	Frozen-fish factory	1 [17]	NA	U	+ for AS	slgE: + for AS	ND	ND
	Oysters handlers	1416	16% (Symptoms of asthma)	Rh-C	+	+	ND	ND
Red soft coral	Spiny lobster fishermen	79	9%	Rh-C; dermatitis	+	ND	ND	ND

Modified and updated with permission from [1]; C, conjunctivitis; PC₂₀, concentration of methacholine or histamine inducing a 20% fall in forced expiratory volume in 1 s (FEV₁); PEF, peak expiratory flow; Rh, rhinitis; Rh-C, rhino-conjunctivitis; SIC, specific inhalation challenge; slgE, specific IgE determined by either RAST or ImmunoCap System; SPT, skin prick test; U, urticaria; WRAS, work-related asthma symptoms.

Although questionnaires on occupational asthma (open and closed) are very sensitive, they are not very specific [48] and the diagnosis should rely on objective means to confirm work-related asthma [49]. Documentation of specific sensitization (prick skin test or specific IgE) to the offending allergens or of increased nonallergenic bronchial responsiveness (NABR) supports the diagnosis but does not confirm it. In crab processing workers, the positive predictive value of a positive skin test to crab extracts or positive specific IgE (as assessed by RAST) was 76 and 89%, respectively [43]. A negative skin test therefore does not exclude the diagnosis of occupational asthma, whereas a positive test is not confirmatory either. Monitoring of peak expiratory flow (PEF) at work and off work is inexpensive, easily available and can confirm the diagnosis of work-related asthma. However, PEF is effort-dependant and often poorly performed by workers who need to be properly coached and supervised [44^{••},50]. PEF may also be combined with monitoring of NABR and sputum induction to improve the accuracy of the diagnosis but the latter test is less accessible [51]. A few studies have used specific inhalation challenges to confirm the diagnosis in seafood asthma. Among the asthmatic reactions observed, early reactions are the most frequent, followed by dual asthmatic reactions with a few isolated late reactions. In crab processing workers, isolated late asthmatic reactions are more frequent [52].

The prognosis of occupational asthma in workers who develop occupational asthma is variable and depends on several factors: duration of exposure, particularly after onset of symptoms, FEV₁ and PC₂₀ at the time of diagnosis, and the type of agent involved [52–54]. Unfortunately, several workers continue to be symptomatic of asthma or have abnormal lung function after work withdrawal. In crab processing workers, Hudson *et al.* [52] found that a better prognosis was seen in workers with shorter duration of exposure after onset of symptoms, higher FEV₁ and PC₂₀ at time of diagnosis. The study also demonstrated that, following work withdrawal, a plateau of improvement was reached after a mean of 1 year for spirometry and 2 years for NABR [55]. Although there was a concomitant decrease in the blood level of specific IgE to crab allergen, no plateau was reached even at 5 years.

Irritant-induced asthma or RADS can be induced by exposure to high concentrations of irritants such as sulphite preservatives [22] or ammonia used as a refrigerant [56] which could be encountered in seafood industries. Furthermore, asthma triggered by exposure to sulphites in prawn and lobster processing workers has been described simulating occupational asthma [21,22], although the exact mechanism of sulphite asthma is unknown [57].

Although no cases of hypersensitivity pneumonitis have been described in the seafood industry, there are reports of hypersensitivity pneumonitis in workers exposed to the dust of molluscs (oyster, sea snail) used in the manufacture of various ornaments such as buttons [58–60].

Determinants of seafood-related respiratory health effects

Individuals with pre-existing asthma are not at increased risk of developing occupational asthma unless they are atopic. Indeed, atopy is the most important host factor associated with the development of sensitization to high molecular allergens such as crabs, prawns, cuttlefish, pilchard and anchovy [1,37^{••},44^{••}] as well as for the development of occupational asthma [44^{••}], although the risk associated with atopy varies between studies. Smoking has been associated with an increased risk of developing sensitization to high molecular agents and in the seafood industry, particularly to prawns [1], crab [44^{••}] and fish (pilchard, anchovy and salmon) [1,37^{••}]. It is also a risk factor for developing occupational asthma in salmon and crab processing workers [37^{••},44^{••}]. The presence of rhino-conjunctivitis has been associated with an increased risk of developing occupational asthma to a number of high molecular agents including seafood [47]. Analysis of fish consumption patterns among seafood processors has shown that high seafood consumption (as measured by serum levels of omega-3 fatty acids) is not positively associated with occupational sensitization or with occupational asthma [14].

