

CRUSTACEAN ALLERGY IN SOUTH AFRICA

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A TRIBUTE TO PAUL POTTER

I have known Prof Paul Potter since 1993, when I joined the National Health Laboratory Services (NHLS) at Groote Schuur Hospital, and I was one of his first doctoral students. Paul was not only my supervisor, but inspired me to investigate new and indigenous allergens causing clinical symptoms in South African allergic subjects. His way of dealing with patients in South Africa, with its unique biodiversity of populations, flora and fauna, was central to my entire career in the field of allergy research.

He introduced me to the importance of focusing on patient service and management and not exclusively on the molecular side of laboratory sciences. Under Paul's guidance, we conducted the first studies in Africa on allergic sensitisation to various indigenous seafood species, for which there were no diagnostics available at the time. We identified a novel allergen in abalone (perlemoen) – the first African allergen given a formal designation by the International Union of Immunological Societies (IUIS), which was subsequently published in 1997 in the Journal of Allergy and Clinical Immunology, the premier journal in the field. A new ImmunoCAP for abalone was subsequently developed (f346).

Our work on indigenous allergens did not stop with perlemoen. We investigated in detail the allergens causing asthma through inhaling dust when breeding locusts. Not only critters but, in addition, pigeons generate dust that causes allergic alveolitis. All these studies were published in several international journals as well as in the South African Current Allergy and Clinical Immunology Journal, and they provided valuable information for practising clinicians.

Through Paul's dedicated training we were able to establish a strong research team, at the University of Cape Town and then the IDM, supported by seven ALLSA grants and several NRF and MRC grants. This team focused on various aspects of seafood allergy and their research resulted in eight doctoral and master's students' successfully completing their degrees in the field of allergy, including murine models on mechanisms of seafood allergy and sensitisation to fish through workplace exposure.

Whereas Paul started the African endeavour into seafood allergies with 100 patients from the Western Cape in 1996, 21 years later we continue this legacy of characterising indigenous allergens now Down Under, in Australia. With funding from Australia, the United States and Europe, our team has identified more than 20 novel seafood allergens and is now translating previous and current findings into the development of the first immunotherapeutic for fish and shellfish allergy.

I would like to highlight our milestone publication on the immunological cross-reactivity of South African patients with crustacean allergy to a range of related indigenous crustacean species. This study was one of the very first international studies to focus on other crustaceans species besides shrimps or prawns. The diagnostic workup of the subjects in this study was challenging as no specific diagnostics were available at the time. Furthermore, this study also demonstrated distinct different immune responses to specific allergens in individual subjects with crustacean allergy, in particular those to our South African crayfish.

INTRODUCTION

Invertebrate species known to elicit adverse food reactions belong mainly to two phyla – arthropods and molluscs. These constitute the artificial grouping known as ‘shellfish’.¹ The group of crustaceans (see Table I) contains more than 35 000 species (including barnacles) and the order Decapoda, including practically all edible species, contains approximately 8 000 species.

The local ‘crayfish’ in the Western Cape of South Africa is in fact a ‘rock lobster’ and it belongs to a different sub-order than the ‘true’ crayfish, which is a freshwater species not found in Africa (see Table II). This can result in missing the diagnosis of a crustacean allergy if the wrong species in the RAST is tested.

The sub-orders include shrimp, crab, lobster and crayfish, all of them closely related to one another. Consequently, similar antigenic structures occur and human IgE antibodies against antigens in one crustacean species may cross-react with those from other species.

The aim of this study was to analyse the immune response of subjects with food sensitivity to South African crustacean species. These subjects are part of a previous study published by our research group on seafood allergy.²

Sera from 80 subjects with perceived seafood allergy were obtained for RAST and Western-blot studies, of which 40 reported sensitivity to crustacean. All the subjects replied to a self-administered questionnaire concerning history and symptoms.

