

REVIEW

Crustacea allergy

J. J. MUSMAND, C. B. DAUL* and S. B. LEHRER

*Section of Clinical Immunology, Tulane University School of Medicine, Department of Medicine, New Orleans, Louisiana, U.S.A. and *Section of Allergy and Clinical Immunology, Ochsner Medical Institutions, New Orleans, Louisiana, U.S.A.*

Introduction

During the last decade, as concerns about dietary fat and cholesterol have increased in the United States and Europe, seafood has become a more prominent component of the diet. In 1990, consumption of seafood reached 15 pounds per capita in the United States, while world consumption averaged 29 pounds per capita. Total United States commercial landings and imports equalled 65 million pounds for 1990. Approximately 6 million pounds were classified as crustacea which includes shrimp, crab, lobster and crawfish [1]. As of 1990, there are estimated to be 72 000 processors, wholesalers, and distributors who work in the seafood industry. An additional 93 500 individuals are employed on fishing vessels ranging from 2-30 workers per boat [1].

Crustacea are recognized as a common cause of food hypersensitivity reactions [2-8]. Allergic reactions in seafood workers develop after occupational exposure and in consumers after preparation and/or ingestion of crustacea. Crustacea belong to the phylum Arthropoda, one of the three phyla of commonly consumed seafood. The other two are the Mollusca (snail, abalone, clam, mussel, oyster, octopus, squid, and scallop) and the Chordata, subphylum Vertebrata (shark and bony fish) (Table 1).

The popularity of seafood, especially shrimp and crawfish, in the Gulf south of the United States is immense. The frequency of hypersensitive reactions to shrimp in the New Orleans area has facilitated our investigation of shrimp allergy. A comprehensive review of shrimp and crustacea allergy will be presented, as well as a discussion of crossreactivity among crustacea and between crustacea and other seafood. Allergic occupational reactions to crustacea are frequent, although few studies investigating the epidemiology, aetiology, diagnosis, and treatment have been undertaken. This article will also review current information on occupational hypersensitivity reactions to crustacea.

Allergic reactions to ingested crustacea

Introduction

Ingestion of crustacea is a common cause of food hypersensitivity in food-allergic individuals [2-5]. Shellfish were the second most commonly implicated food in a recent study of subjects with food-induced rhinitis or asthma [9]. The pattern of immediate allergic reactions following the ingestion of crustacea is similar to that reported for other foods [3-5,10-14]. Dermatological manifestations include flushing, urticaria, angioedema [4,13,14], and, less commonly, atopic dermatitis [15-17]. Other reactions include gastrointestinal (nausea, emesis, diarrhoea, and/or abdominal cramping), respiratory (wheezing and/or rhinitis) and ocular (conjunctivitis) [4,13,14]. Anaphylaxis, exercise-induced anaphylaxis, and, in extreme cases, fatal reactions have been reported [4,18,19]. Atopic and non-atopic individuals reported similar symptoms; however, anaphylaxis was more frequently described by the atopics [13]. Some studies have similarly indicated that atopic individuals are at greater risk for severe food-related allergic reactions [20]. Several of our subjects reported adverse reactions from the 'smell' of crustacea during preparation [21,22]. The 'smell' of fish and other food has been reported to induce similar adverse responses [23,24]. Laboratory studies have demonstrated that shrimp and other crustacea retain significant allergenicity despite boiling [21,22,25,26].

Shrimp allergy

In order to better understand the pathogenesis of shrimp and crustacea allergy, double-blind, placebo controlled food challenges (DBPCFCs) were performed in 30 subjects with convincing histories of immediate adverse reactions to shrimp [14]. These subjects reported historical symptoms of oropharyngeal pruritus (90%), urticaria (61%), angioedema (52%), wheezing (42%), gastrointestinal distress (35%), and anaphylaxis or shock (10%) following ingestion of shrimp [14]. A major difficulty encountered in such investigation of food hypersensitivity is that often only 10-15% of subjects claiming food sensitivity will demonstrate an objective reaction by DBPCFC [27,28].

Correspondence: Dr S. B. Lehrer, Section of Clinical Immunology, Tulane University School of Medicine, Department of Medicine, 1700 Perdido Street, New Orleans, LA 70112, U.S.A.

Table 1. Seafood classification

Phylum	Class	Genus/species-common name
Molluscs	Gastropoda	Snail, abalone
	Bivalvia	Clam, mussel, oyster
	Cephalopoda	Octopus, squid, scallop
Arthropods	Crustacea	Crab, crawfish, lobster, shrimp, prawn
Chordata	Condrichthyes	Ray, shark
	Osteichthyes	Bony fish (cod, salmon, tuna, whitefish)

The DBPCFC was conducted in two phases [14]. In the first, blinded phase, increasing doses of shrimp-allergen extract or placebo were administered masked in grape flavoured, vanilla ice cream milkshakes at hourly intervals. If the blinded challenge was negative, the second phase, an open challenge with 16 boiled shrimp (approximately 64 g) was conducted. If the subject displayed an objective dermatological, gastrointestinal, or respiratory response to the shrimp, the challenge was considered positive.

Of the 30 subjects challenged, nine (30%) had a negative challenge; nine of the remaining individuals (30%) had a positive challenge; six of the nine subjects reacted during the blinded phase, and three responded objectively during the open challenge. All positive responses occurred within 60 min of shrimp ingestion and most within 15 min. Except for two individuals who required treatment (one for persistent emesis and one for wheezing), all reactions spontaneously resolved within 1–2 hr [14]. A third group of 12 subjects (40%) who reported oropharyngeal symptoms after ingestion of shrimp but not placebo failed to manifest objective signs.

Subjects with a positive DBPCFC complained of oropharyngeal pruritus at a significantly lower shrimp dose than that which ultimately led to an objective response [14]. Additionally, the dose of shrimp which induced this pruritus was significantly lower in those subjects with a positive challenge than in those who manifested only subjective symptoms. Whether individuals with only oropharyngeal pruritus would have developed objective responses if larger doses of shrimp had been administered remains unanswered. This oral allergy syndrome, alone or preceding a more generalized reaction, has been previously reported with other foods [12,29,30].

Shrimp skin tests were positive in 8/9 subjects with objective responses to shrimp by DBPCFC and in 12/12 subjects with only oropharyngeal pruritus [14]. The subject with a positive challenge and a negative shrimp skin test did not react until the open challenge and then

only with urticaria [14]. RAST reactivity was significantly higher for the positive challenge group than for the negative challenge group [14]. Although there was a difference in the RAST values of the group reporting only oropharyngeal pruritus compared with the negative challenge group, it was not statistically significant [14]. RAST reactivity correlated significantly with both the threshold dose for inducing pruritus and a positive challenge [14].

