Review

Allergologie select, Vol. 5/2021 (33-44)

Assessment of the effects of a work-related allergy to seafood on the reduction of earning capacity in the context of BK No. 5101

Heinrich Dickel[1], Annette Kuehn[2], Beate Dickel[3], Andrea Bauer[4], Detlef Becker[5], Manigé Fartasch[6], Michael Haeberle[7], Swen Malte John[8], Vera Mahler[9], Christoph Skudlik[8], Elke Weisshaar[10], Thomas Werfel[11], Johannes Geier[12], and Thomas Ludwig Diepgen[13†] for the working group "Evaluation of Allergens with regard to BK No. 5101" of the ABD and the DKG in the DDG

[1]Department of Dermatology, Venerology and Allergology, St. Josef-Hospital, University Hospital of the Ruhr University Bochum (UK RUB), Bochum, Germany, [2]Department of Infection and Immunity, Luxembourg Institute of Health, Esch-sur-Alzette, Luxembourg, [3]Dermatological Practice Dr. med. Peter Wenzel, Hattingen, Germany, [4]Department of Dermatology, University Allergy Center, University Hospital Carl Gustav Carus, Technical University, Dresden, Germany, [5]Department of Dermatology, University Medical Center, Mainz, Germany, [6]Institute for Prevention and Occupational Medicine (IPA) of the German Social Accident Insurance, Department of Clinical and Experimental Occupational Dermatology, Ruhr University Bochum, Bochum, Germany, [7]Dermatological Practice, Künzelsau, Germany, [8]Department of Dermatology, Environmental Medicine and Health Theory, University of Osnabrück and Institute for Interdisciplinary Dermatological Prevention and Rehabilitation (iDerm) at the University of Osnabrück, Osnabrück, Germany, [9]Paul-Ehrlich-Institut (PEI), Langen, Germany, [10]Division of Occupational Dermatology, Department of Dermatology, University Hospital Heidelberg, Heidelberg, Germany, [11]Department of Dermatology and Allergy, Hannover Medical School, Hannover, Germany, [12]Information Network of Departments of Dermatology (IVDK), Institute at the University Medical Center Göttingen, Göttingen, Germany, [13]University of Heidelberg, Heidelberg, Germany

ISSN 2512-8957

DOI 10.5414/AL0DB380E
e-pub: January 14, 2021

Key words
immediate-type allergy – occupational dermatology – BK No. 5101 – fish – crustaceans – shellfish – seafood – reduction of earning capacity – mollusks

German version published in Dermatologie in Beruf und Umwelt. Vol. 68, No. 3/2020, pp. 113-125 DOI 10.5414/DBX00380

[†]The authors dedicate the present work to Prof. Dr. med. Thomas Ludwig Diepgen who founded the working group "Evaluation of Allergens with regard to BK No. 5101" and who was a committed leader of this group until his much too early death.

Received
October 1, 2020;
accepted in revised form
November 11, 2020

Correspondence to
Priv.-Doz. Dr. med. Heinrich Dickel
Department of Dermatology, Venerology and Allergology, St. Josef-Hospital, University Hospital of the Ruhr University Bochum (UK RUB), Gudrunstraße 56, 44791 Bochum, Germany
heinrich.dickel@ruhr-uni-bochum.de

Abstract. Fish, crustaceans, and mollusks are among the most potent allergenic foods of animal origin and are thus important triggers of work-related immediate-food allergies. In Germany, work-related seafood allergies are of great importance in the fishing and processing industries as well as in the areas of food preparation, food control, and food sales. There is no causal therapy of seafood allergy, only the strict and lifelong avoidance of allergens remains. The following recommendations serve to assess the impact of a seafood allergy with regard to the work opportunities ended by it for the assessment of the reduction of earning capacity (MdE (German for Minderung der Erwerbsfähigkeit)) in the context of the occupational disease number 5101 of the Annex to the German regulation for occupational diseases. As a special feature of work-related seafood allergy with regard to insurance law aspects, it must be taken into account that there is a potential risk of systemic reaction with subsequent multi-organ involvement. For the estimation of MdE in the general labor market, the impact of a seafood allergy can therefore be assessed, depending on its clinical severity, as generally "mild" to "severe" in justified individual cases.