SPECIES

The most frequently reported sensitivity to crustacean species was to prawn (47%), followed by rock lobster (44%), shrimp (13%) and crab (12%) (see Figure 1).

SYMPTOMS

The symptoms experienced by the subjects included:

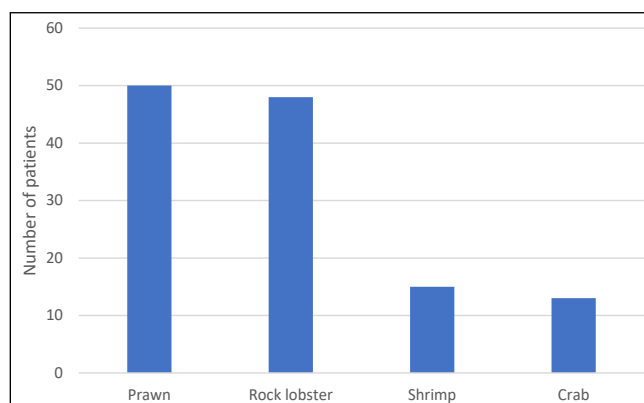


Figure 1: Frequency of crustacean species implicated in allergic reactions reported in the questionnaire by subjects with perceived seafood allergy

cutaneous, gastro-intestinal, respiratory and miscellaneous (see Table II).

Itching and swelling of the throat, lips and/or tongue were the most common symptoms; nausea and vomiting (78%) and, surprisingly, respiratory problems were also very common (61%).

The vast majority of IgE-mediated allergic reactions to crustaceans result from ingestion. However, we found that approximately one-third of the study group experienced clinical symptoms after handling seafood. The allergens from crustaceans can enter the atmosphere in steam aerosols and this explains the respiratory symptoms after ‘smelling’ cooked or grilled rock lobster, for example.³ The inhalation of these aerosols could be a means of inadvertent exposure to crustacean allergens, producing reactions in sensitive patients; they could also be responsible for the fact that hypersensitive patients rarely lose their clinical reactivity. Aerosolised allergens are of particular importance in the occupational environment.^{4,5}

IgE RESPONSE

In order to study the immune response of 40 subjects

TABLE I: CLASSIFICATION OF CRUSTACEANS, THEIR COMMON AND SCIENTIFIC NAMES AND AVAILABLE CAP-RAST

Class	Sub-orders	Common names	Some local species (scientific names)	Common southern African names	Available commercial CAP-RASTs
Crustacea	NATANIA	True schrimp; prawn	Tiger prawn: <i>Penaeus monodon</i>	Tiersteurgarnaal	Shrimp: <i>Pandalus borealis</i> , f24
	REPTANTIA	Spiny lobster	Rock lobster - West Coast: <i>Jasus Lalandi</i> Rock lobster - East Coast: <i>Paralurus homarus</i>	Crayfish/kreef	
		Langoustine (Rock lobster)	Rock lobster - West Coast: <i>Palinurus gilchristii</i> Langoustine: <i>Nephrops andamanicus</i>		Langoustine/Spiny lobster: <i>Palinurus</i> sp, Rf304
	ASTACURA	Lobster; crayfish (freshwater crayfish)	No local species		Lobster: <i>Homarus gammarus</i> , f80 Crayfish: <i>Astacus astacus</i> , Rf320
	BRACHYURA	Shore, Stone and Fiddler crab	Cape stone crab: <i>Neolithodes capensis</i> Red crab: <i>Chaceon</i> sp.	Spinnekopkrap	Crab: <i>Cancer pagurus</i> , f23

TABLE II: FREQUENCY OF REPORTED SYMPTOMS IN 40 SUBJECTS WITH PERCEIVED CRUSTACEAN SENSITIVITY

SYMPTOMS	PERCENTAGE (%)
Oropharyngeal itching/swelling	100
Nausea/vomiting/abdominal pain	78
Asthma/wheezing	61
Anxiety	48
Urticaria/eczema	44
Flushing	22
Diarrhoea	17
Dizziness	13
Headache	9

with crustacean sensitivity their specific IgE reactivity was analysed in more detail.