The combination of a positive shrimp skin test and a RAST greater than 11% bound had a positive predictive value of 87% for a positive challenge [14]. It is important to emphasize that several subjects with a positive skin test had a negative DBPCFC and that one subject with a negative skin test and RAST had a positive open food challenge [14]. Similarly, skin testing and RAST have been reported to be sensitive and specific for certain foods; however, these tests cannot be solely relied upon to diagnose food allergy [27,28,31,32,33]. The DBPCFC remains the 'gold standard'.

Serum shrimp specific IgG, IgA, IgM and salivary IgG did not differ among positive and negative DBPCFC groups. Salivary shrimp-specific IgA was significantly higher in the positive and oropharyngeal pruritus groups than the negative group, and serum IgG subclass (IgG2, IgG4) levels were increased in subjects with documented shrimp sensitivity; however, none of these were predictive of a positive DBPCFC [34,35].

The persistence of shrimp antibodies was studied in 11 shrimp allergic individuals over a 24-month period. Seven of these subjects had a positive DBPCFC, and four had subjective oropharyngeal pruritus during challenge [36]. Shrimp-specific IgE levels were elevated in all subjects, remained relatively constant during the 24 months of follow-up, and were not affected by the shrimp challenge. Since most (8/11) subjects carefully excluded shrimp from their diets for many years prior to study, the persistent elevation of shrimp-specific IgE levels and positive DBPCFC after shrimp avoidance suggests a persistent

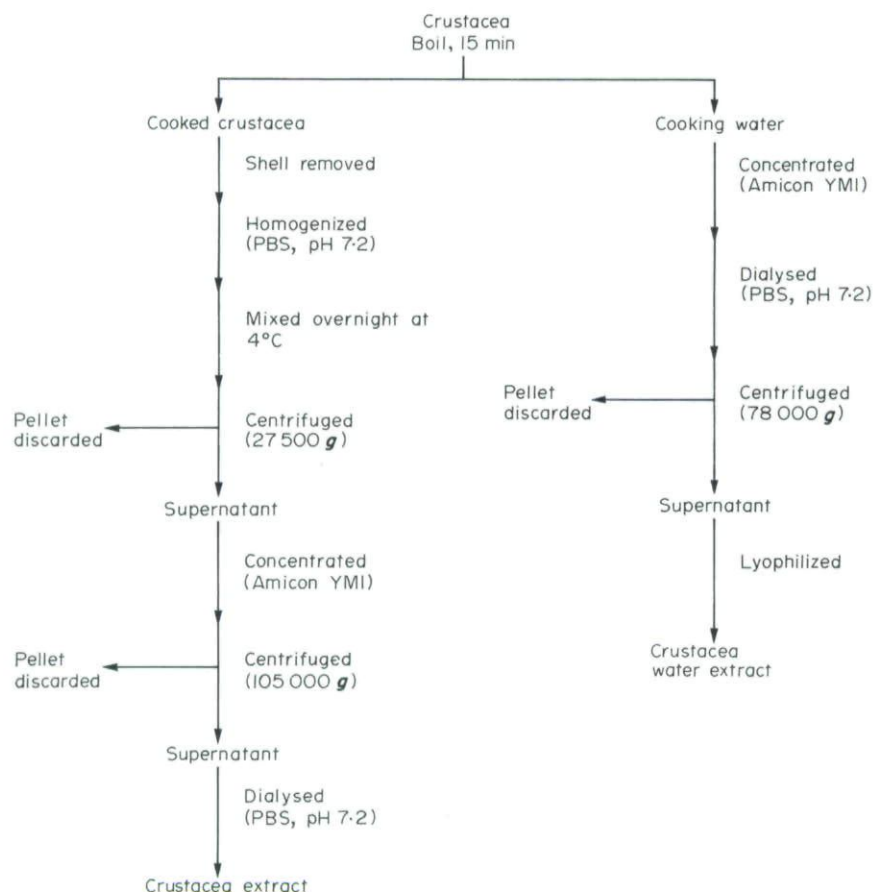


Fig. 1. Extraction of crustacea allergens. The standard extraction for crustacea allergens was developed with shrimp. Crustacea are boiled in ion-depleted water for 15 min. The cooked crustacea are removed, the meat extracted and the extract processed. The cooking water also provides a source of allergen, and is processed as described.

nature of this hypersensitivity. Similar reports of long-lasting sensitivity to crustacea have been reported by other investigators [17,37,38].

Identification and isolation of the major shrimp allergen

To better understand the pathogenic mechanisms of shrimp sensitivity, work in our laboratory has also centred on crustacea allergen identification, isolation, and crossreactivity among crustacea. Extracts for allergen analysis were prepared from the meat of fresh, boiled brown shrimp (*Panaeus aztecus*) and the water in which the shrimp were boiled. The extraction process is outlined in Fig. 1.

IgE antibody reactivity of sera from 13 shrimp allergic, RAST-positive individuals was analysed by SDS-PAGE of shrimp extracts followed by Western blotting [39]. This analysis revealed nine IgE binding bands present in both meat and water extracts [39]. Twelve of 13 (92%) sera bound to the band at 36 kD [40,41]. After isolation by preparative SDS-PAGE, the 36 kD allergen, *Pen a I* was determined to constitute at least 20% of the shrimp extract's soluble protein and inhibit 75% of the RAST reactivity to whole shrimp [40,41]. *Pen a I*'s isoelectric point is 5.2. This protein contains 2.9% carbohydrate and

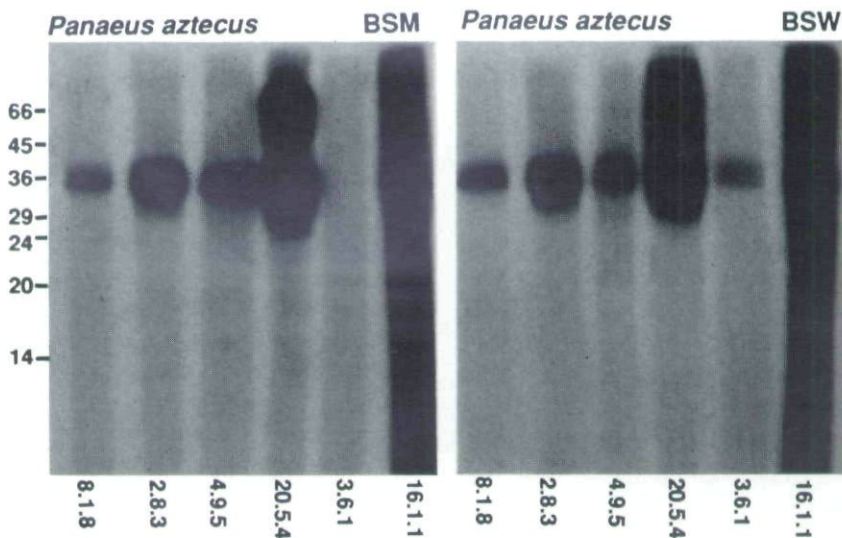
has an amino acid composition rich in aspartic and glutamic acid [40,41].