Regarding environmental factors, exposure to the causative agent/substance in the food matrix, its physical state and the exposure dose (duration and level of exposure) all appear to play a role. Several studies have shown dose–response relationships between the level of exposure to occupational sensitizers and the development of either symptoms or sensitization [61]. As reported previously, Gaddie *et al.* reported that 15 out of 18 workers in a prawn processing plant experienced relief of allergy symptoms including asthma when compressed air jets used to extrude prawns from their carapace were replaced by cold water jets, the wet weight of material filtered in the air decreasing from 1.8–3.3 mg/m³ to 0.1–0.3 mg/m³ [1]. Similarly, Douglas *et al.* reported that adding an exhaust ventilation over gutting machines in a salmon processing facility reduced respirable aerosol levels from a mean of 3.14 mg/m³ to less than 0.01 mg/m³. Since then, no new cases of occupational asthma occurred over 24 months versus an initial prevalence of 8% over an 18-month period [1]. Recently, Gautrin *et al.* [44^{••}] showed that cumulative exposure to snow crab allergens is positively associated with occupational asthma and allergy in a dose–response manner. Exposure response relationships

in fish processing workers have also demonstrated that workers with work-related asthma symptoms have a two-fold increased risk of being exposed to pilchard-antigen concentrations above 30 ng/m³ at the time of onset of new symptoms [62]. Finally, there is also some evidence that processing raw versus cooked crustaceans and fish may be less sensitizing (Lopata AL, Jeebhay MF, unpublished observation) [44^{••},63].

Prevention

Although a number of studies suggest that atopic individuals are at higher risk of developing occupational asthma, there is no way of predicting which individuals will become symptomatic. Furthermore, even pre-existing sensitization to a work-related allergen is not sufficient to predict which individual will develop allergic symptoms. As a result there is general consensus that there is no place for prescreening and exclusion from employment of atopic individuals [49]. Primary prevention measures to minimize exposure to offending agents are therefore keys to reducing the risk of occupational allergy and asthma among workers in the seafood industry. However, regular follow-up of exposed workers employed particularly in high-risk industries such as crab and prawn processing is warranted. Although regular assessment using skin prick tests to specific occupational allergens has been used successfully in the enzyme industry to detect those at risk of developing symptoms [64], this may not be as useful in some seafood industries such as snow crab processing in which skin prick tests appear to be less sensitive [43]. Short questionnaires administered on a regular basis may allow early detection of allergic symptoms. Prior to work withdrawal, proper evaluation should be conducted to confirm the diagnosis of occupational allergy or asthma. Affected individuals should be transferred to a low allergen exposure environment, while measures are undertaken to reduce allergen exposures in high risk work processes.

Monitoring of allergen exposure in seafood processing plants would be ideal but is not readily available. Furthermore, there are currently no regulatory exposure standards for seafood allergens and these should be developed once standardized assays for quantifying these allergens become available [65]. An alternative strategy may be to monitor total particulate or proteins in the air as a proxy for allergen exposure, provided that these exposure metrics are highly correlated. Identifying departments and activities with high aerosol exposure such as fishmeal bagging [37^{••}], gutting machines [66], cleaning and brushing crab [44^{••}], compressed air jets [67]) should lead to the introduction of improved local exhaust ventilation systems and change in work processes to reduce aerosol exposures. Preliminary studies suggest that processing (cleaning and brushing) raw crab before it

is cooked may help reduce exposures; however, further studies are needed to confirm this.

Conclusion

In conclusion, this review has pointed to the following areas for further research:

- (1) Detailed exposure assessment studies using standardized immunoassays for seafood allergens and non-immunologically based agents (proteases, sulphites, toxins) to investigate single and mixed exposures in the seafood industry.
- (2) Further molecular characterization of putative seafood allergens in order to better understand their biological activity and the pathophysiological mechanisms through which they cause disease. The relevance of raw versus cooked seafood in causing sensitization and allergic symptoms through inhalation needs further elucidation.
- (3) Establishing sentinel health surveillance for high risk exposure groups with specific reference to
 - (a) conducting detailed epidemiological studies of workers aboard seafood vessels
 - (b) establishing dose-response relationships in order to establish the utility of exposure threshold limits for minimising exposure to seafood allergens
 - (c) investigating the interaction of exposures (allergic and irritant) with host factors in modifying the asthmatic response
 - (d) investigating the relationship between ingestion related seafood allergy and respiratory sensitization
- (4) Establishing whether diagnostic decision points using seafood-specific IgE levels are more useful in predicting clinical reactivity to inhaled seafood allergens in the context of insensitive skin prick tests and generally poor access to bronchial challenge tests.
- (5) Evaluating effective intervention packages (exposure control/best practice) in seafood processing environments aboard vessels and ashore.
- (6) Evaluating the role of recombinant allergens in treating individuals with occupational seafood allergy and asthma in the absence of effective allergen avoidance measures.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 163).

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