Background

The edible seafoods fish and shellfish are regarded as extremely high-quality and particularly digestible foods [86, 87] containing easily assimilable proteins, essential polyunsaturated omega-3 fatty acids (e.g., eicosapentaenoic acid, docosahexaenoic acid) as well as a large number of important vitamins (e.g., vitamin D), minerals, and trace elements (e.g., iodine, iron, selenium, zinc) [11]. Fish is divided into saltwater fish (62%

market share in Germany in 2018; https://www.fischinfo.de/index.php/markt/92-datenfakten/4979-marktanteile-2019, last access: 11/07/2020) and freshwater fish (26% market share in 2018). In Germany, the most popular edible fish include pollack, salmon, tuna, herring, and trout. Shellfish (12% market share 2018) includes crustaceans and mollusks [29]. Commonly eaten crustaceans include shrimp, crawfish, crayfish, and lobster [42] while the most popular mollusks are mussels, octopus, and squid [53].

Seafood, however, is considered to be the most potent allergenic food of animal origin [11, 87], and thus regarded as one of the most common triggers of food allergies [6, 87, 100]. In addition, seafood is also an important trigger of occupational allergies [12, 87, 100]. The most widely studied seafood allergies are those based on an IgE-mediated mechanism [42]. Parvalbumins, enolases, aldolases, and collagens are allergens of primary importance in fish allergies [40, 57]. For shellfish allergies, tropomyosins, arginine kinases, sarcoplasmic calcium binding proteins, myosin light chains, troponin C, and triose phosphate isomerases have been described as important allergens [57, 67]. Clinical cross-reactions between fish and shellfish are not known [40].

An important aspect of seafood allergies is that clinical symptoms may occur not only during consumption but also during food processing and preparation. In the context of professional activities, the impact can be significant for the affected person, leading to allergic reactions so severe that the person has to give up work [12]. Until now, there has been no framework for the assessment of the "impact of an allergy" for occupational seafood allergies [12], respective cases could only be assessed in the declaratory procedure by analogy with the work-related immediate-type allergy to natural rubber latex [77], because proteins with the potential risk of anaphylaxis and systemic disease also play a significant role in natural rubber latex.

Epidemiology

The prevalence of seafood allergies varies greatly depending on country-specific eating habits, the size of the seafood processing industries, and the density of gastronomy [42, 53]. Countries with a high proportion of coastal regions, such as the Mediterranean countries, Scandinavia, and Japan, are particularly affected [59, 63, 86, 87]. In general, shellfish allergies seem to be more common than fish allergies [10, 29]. For the adult population in Europe, prevalence (based on self-assessment/sensitization/medical history and sensitization/provocation testing) of up to 1.5% (95% confidence interval (CI) 1.0 – 2.2%)/2.9% (95% CI 2.2 – 3.9%)/0.8% (95% CI 0.2 – 2.5%)/0.2% (95% CI 0 – 0.9%) for fish allergies and up to 2.0% (95% CI 1.2 – 3.3%)/10.3% (95% CI 7.0 – 14.9%)/0.2% (95% CI 0.1 – 0.5%)/0.3% (95% CI 0.1 – 1.0%) for shellfish allergies have been reported [58].

In the fish- and shellfish-processing industry, the prevalence of occupational allergic contact urticaria or protein contact dermatitis ranges from 3 to 11% worldwide [34], that of work-related allergic rhinitis from 5 to 24% [33, 52], and that of work-related allergic asthma from 2 to 36% [21, 31, 33]. Occupational allergic asthma seems to be more often associated with shellfish (4 – 36%) than with fish (2 – 8%) [33].