Pen a I is similar to shrimp antigen II described by Hoffman *et al.* [42]. They reported that shrimp antigen II had a molecular weight of 38 kD, an isoelectric point of 5.4, and a carbohydrate composition of 4.0%. A similar 34 kD protein was isolated from shrimp by Nagpal *et al.* and designated as Sa-II [43]. The amino acid content of both antigen II and Sa-II was remarkably similar to *Pen a I* (Table 2). Nagpal *et al.* also reported that shrimp tRNA could bind IgE; however, a protein-free nucleic acid preparation could not be prepared [44]. Since only two patients' sera were tested, the clinical importance of the tRNA allergen is unclear.

Pen a I was digested by an endopeptidase and a 21-residue peptide isolated by HPLC. The amino acid sequence of the peptide was compared for homology with other proteins in the Swiss protein database. The greatest homology (72–87%) was with the fruit fly muscle protein tropomyosin [40,41]. Both fruit fly and shrimp are members of the phylum Arthropoda. Monoclonal antibodies (MoAb) were raised against *Pen a I* [41,45]. Reactivity of six MoAb to *Pen a I* in shrimp meat (BSM) or water (BSW) extracts is shown in Fig. 2.

Table 2. Amino acid composition of the major shrimp allergen as isolated by different investigators

	Number of residues		
	<i>Pen a I</i> (Daul <i>et al.</i>)	Antigen II (Hoffman <i>et al.</i>)	Sa-II (Nagpal <i>et al.</i>)
MW (kD)	36	38	34
Aspartic Acid	40	58	39
Threonine	12	12	9
Serine	14	15	12
Glutamic Acid	80	61	75
Proline	2	6	3
Glycine	10	20	6
Alanine	33	31	21
Cysteine	ND	2	3
Valine	13	19	15
Methionine	8	9	6
Isoleucine	6	12	6
Leucine	35	30	30
Tyrosine	4	7	6
Phenylalanine	4	9	6
Histidine	1	4	3
Lysine	26	27	27
Arginine	26	19	30
Tryptophan	ND	ND	4
Total	312	341	301

**Fig. 2.** Western Blot analysis of a shrimp (*Panaeus aztecus*) meat (BSM) and cooking water (BSW) extracts with monoclonal antibodies. Six monoclonal antibodies were tested for reactivity to shrimp extracts. Five of the six showed significant reactivity to the shrimp allergen, *Pen a I* in meat extracts, and 6/6 reacted to *Pen a I* in the water extracts.

Common crustacea allergens

As many shrimp-allergic individuals demonstrated positive skin tests and RASTs to other crustacea even in the absence of prior exposure, it was proposed that crustacea possess common allergens [4,21,46–49]. Evidence for

common crustacea allergens was obtained from shrimp RAST inhibition analysis with increasing doses of different crustacea extracts. As expected, shrimp extract was the most potent inhibitor [21,46,47]; lobster and crawfish extract were the next most effective inhibitors, and crab

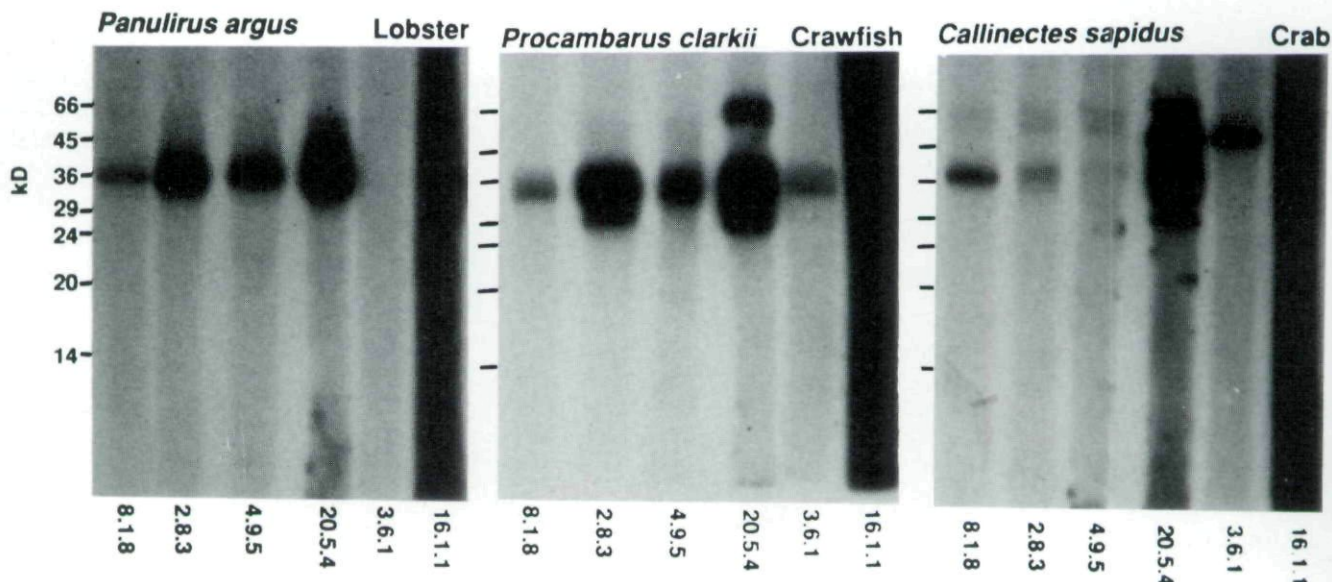


Fig. 3. Western Blot reactivity of *Pen a I* reactive monoclonal antibodies to lobster (*Panulirus argus*), crawfish (*Procambarus clarkii*), and crab (*Callinectes sapidus*).

extract was the least. Crossed-line immunoelectrophoresis also demonstrated the presence of shared antigenic determinants in shrimp, lobster, crawfish and crab extracts [21,46,47]. Crossed-line and crossed radioimmunoelectrophoresis of the extracts confirmed that crustacea have shared allergens [21,46,47].

Monoclonal antibodies (MoAbs) prepared to shrimp *Pen a I* were tested for reactivity to crawfish, crab, and lobster antigens [48,49]. All six MoAbs demonstrated similar reactivity patterns with all three crustacea extracts (Fig. 3). Five of the six MoAbs which reacted with *Pen a I* also reacted with a 36 kD protein in crawfish, crab, and lobster extracts. These results strongly support the existence of common major crustacea allergens and the presence of *Pen a I* like molecules in other crustacea [48,49].