The IgE response of 24 crustacean-sensitive subjects to langoustine, crayfish, lobster, shrimp and crab is illustrated in Figure 2A with means of 13.6, 6.4, 6.0, 5.0 and 5.0 ku/L respectively. The mean value for the langoustine RAST was far higher than the means for the other four crustacean species. Co-reactivity to all five crustacean species analysed was found in six subjects (see Figure 2B). However, the immune responses observed to the different crustacean species are not very different from one another.

ALLERGENS

Allergens from shrimp have been reported to be heat stable and to have molecular weights between 8.2 and 29 kDa.⁶ However, few studies have focused on different lobster and crab species. More knowledge about the molecular characteristics of the allergens is needed to make a more specific diagnosis or prediction of cross-allergenicity among crustacean species. We therefore analysed six South African crustacean species by SDS-gel electrophoresis and Western-blotting to identify species-specific allergens.

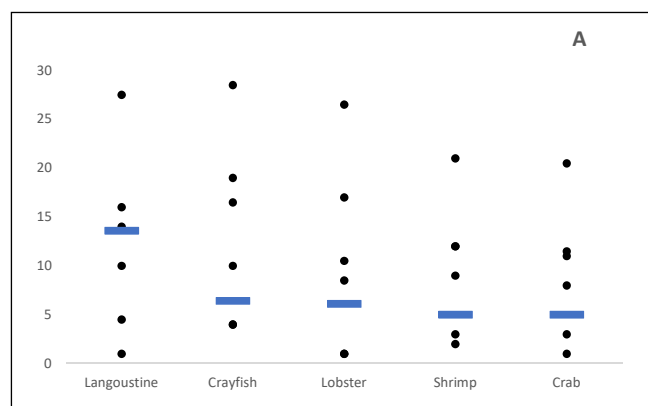


Figure 2A: Distribution of specific IgE response to different crustacean species in 24 subjects with seafood allergy and their mean values for each species: 13.6, 6.4, 6.1, 5.0 and 5.0 ku/L respectively. The following CAP-RASTs were used: langoustine (rf304), crayfish (rf320), lobster (f80), shrimp (f24), crab (f23)

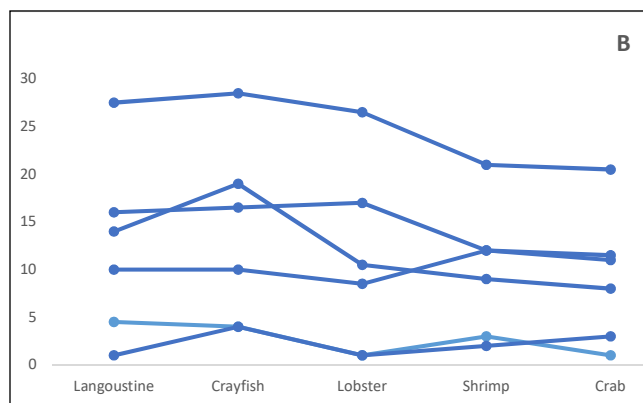


Figure 2B: Comparison of concurrent IgE response of six subjects for five different crustacean species

Immunoblots of several crustacean extracts with sera of two sensitised subjects (see Figure 3) demonstrated for subject A allergens in the molecular range of approximately 22 kDa for three of the six species investigated. In addition, all six crustacean species showed binding at approximately 70 kDa for subjects A and B. Both subjects also demonstrated binding to allergens between 36 and 40 kDa in all analysed species. However, the immune response of subject A showed distinctly different allergens in rock lobster from the east coast compared to the other,