Clinical findings

Seafood contains extremely potent IgE-reactive allergens that can cause mild to moderate reactions but also life-threatening anaphylaxis upon skin contact, inhalation, or ingestion [18, 49, 55, 100]. These are immediate-type reactions characterized by common manifestation within the first 2 hours after exposure [19, 50, 54, 67]. Biologically active seafood allergens could be detected in sera of healthy subjects only 10 minutes after ingestion [91]. Late reactions, of up to 8 hours after ingestion, have also been reported [67].

The clinical reactions are manifold. They can affect single organs but also several organ systems [40, 50, 54, 83]. They frequently occur in combination on the skin and mucous membranes of the respiratory and gastrointestinal tract, ranging from contact urticaria and protein contact dermatitis to the oral allergy syndrome (itching, angioedema, dysphagia) [12, 15], upper (rhinitis, conjunctivitis, dyspnea) and lower respiratory symptoms (asthma) [5, 32, 52] as well as gastrointestinal (nausea, vomiting, cramps, diarrhea) [54] and circulatory problems up to the life-threatening or lethal-ending anaphylactic shock [7, 11, 12, 18, 55, 67, 84, 85, 86, 87].

Allergic skin reactions are usually triggered by direct contact [54]. Both the oral allergy syndrome and upper respiratory tract symptoms are commonly caused by ingestion and inhalation [12]. Upper respiratory symptoms can be seen as an early risk marker for the pathogenesis of allergic asthma [32, 33, 34, 52], which might develop after weeks, months, or several years [32, 64]. Severe to life-threatening anaphylaxis is usually observed after ingestion [12, 18, 50, 55, 59, 75]. However, skin reactions – especially generalized urticaria – can occur in addition to the direct contact in the context of a systemic allergic reaction after ingestion or inhalation [12, 26, 28, 32, 34]. On the other hand, in the case of highly sensitized individuals, direct skin contact alone might induce systemic reactions [12, 26, 32, 34]. Individuals suffering from isolated contact urticaria after exclusive skin contact with seafood, who may develop a generalized urticaria over time [26], are exceptional cases, and so far, have only been observed in cooks and fishmongers [12, 20, 61].

In the occupational environment, irritant hand eczema often manifests first, co-triggered and maintained by a high moisture exposure and simultaneous contact with primarily skin-irritating seafood components (e.g., fluids with enzymatic activity of trypsin and pepsin), often based on an atopic skin diathesis [12, 13, 25, 32, 96, 97]. With such an impaired skin barrier, an allergic contact urticaria in the sense of a “two-phase eczema” can develop [71] and with increasing chronicity, an allergic protein contact dermatitis – the latter being the second most frequent occupational dermatosis in patients with occupational food contact [96].

However, IgE-mediated reactions are not the only cause of seafood intolerances [10, 67, 86, 87]. Adverse effects can also be caused by toxic compounds, bacterial spoiling, or pharmacological effects. The latter are mostly due to biogenic amines and, of these, especially histamine [30], which is only present in small amounts in fresh seafood. Under microbial influence, histamine can be produced in large quantities [40]. In addition, seafood allergies can also be mimicked by reactions to food additives or to parasites, especially to the parasitic nematode *Anisakis simplex* [10, 40, 59, 82, 100].