Crossreactivity between crustacea and other seafood

Allergenic crossreactivity between crustacea and molluscs has also been reported [50,51] and was first investigated by our laboratory after several of our crustacea-sensitive subjects reported allergic reactions to oysters. Crustacea extracts inhibited oyster RASTs, and rabbit antisera to crustacea reacted with oyster antigens [50]. However, since oyster skin testing and RAST were not useful in diagnosing oyster sensitivity [50], the clinical importance of these observations is unclear. Another group of subjects reported concomitant squid and shrimp sensitivities [51]. A modified reverse ELISA demonstrated cross-reactivity between squid, shrimp and other crustacea;

however, crossreactivity was not detected between squid and other molluscs, except for oyster, which demonstrated limited crossreactivity [50]. One case report described a seafood handler sensitive to both shrimp and scallop [52]. Immunoblot inhibition analysis with both seafood extracts demonstrated several crossreactive allergens, including a major one of 34–35 kD molecular weight [52].

Because almost 50% of 39 fish-allergic subjects whom we studied reported crustacea sensitivity, crossreactivity between crustacea and fish was investigated by RAST inhibition (unpublished results, A. Helbling, J. J. Musmand and S. B. Lehrer). None of the six fish (pollock, salmon, tuna, mackerel, trout and anchovy) tested significantly inhibited the shrimp RAST, suggesting that sensitivity of fish-allergic individuals to crustacea is probably a concomitant sensitivity and not crossreactivity [53]. Until reports demonstrating cross-sensitivity between crustacea and bony fish are substantiated, crustacea allergic individuals can be advised to cautiously eat bony fish.

Shrimp species-specific allergens

Several shrimp-sensitive individuals report only occasional adverse reactions after shrimp ingestion. To determine if species-specific reactivity explained their clinical symptoms, white shrimp (*Penaeus setiferus*) and brown shrimp (*Penaeus aztecus*), the two most commonly consumed shrimp species in our area were investigated [53]. Three out of 31 subjects reacted by skin tests and RASTs with only one of the two shrimp species. Testing their sera

by RAST inhibition suggested the presence of unique allergens. These studies support the existence of shrimp species-specific allergens and could explain the intermittent symptoms reported by some individuals. Thus, caution must be exercised when using only one species for testing, RAST, or DBPCFC in the evaluation of patients who claim shrimp sensitivity. However, this is probably not a concern for the majority of shrimp-sensitive patients [53].

Treatment

Currently, the only accepted therapy for food allergy is strict avoidance of the offending food. Cromoglycate, ketotifen, H₁- and H₂-histamine receptor antagonists, and prostaglandin synthetase inhibitors cannot be recommended for the prophylactic treatment of food allergy due to conflicting reports of their efficacy [54–56]. Although at some risk, immunotherapy has recently been reported to be successful and may hold promise in food allergy treatment; however, recommendations await additional studies [58]. Patients who have food-induced, life-threatening reactions must be instructed in the use of self-injectable epinephrine, which they should carry with them at all times. Additionally, they should be advised to wear identification bracelets (MedicAlert® Bracelets assumed to be worn on wrist), stating their food sensitivity, to help health-care professionals treat any life-threatening reactions when a history cannot be obtained [58].

Summary

Crustacea allergic reactions are an important and prevalent problem. Recent studies have provided significant advances in the identification and management of crustacea-allergic individuals. When evaluating individuals for crustacea allergy, it is important to determine if the patient's history is consistent with an immediate, IgE-mediated hypersensitive reaction. Adverse reactions following crustacea ingestion range from mild (oral allergy syndrome) to life-threatening (systemic anaphylaxis). Patients with a history of a severe reaction to crustacea should avoid locations where crustacea are cooked as these individuals may be sensitive enough to react to allergens present in the vapours from cooking crustacea. Research has shown that, in those patients with a convincing history, skin-test and RAST reactivity to shrimp have a high sensitivity and positive predictive value; however, the double-blind, placebo-controlled, food challenge remains the 'gold standard' for diagnosis.

Several factors must not be forgotten when diagnosing shrimp allergy. Exercise care when dismissing a patient as non-allergic based on negative skin-test and RAST results; our shrimp challenge studies have demonstrated

that shrimp may still rarely elicit mild adverse reactions in such individuals. Similarly, those who claim intermittent difficulty after shrimp ingestion should not be dismissed since species-specific shrimp allergens have been demonstrated, although again, such specific reactivity is indeed, unusual.

Patients sensitive to a single crustacea species should be tested to all crustacea because significant crossreactivity among crustacea has been demonstrated. Crustacea-allergic individuals should be cautious when ingesting squid and oyster; preliminary studies have determined that cross-sensitivity may exist although clinical relevance remains to be determined. Note that oyster skin testing and RAST may not always be helpful when assessing oyster sensitivity. Although a number of individuals with fish allergy also report sensitivity to crustacea, recent evidence indicates that this most likely represents a concurrent allergy and not allergen crossreactivity.

Occupational hypersensitivity reaction to crustacea

Introduction

Occupational hypersensitivity reactions to seafood have been reported in workers involved in every stage of seafood processing and delivery. These reactions include dermatitis, urticaria, rhinitis, conjunctivitis, asthma, and hypersensitivity pneumonitis [59]. This spectrum of reactions has been reported in fishermen, processing workers, shell grinders, fish meal factory workers, oyster shuckers, as well as caterers and restaurant cooks [59–65]. Crustacea, in particular, are recognized as important occupational allergens. Lobster, snowcrab, crab, shrimp, and prawn have been documented to cause occupational dermatitis, rhinitis, conjunctivitis, and asthma [26,59,65–71]; however, crustacea-induced hypersensitivity pneumonitis has not been documented.

Occupational dermatological diseases

The prevalence of occupational skin disease in fishermen and seafood workers ranks among the top five of all industries in which such reactions are recognized to occur in the United States [8]. Among food handlers, contact reactions to crustacea are some of the most commonly reported [72–74]. Crustacea most often produce an immediate IgE-mediated contact urticaria, although a delayed contact dermatitis may also develop in certain individuals [72–75]. In several instances, contact urticaria can only be induced with fresh, raw crustacea and not with cooked crustacea, suggesting the presence of heat labile allergen(s) [73,75,76]. The development of immediate contact reactions often requires trauma to the skin although reactions on intact skin have been reported