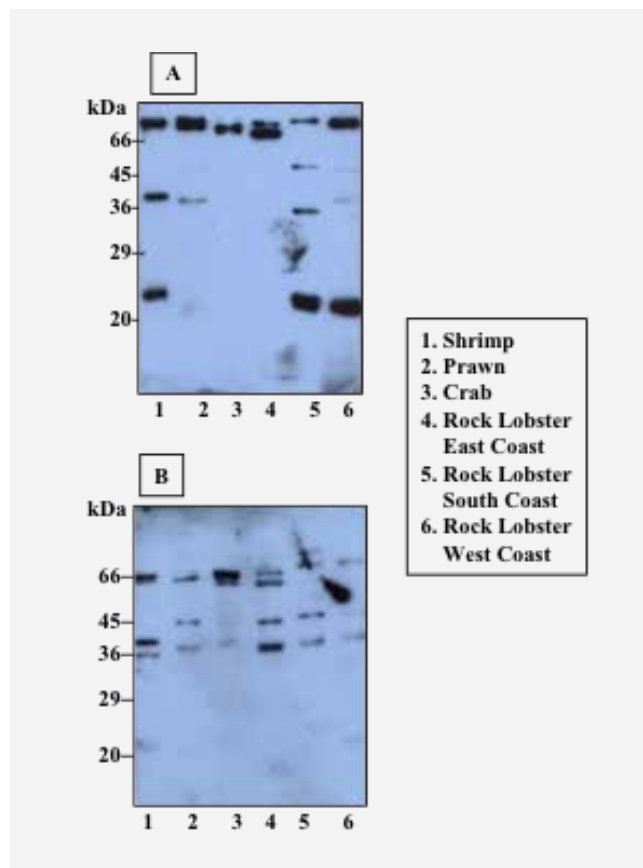


Figure 3: Western blot of IgE reactivity of two sensitised subjects (A and B) to South African crustacean species. The species' names are labelled from 1 to 6 and the molecular weights are indicated on the left side of kilodalton (kDa)