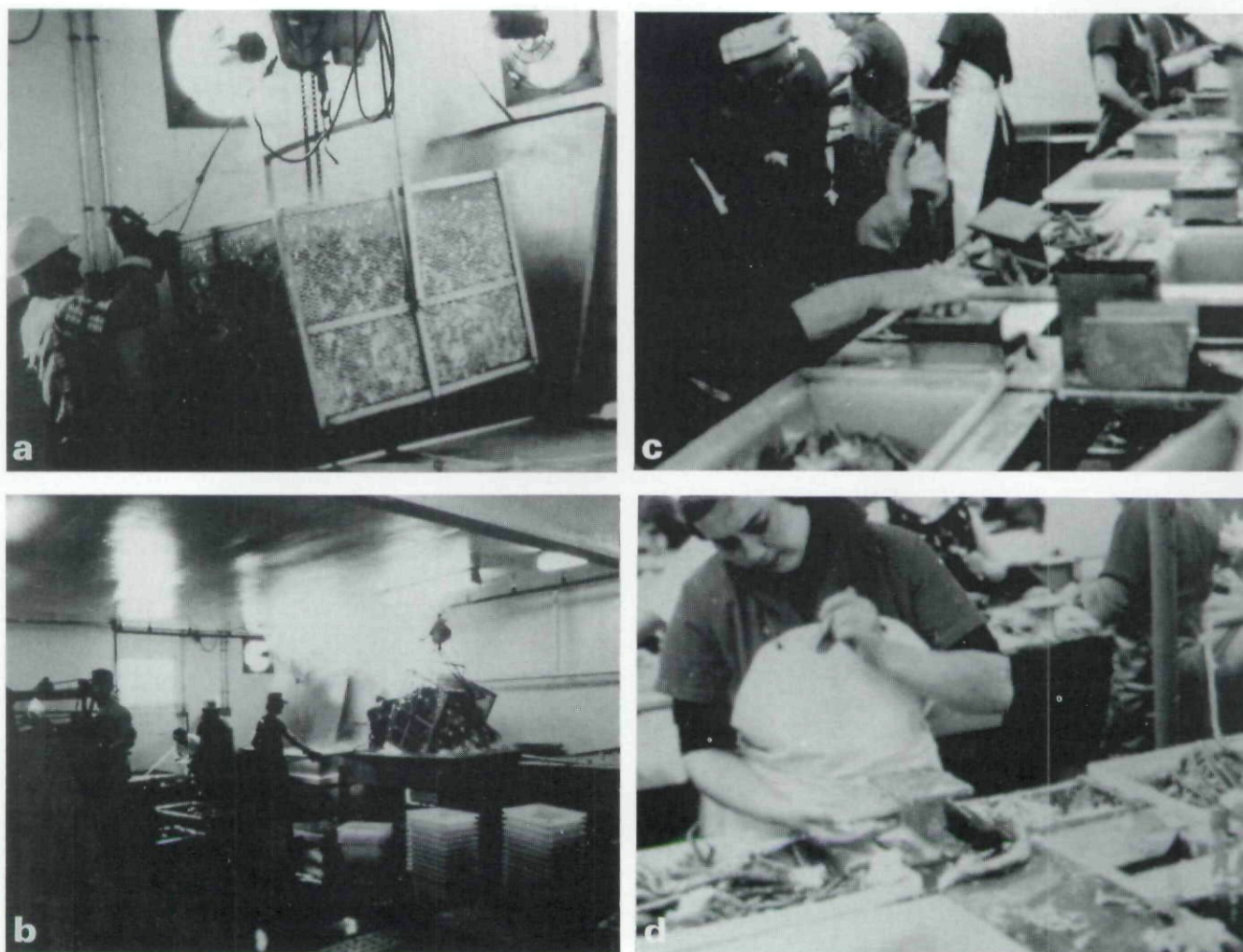


Fig. 4. Processing of crabmeat in a snowcrab manufacturing plant. The cooked crabs, contained in a large basket, are removed from the boiling water vat (a), and dumped (b) into a large metal tray for cooling. Note the considerable amounts of steam and water vapour that escape into the atmosphere during this process. Crabmeat is then removed from the cooked crabs, by extracting (c) and shaking the crab parts (d). Note the absence of protective masks and, in some cases, gloves, during this process.

[73,75]. Atopy is a significant risk factor for the development of crustacea-induced occupational skin diseases [73,74]. It has been estimated that up to one-third of food handlers and caterers with occupational skin disease may need to find alternative employment because of debilitating symptoms. Moreover, despite cessation of continued shellfish exposure, some individuals may have persistent dermatitis [74].

Occupational asthma in snowcrab workers

Asthma is the most serious occupational reaction to crustacea. Symptoms can be chronically disabling, even years after the worker has been removed from exposure [7,59,77]. The most thorough investigation of occupatio-

nal asthma in seafood workers was conducted by Cartier *et al.* of snowcrab workers [26,78,79].

During 1982, two companies in Canada's Iles de la Madeleine were surveyed to determine the prevalence of allergic occupational symptoms among snowcrab (*Chionoecetes opilis*) workers [78]. Processing of crabs in both factories was similar. Fresh crabs were brushed clean, then the legs and claws were separated from the body and boiled. Each time crabs were removed from the boilers, abundant amounts of steam were released (Fig. 4). Exposure to steam induced adverse reactions in a significant number of workers. Of the 303 employees who were studied, 103 (34%) reported pulmonary symptoms, 72 (24%) dermatological symptoms, and 55 (18%) rhinitis and/or conjunctivitis [78].

Occupational asthma was diagnosed in 48/303 (16%) workers by provocative inhalation challenge with nebulized crab boiling water or by a demonstration of increased bronchial hyperresponsiveness to histamine, pulmonary function measurements, and changes in peak expiratory flow rates while at work [78].

Skin-test reactivity to crabmeat or boiling water extracts was significantly associated with a diagnosis of occupational asthma, rhinitis/conjunctivitis, or dermatitis [78]. The boiling water extract was more active than the meat extract, and both were more potent than commercial extracts in identifying workers with allergic occupational diseases. Skin testing had a sensitivity of 61% and a specificity of 85% in workers with occupational asthma [78]. A significant relationship was also demonstrated between RAST level to crab extract and occupational asthma. The association between immediate skin-test and RAST reactivity and occupational asthma implicates an IgE-mediated mechanism [26,78,79]. Atopy was not a risk factor in the development of occupational asthma, however smoking was [78].

An important finding of this study was that even 5 years after cessation of exposure, symptoms persisted in a majority of workers with occupational asthma [26,79]. Although the number of employees who required medication decreased, bronchial hyperreactivity, as measured by response to inhaled histamine, remained heightened in approximately 80% of the workers [26,79]. By the first year of follow-up, spirometry normalized in almost all workers. Improvement in bronchial hyperreactivity plateaued by the second year of follow-up, although it remained abnormal in the majority of workers after 5 years. In contrast, levels of crab-specific IgE antibodies, although slowly falling, remained elevated even 5 years after cessation of exposure [26,79].

Occupational asthma in other crustacea workers

Occupational asthma has been reported in workers exposed to king or other crab species, prawn, shrimp meal, and lobster [66–71]. The prevalence and pattern of development are similar to those reported for snowcrab workers [66–71].

As with snowcrab workers, development of occupational asthma in other crustacea workers was related to cooking steam or aerosolized crustacea particulate exposure [69,78]. Prawn workers in England developed occupational asthma 6 weeks after the method of meat extraction was changed from hand peeling to air-blowing [69]. Symptoms disappeared in most workers after compressed-air jets were replaced with cold-water jets and aerosolized particulates were reduced from 1.8–3.3 mg/m³ to 0.1–0.3 mg/m³. Air sampling of king crab process-

ing factories having workers with occupational asthma revealed measurable amounts of airborne crab antigen; 30% of the aerosolized crab dust was of respirable size ($< 5 \mu\text{m}$) [67]. Studies of crawfish, lobster, shrimp and crab allergens disclosed that cooking/boiling water possesses significant allergenic activity [21,22,25,26]. Together, these investigations strongly suggest that workers can be sensitized to aerosolized crustacea allergens which are released and, thus, encountered during processing.

Investigations of other crustacea workers support the finding in snowcrab processors that occupational asthma is IgE mediated. Skin testing and RAST of prawn workers demonstrated that prawn-specific IgE occurred more commonly in workers with occupational asthma [69,70]. Interestingly, as reported in the snowcrab study, prawn workers who smoked were more likely to develop occupational asthma than non-smokers [69,70,78]. Smoking has been reported in some other, but not all industries, to increase the risk of occupational asthma [80,81], although the pathophysiology is not currently understood.

Smith, in an unpublished report, suggests that occupational exposure to the *Opilio* crab can induce 'crab worker's bronchitis', a syndrome separate from occupational asthma. This syndrome, as theorized, is induced through a non-immunologic mechanism, by a yet to be defined toxin which is released by the crab (unpublished results, D. Smith Everett, WA, U.S.A.). The clinical relevance of this report awaits better delineation of the toxin and additional confirmatory studies.

Diagnosis and treatment of occupational asthma

The diagnosis of occupational asthma begins with a convincing history and physical exam. Supporting evidence for the diagnosis of occupational asthma includes skin testing, RAST, serial monitoring of peak expiratory flow rates, measurement of bronchial reactivity and spirometry. Although not usually necessary, provocative inhalation challenge with the putative agent remains the definitive diagnostic test. A complete discussion of the diagnosis and treatment of occupational allergic diseases is beyond the scope of this review and has been published in detail elsewhere [7].

It is important to emphasize that, once occupational asthma develops, the only proven therapy is complete cessation of further exposure. Continued exposure after onset of symptoms may lead to progressive lung function impairment [7,59,77,81]. Minute levels of exposure may induce symptoms in sensitized individuals, and, once occupational asthma has developed, protective masks or improved ventilation to reduce allergen levels are unsatisfactory. Although sporadic successes using immuno-

therapy have been described in some workers with occupational asthma, these reports require confirmation before adopting immunotherapy as a treatment modality [7,59,80,82-84].

Summary

Occupational allergic reactions are a significant problem in the crustacea industry. Workers with occupational dermatitis and asthma often have persistent, debilitating symptoms. Based on the results of the Canadian snow-crab study in which 16% of workers developed occupational asthma, a significant number of crustacea workers in the United States and Europe are at risk of developing occupational asthma. Workers with respiratory symptoms require urgent evaluation. Those diagnosed with occupational asthma should be removed from further exposure. Strict monitoring of processing methods, air-environment allergen levels, and work practices is vital, as decreased allergen exposure will prevent or reduce the development of occupational hypersensitivity diseases.

Conclusion

Seafood, in general, and crustacea in particular, is recognized as a common cause of food allergy. Because of current dietary concerns, the consumption of crustacea is predicted to increase. As the exposure to crustacea increases, it can be expected that the number of workers and consumers who develop hypersensitivity reactions to crustacea will also increase. The last decade has been marked by a number of advances in our understanding of the pathogenesis of hypersensitivity reactions to crustacea. However, there are still a number of areas that warrant further study. As with many food allergies, the question arises why some individuals develop such reactions and others do not. What is the role of mucosal permeability to food allergens in establishing disease pathogenesis? How important is exposure to crustacea allergen vapours in disease pathogenesis? In some individuals, can these reactions be provoked only by inhaled allergens and not by ingestion? Finally, can better, more precise methods be developed to identify, diagnose, and ultimately, treat crustacea-sensitive individuals?

The necessity of therapeutic interventions for food allergy has been questioned. Why can't sensitized individuals merely avoid exposure to such foods? Reports of fatalities following the ingestion of foods by highly sensitized subjects suggests that avoidance is not always that easy or effective. Furthermore, employment patterns in small communities where the seafood industry is the major source of employment suggests that a change of

jobs may not be a viable alternative for many crustacea hypersensitive workers.

The identification and isolation of a major shrimp allergen holds the promise for advancing our understanding, diagnosis and treatment of crustacea as well as other food hypersensitivity reactions. Through study of the molecular structure and biological activity of shrimp-induced allergic reactions, it is hoped that we can develop better reagents for treatment. The recent progress in molecular biology techniques suggests that substantial amounts of any allergen can be produced by cost effective methods. Thus, it should be possible in the near future to develop a clinically efficacious agent for the diagnosis and the treatment of hypersensitive individuals.

Acknowledgements

The authors gratefully acknowledge the word processing help of Mrs Carin Fernandez. This review was supported in part by a grant from the National Fisheries Foundation, and the Alton Ochsner Medical Foundation.

References

- 1 Martin RE. Vice President, Science and Technology, National Fisheries Institute. Personal communications, 1992.
- 2 Koerner CB, Sampson HA. Diets and nutrition. In: Metcalfe DD, Sampson HA, Simon RA, eds. Food allergy: adverse reactions to foods and food additives. Boston: Blackwell Scientific Publications, 1991:332-54.
- 3 Atkins FM, Steinberg SS, Metcalfe DD. Evaluation of immediate adverse reactions to foods in adult patients. I. Correlation of demographic, laboratory, and prick skin test data with response to controlled oral food challenge. *J Allergy Clin Immunol* 1985; 75:348-55.
- 4 Waring NP, Daul CB, deShazo RD, McCants ML, Lehrer SB. Hypersensitivity reactions to ingested crustacea: Clinical evaluation and diagnostic studies in shrimp-sensitive individuals. *J Allergy Clin Immunol* 1985; 76:440-5.
- 5 Metcalfe DD. Food hypersensitivity. *J Allergy Clin Immunol* 1984;73:749-64.
- 6 Lehrer SB. Hypersensitivity reactions in seafood workers. *Allergy Proc* 1990; 11:67-8.
- 7 Cockcroft DW. Occupational asthma. *Ann Allergy* 1990; 65:169-76.
- 8 Emmett EA. Occupational skin disease. *J Allergy Clin Immunol* 1983; 72:649-56.
- 9 Oehling A, Garcia B, Santos F *et al.* Food allergy as a cause of rhinitis and/or asthma. *J Invest Allergol Clin Immunol* 1992; 2:78-83.
- 10 Atkins FM, Steinberg SS, Metcalfe DD. Evaluation of immediate adverse reactions to foods in adult patients. II. A detailed analysis of reaction patterns during oral food challenge. *J Allergy Clin Immunol* 1985; 75:356-63.
- 11 Golbert TM, Patterson R, Pruzansky JJ. Systemic allergic reactions to ingested antigens. *J Allergy* 1969; 44:96-107.