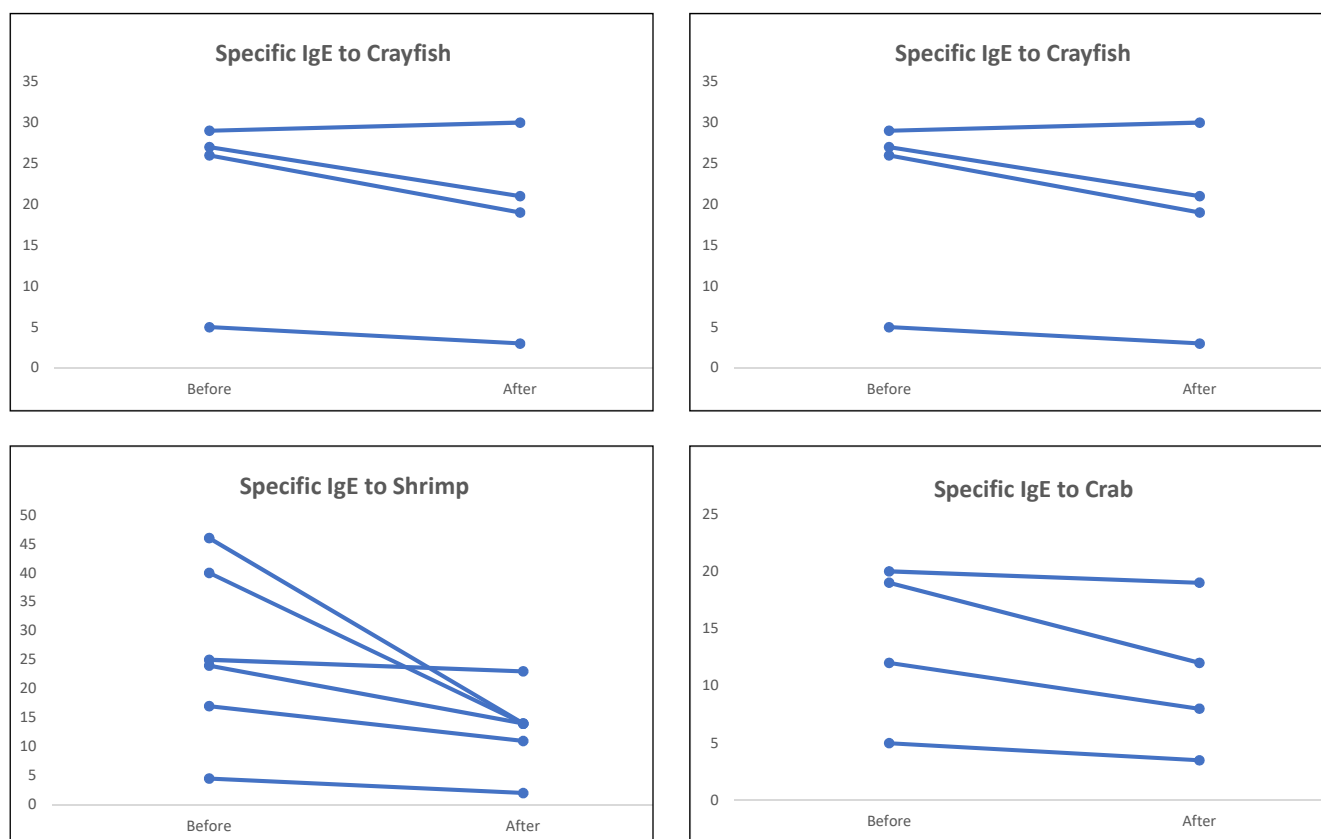


Figure 4: Specific IgE reactivity of six crustacean-sensitive subjects before consultation in our clinic and after 3–4 years, as measured by CAP-RAST in ku/L. All subjects, except one, demonstrated a decrease in IgE reactivity

very closely related rock lobsters from the south and west coasts.

Western-blot analysis of cooked crustacean species indicated decreased allergenicity. Nevertheless, some of the allergens are remarkably resistant to heat treatment. Other research groups have demonstrated that crustacean allergens are very stable; tropomyosin, a muscle protein of approximately 38 kDa, has been implicated in several other studies to be the major allergen of different crustacean species.⁷

However, the immunoblots produced in our study demonstrated higher molecular weight allergens in most of the species analysed. These results clearly indicate that specific allergens can vary among species and among individual subjects. Therefore, a detailed analysis of crustacean-sensitive individuals is important.

PERSISTENCE OF THE IMMUNE RESPONSE TO SEAFOOD

Six subjects, with concurrent allergy to crustaceans, were followed up 3–4 years after their first consultation in our clinic and the immune response to different crustacean species was compared by RAST reactivity (see Figure 4). In five subjects, the concentration of specific IgE antibodies to tested seafood species decreased by approximately 50%. The one subject who did not demonstrate a

decreased immune response over three years admitted to occasionally ingesting seafood, in particular rock lobster and prawns, and taking oral antihistamines before meals to control symptoms.

CONCLUSIONS

Crustaceans are among the most frequently mentioned seafoods causing adverse reactions in food-sensitive individuals. Sensitivity should be regarded as lifelong.

The CAP-RAST results indicate a stronger immunoreponse to the langoustine RAST with decreasing reactivity to crayfish, lobster, shrimp and crab. Because of the close phylogenetic relationship of our local rock lobster to langoustine, we recommend the use of langoustine CAP-RAST for identifying specific rock lobster IgE. We noted that crayfish is a freshwater crustacean species and lobster is a European crustacean species.

We observed that the IgE reactivity on Western-blots of the different local species is similar but not identical. Binding occurred to a 38 kDa allergen, which is probably the well-described tropomyosin also found in shrimps and prawns. However, additional allergens in the higher molecular weight ranges were also identified which have not been described previously in the literature.