- 12 Berstein M, Day JH, Welsh A. Double-blind food challenge in the diagnosis of food sensitivity in the adult. *J Allergy Clin Immunol* 1982; 70:205-10.
- 13 Daul CB, Morgan JE, Waring NP, McCants ML, Hughes J, Lehrer SB. Immunologic evaluation of shrimp-allergic individuals. *J Allergy Clin Immunol* 1987; 80:716-21.
- 14 Daul CB, Morgan JE, Hughes J, Lehrer SB. Provocation-challenge studies in shrimp-sensitive individuals. *J Allergy Clin Immunol* 1988; 81:1180-6.
- 15 Sampson HA. Role of immediate food hypersensitivity in the pathogenesis of atopic dermatitis. *J Allergy Clin Immunol* 1983; 107:669-75.
- 16 Sampson HA, McCaskill CC. Food hypersensitivity and atopic dermatitis: Evaluation of 113 patients. *J Pediatr* 1985; 107:669-75.
- 17 Sampson HA, Scanlon SM. Natural history of food hypersensitivity in children with atopic dermatitis. *J Pediatr* 1989; 115:23-7.
- 18 Maulitz RM, Pratt DS, Schocket AL. Exercise-induced anaphylactic reaction to shellfish. *J Allergy Clin Immunol* 1979; 63:433-4.
- 19 Yunginger JW, Sweeney KG, Sturner WQ *et al.* Fatal food-induced anaphylaxis. *J Am Med A* 1988; 260:1450-2.
- 20 Sheffer AL. Anaphylaxis. *J Allergy Clin Immunol* 1985; 75:227-33.
- 21 Halmepuro L, Salvaggio JE, Lehrer SB. Crawfish and lobster allergens: identification and structural similarities with other crustacea. *Int Archs Allergy Appl Immunol* 1987; 84:165-72.
- 22 Lehrer SB, Ibanez MD, McCants ML, Daul CB, Morgan JE. Characterization of water-soluble shrimp allergens released during boiling. *J Allergy Clin Immunol* 1990; 85:1005-13.
- 23 Danneaus A, Inganas M. A follow-up study of children with food allergy. Clinical course in relation to serum IgE- and IgG-antibody levels to milk, eggs and fish. *Clin Allergy* 1981; 11:533-9.
- 24 Aas K. Studies of hypersensitivity to fish. *Int Arch Allergy* 1966; 29:346-63.
- 25 Bush R, Olsen E, Meier-Davis S, Czapinski MT. Characterization of an allergen in a case of snow crab asthma. *J Allergy Clin Immunol* 1986; 77:121.
- 26 Cartier A, Malo JL, Ghezzi H, McCants M, Lehrer SB. IgE sensitization in snow crab-processing workers. *J Allergy Clin Immunol* 1986; 78:344-8.
- 27 Bernhisel-Broadbent J, Scanlon SM, Sampson HA. Fish hypersensitivity. *J Allergy Clin Immunol* 1992; 89:730-7.
- 28 Sampson HA, Metcalfe DD. Immediate reactions to foods. In: Metcalfe DD, Sampson HA, Simon RA, eds. *Food allergy: adverse reactions to foods and food additives*. Boston: Blackwell Scientific Publications, 1991:99-112.
- 29 Ortolani C, Ispano M, Pastorello E, Bibi A, Ansaloni R. The oral allergy syndrome. *Ann Allergy* 1988; 61:47-52.
- 30 Enberg RN. Food-induced oropharyngeal symptoms. *Food Allergy* 1991; 11:767-72.
- 31 Ownby DR. *In vitro* assays for the evaluation of immunologic reactions to foods. *Food Allergy* 1991; 11:851-62.
- 32 Aas K. The diagnosis of hypersensitivity to ingested foods. *Clin Allergy* 1978; 8:39-50.
- 33 Aas K, Lundkvist U. The radioallergosorbent test with a purified allergen from codfish. *Clin Allergy* 1973; 3:255-61.
- 34 Morgan JE, Lehrer SB, Daul CB. Shrimp-specific salivary antibodies. *J Allergy Clin Immunol* 1991; 87:192.
- 35 Morgan JE, Daul CB, Lehrer SB. The relationship among shrimp-specific IgG subclass antibodies and immediate adverse reactions to shrimp challenge. *J Allergy Clin Immunol* 1990; 86:387-92.
- 36 Daul CB, Morgan JE, Lehrer SB. The natural history of shrimp hypersensitivity. *J Allergy Clin Immunol* 1990; 86:88-93.
- 37 Fries JH. Factors influencing clinical evaluation of food allergy. *Ped Clin N Am* 1957; 6:867-81.
- 38 Bock SA. The natural history of food sensitivity. *J Allergy Clin Immunol* 1982; 69:173-7.
- 39 Morgan JE, Daul CB, Lehrer SB, English M. Characterization of important shrimp allergens by immunoblot analysis. *J Allergy Clin Immunol* 1990; 85:170.
- 40 Daul CB, Slattery M, Morgan JE, Lehrer SB. Isolation and characterization of an important 36 kD shrimp allergen. *J Allergy Clin Immunol* 1991; 87:192.
- 41 Lehrer SB, Daul CB, Helbling A. Identification of shrimp allergens and their ability to reproduce clinical reactions. *Ann Allergy* in press.
- 42 Hoffman DR, Day ED, Miller JS. The major heat stable allergen of shrimp. *Ann Allergy* 1981; 47:17-22.
- 43 Nagpal S, Rajappa K, Metcalfe DD, Subba Rao PV. Isolation and characterization of heat-stable allergens from shrimp (*Penaeus indicus*). *J Allergy Clin Immunol* 1989; 83:26-36.
- 44 Nagpal S, Metcalfe DD, Subba Rao PV. Identification of a shrimp-derived allergen as tRNA. *J Immunol* 1987; 138:4169-174.
- 45 Daul CB, Morgan JE, Lehrer SB, English M. Production of murine monoclonal (Mab) antibodies to shrimp antigens. *J Allergy Clin Immunol* 1990; 85:276.
- 46 Lehrer SB, McCants ML, Salvaggio JE. Identification of crustacea allergens by crossed radioimmunoelectrophoresis. *Int Arch Allergy Appl Immunol* 1985; 77:192-4.
- 47 Lehrer SB. The complex nature of food antigens: Studies of cross-reacting crustacea allergens. *Ann Allergy* 1986; 57:267-72.
- 48 Daul CB, Slattery M, Morgan JE, Lehrer SB. Identification of a common major crustacea allergen. *J Allergy Clin Immunol* 1992; 89:194.
- 49 Daul CB, Slattery M, Morgan JE, Lehrer SB. Common crustacea allergens: Identification of B cell epitopes with the shrimp specific monoclonal antibodies. *Int Arch Allergy Appl Immunol* in press.
- 50 Lehrer SB, McCants ML. Reactivity of IgE antibodies with crustacea and oyster allergens: Evidence for common antigenic structures. *J Allergy Clin Immunol* 1987; 80:133-9.
- 51 Carrillo T, Castillo R, Caminero J *et al.* Squid hypersensitivity: a clinical and immunologic study. *Ann Allergy* 1992; 68:483-7.

- 52 Goetz DW, Whisman BA. Crossreactive allergens of shrimp and scallops identified by ELISA and immunoblot inhibitions. *J Allergy Clin Immunol* 1990; 85:276.
- 53 Morgan JE, O'Neil CE, Daul CB, Lehrer SB. Species-specific shrimp allergens: RAST and RAST-inhibition studies. *J Allergy Clin Immunol* 1989; 83:1112-7.
- 54 Micallef E. Effect of oral sodium cromoglycate and ketotifen in fish-induced bronchial asthma. *Thorax* 1983; 38:537-30.
- 55 Sogn D. Medications and their use in the treatment of adverse reactions to foods. *J Allergy Clin Immunol* 1986; 78:238-43.
- 56 Ciprandi G, Scordamaglia A, Bagnasco M, Canonica GW. Pharmacologic treatment of adverse reactions to foods: Comparison of different protocols. *Ann Allergy* 1987; 58:341-3.
- 57 Oppenheimer JJ, Nelson HS, Bock SA, Anistensen F, Leung DYM. Treatment of peanut allergy with rush immunotherapy. *J Allergy Clin Immunol* 1992; 90:256-62.
- 58 Atkins FM. Food-induced urticaria. In: Metcalfe DD, Sampson HA, Simon RA, eds. *Food allergy: adverse reactions to foods and food additives*. Boston: Blackwell Scientific Publications, 1991:129-38.
- 59 Lehrer SB, O'Neil CE. Occupational reactions in the food industry. *Food Technol* 1992; 46:153-6.
- 60 Nakashima T. Studies of bronchial asthma observed in cultured oyster workers. *Hiroshima J Med Sci* 1969; 18:141-84.
- 61 Droszcz W, Kowalski J, Piotrowska B, Pawlowicz A, Piebruszezewska E. Allergy to fish meal in fish meal factory workers. *Int Arch Occup Environ Health* 1981; 49:13-19.
- 62 Jyo T, Komoto K, Tsubai S, Katsutani T, Otsuka T, Oka S. Sea squirt asthma—occupational asthma induced by inhalation of antigenic substances contained in sea squirt body fluid. *Allergy Immunol* 1974/1975; 20/21:435-48.
- 63 Avila R. Extrinsic allergic alveolitis in workers exposed to fishmeal and poultry. *Clin Allergy* 1971; 1:343-6.
- 64 Zhoutyi VR, Botzov MV. Dermatitis in workers processing mussels. *Vestn Dermatol Venerol* 1973; 47:71-3.
- 65 Goransson K. Contact urticaria to fish. *Contact Dermatitis* 1981; 7:282-3.
- 66 Patel PC, Cockcroft DW. Occupational asthma caused by exposure to cooking lobster in the work environment: a case report. *Ann Allergy* 1992; 68:360-1.
- 67 Orford RR, Wilson JT. Epidemiologic and immunologic studies in processors of the king crab. *Am J Ind Med* 1985; 7:155-69.
- 68 Asthma-like illness among crab-processing workers—Alaska. *MMMR* 1982; 31:95-6.
- 69 Gaddie J, Legge JS, Friend JA. Pulmonary hypersensitivity in prawn workers. *Lancet* 1980; 2:1350-3.
- 70 McSharry C, Wilkinson PC. Serum IgG and IgE antibody against aerosolized antigens from *Nephrops Norvegicus* among seafood process workers. In: *Recent Advances in Mucosal Immunology*. New York: Plenum Press, 1986:865-8.
- 71 Carino M, Elia G, Molinini R, Nuzzaco A, Ambrosi L. Shrimp-meal asthma in the aquaculture industry. *Med Lab* 1985; 76:471-5.
- 72 Hjorth N, Petersen-Roed J. Occupational protein contact dermatitis in food handlers. *Contact Dermatitis* 1976; 2:28-42.
- 73 Fisher AA. Allergic contact urticaria of the hands due to seafood in food handlers. *Cutis* 1988; 42:388-9.
- 74 Cronin E. Dermatitis of the hands in caterers. *Contact Dermatitis* 1987; 17:265-9.
- 75 Nagano T, Kanao K, Sugai T. Allergic contact urticaria caused by raw prawns and shrimps: three cases. *J Allergy Clin Immunol* 1984; 74:489-93.
- 76 Maibach HI. Regional variation in elicitation of contact urticaria syndrome (immediate hypersensitivity syndrome): shrimp. *Contact Dermatitis* 1986; 15:100.
- 77 Chan-Yeung M. Evaluation of impairment/disability in patients with occupational asthma. *Am Rev Respir Dis* 1987; 135:950-1.
- 78 Cartier A, Malo JL, Forest F *et al.* Occupational asthma in snow crab-processing workers. *J Allergy Clin Immunol* 1984; 74:261-9.
- 79 Hudson P, Cartier A, Pineau L *et al.* Follow-up of occupational asthma caused by crab and various agents. *J Allergy Clin Immunol* 1985; 76:682-8.
- 80 Zetterström O, Osterman K, Machado L, Johansson SGO. Another smoking hazard: raised serum IgE concentration and increased risk of occupational allergy. *Br Med J* 1981; 283:1-7.
- 81 O'Neil CE, Salvaggio JE. The pathogenesis of occupational asthma. *Bailliere's Clin Immunol and Allergy* 1977; 2:143-75.
- 82 Carlston J. Injection immunotherapy trial in inhalant food allergy. *Ann Allergy* 1988; 61:80-2.
- 83 Armentia A, Martin-Santos JM, Wuintero A *et al.* Bakers' asthma: prevalence and evaluation of immunotherapy with a wheat flour extract. *Ann Allergy* 1990; 65:265-72.
- 84 O'Neil CE, Lehrer SB. Occupational reactions to food allergens. In: Metcalfe DD, Sampson HA, Simon RA, eds. *Food allergy: adverse reactions to food and food additives*. Boston: Blackwell Scientific Publications, 1991:207-36.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.