Although we have encountered patients with sensitivity to

one crustacean but not to another, it is advisable to be very careful about avoiding all crustaceans if sensitivity to one is shown, unless double-blind challenges can be conducted to demonstrate that another crustacean is in fact safe to eat.

REFERENCES

1. Lopata AL, Potter PC. Allergy and other adverse reactions to seafood. *Allergy Clin Immunol Intern* 2000;12(6):271.
2. Zinn C, Lopata AL, Visser M, Potter PC. The spectrum of allergy to South African bony fish (Teleostil). Evaluation by double-blind, placebo-controlled challenge. *S Afr Med J* 1997;87(2):146.
3. Daul CB, Morgan CE, Lehrer SB. Hypersensitivity reactions to crustacea and molluscs. *Clin Rev Allergy* 1993;11(2):20.
4. Jeebhay MF, Lopata AL, Robins TG. Seafood processing in South Africa: a study of working practices, occupational health services and allergic health problems in the industry. *Occup Med (Lond)* 2000;50(6):406.
5. Jeebhay MF, Robins TG, Lopata AL. Occupational seafood allergy. *Curr Allergy Clin Immunol* 2000;13(3):20.
6. Leung PS, Chu KH. Molecular and immunological characterisation of shellfish allergens. *Front Biosci* 1998;3:306.
7. Leung PS, Chow WK, Duffey S, Kwan HS, et al. IgE reactivity against a cross-reactive allergen in crustacea and mollusc: evidence for tropomyosin as the common allergen. *J Allergy Clin Immunol* 1996;98(5):954.

A SAD FAREWELL TO DR JOHAN JANEKE



Dr Johan Benjamin Janeke, an esteemed ENT surgeon died in September, 2017. He was a loyal member of ALLSA since it's founding in 1988.

After obtaining his MB ChB degree at the University of Pretoria Medical School in 1963, he went on to complete his PhD thesis in Otolaryngology at the University of Amsterdam in

1969. He continued his training in Otolaryngology at Baylor College of Medicine in Houston, Texas. Here he received the prestigious Ben Schuster Award for his outstanding research in nasal reconstruction. He returned to South Africa in 1975 and entered private practice as an ENT surgeon in Johannesburg.

Dr Janeke had the good fortune to meet many famous people during his career. Included among these were Elvis Presley and Bob Hope. He was a demonstrator in Anatomy under Prof Phillip Tobias at the University of the Witwatersrand. Most precious and memorable to him was a meeting with Nelson Mandela.

Dr Janeke was passionate about his profession and he had the ability to connect with his patients and their families in a special way. Although he was learned and gifted with great wisdom, he was a humble man who made it his mission to treat all of his patients with the greatest respect and compassion. He gave all of his patients the same level of care, dignity and respect no matter what their station in life. In recognition of his unique ability, skills and dedication to his calling, he was awarded the prestigious



ENT Out of Africa, Dr Janeke's book

Christiaan Barnard Memorial Award for his contribution to medicine and to the people of South Africa.

Alongside his private practice career, Dr Janeke was a passionate scholar, academic and author. He wrote and published several books in the field of Otolaryngology including 'ENT Out of Africa'. This book was translated into French and used for medical training in the Francophone countries of Africa. The English version was used as a textbook at the University

of Witwatersrand Medical School and at several other medical schools in South Africa. He published articles in several peer reviewed journals in his field and was on the editorial Board of several journals in this country, including *Modern Medicine*

He was always innovative and sought new low cost ways to help the hearing impaired. He was the first ENT surgeon in South Africa to perform a cochlear implant. He developed the ABC implant as an alternative to the costly cochlear implant. When no longer able to practice, Dr Janeke turned his hand to painting. He soon developed his own unique style which he used to capture his fascination with nature, particularly trees.

Dr Janeke succumbed to pneumonia after a valiant 40 day battle. He was a committed Christian throughout his life. These values were constantly demonstrated in his personal life and in his practice. He leaves his wife Margaret, six children and six grandchildren.