Seafood allergens and sensitization profiles

Fish allergens

Parvalbumin (10 – 12 kDa) is the main allergen in fish muscles [27, 29, 40, 42, 67]. More than 70% of fish allergic patients are sensitized to this major allergen [24, 49, 50, 75]. The parvalbumin content varies considerably between different fish species and thus influences their allergenicity [48, 84, 87]. Herring and carp, for example, have a high parvalbumin content of up to 5 mg allergen/g muscle tissue, whereas tuna is virtually free of this allergen (≈ 0.03 mg/g muscle tissue) [48, 86]. All parvalbumins are characterized by an extraordinary molecular stability against heat, denaturing agents, and proteolytic enzymes [27, 43, 49, 84, 85, 87, 89]. This high stability as well as their high content in many fish species is probably the reason why even low amounts of fish can be sufficient to trigger allergic reactions [87, 100]. Enolases (50 kDa) and aldolases (40 kDa) are also allergenic muscle proteins. They have been isolated from salmon, tuna, and cod [27, 29, 45, 87]. Their stability is significantly lower as compared to parvalbumins [40, 67]. Collagens (330 kDa) have been identified as further fish allergens [27, 40, 67]. IgE-reactivity has been shown for both fish collagen and fish gelatin, a hydrolyzed collagen product [41, 44, 45]. The correlation between anti-collagen IgE-reactivity and clinical reactions has been best described in Japanese patients [39]. Vitellogenin (118 kDa) is only found in fish roe, but at high levels [82]. Beyond parvalbumin, up to one third of the fish allergic patients are sensitized to the minor allergens described above for individual fish species [29, 45, 49, 75, 82, 87, 92].

Shellfish allergens

Tropomyosin is the main allergen in shellfish species [24, 29, 42, 50, 53, 54, 67].

It is a 65 – 70 kDa water-soluble muscle protein. Arginine kinases (minor allergens) are 40 – 45 kDa muscle proteins that play a key role in the energy production of invertebrates and therefore occur in significant amounts in crustaceans and mollusks [29, 53, 67]. Homologous allergens in house dust mites, cockroaches, and flour moths are known [10, 17, 54]. Tropomyosin, the low-molecular minor allergens myosin light chains (17 – 20 kDa) and sarcoplasmic calcium-binding proteins (20 – 25 kDa) are heat-stable [17, 29, 53, 67].

Other proteins that are vital for the muscle function were purified as crustaceans' allergens, troponin C and I (21 and 30 kDa), and triose phosphate isomerase (28 kDa) [17, 29, 53, 67]. Finally, hemocyanin (75 kDa), the blood pigment of crustaceans, has been described as an allergen in the context of clinical anaphylaxis to shrimp [17, 29, 67].

Immunological cross-reactions

Cross-reactions between fish and shellfish allergens are not known so far [11, 17, 27, 40, 42, 54]. Consequently, allergic persons do not necessarily have to avoid all types of seafood [63]. According to epidemiological studies [90, 94], ca. 20 – 40% of patients suffer from co-allergies to fish and shellfish [86].

Relevant cross-reactions among different fish species are well known [29, 67, 86], with different phenotypes being observed. Most fish allergic patients react to a broad range of different fish species [40]. Parvalbumins are of great importance as cross-reactive allergens [87], as they are characterized by a high protein sequence homology (60 – 80%) and structural similarity [54, 85] – prominent examples are Gad c 1 from cod and Cyp c 1 from carp. Cross-reactions between minor allergens of different fish species (e.g., enolase, aldolase, or collagen) may also occur. Importantly, other patients might react to only a few or even only to single fish species [16, 29, 40, 46, 67]. This points to both the existence of additional fish species-specific lgE-binding epitopes on parvalbumins and other distinct allergy triggers [86, 87]. Furthermore, parvalbumins, enolases, and aldolases have been identified as cross-reactive allergens in fish/chicken meat (so-called "fish-chicken syndrome") [11, 27, 41, 47, 87]. Parvalbumins from frog and crocodile meat are also known as cross-reactive allergens [27, 40, 87].

Due to the high sequence homologies among crustacean tropomyosins (82 – 100%) and among mollusk homologs (65 – 99%) [50, 53, 67], commonly observed cross-reactions can be explained in shellfish allergic patients [17, 29, 54, 76, 100]. The cross-reactivity rate of shellfish tropomyosins (75%) is significantly higher than the cross-reactivity rate of fish parvalbumins (50%) [10, 67, 75, 89]. However, since the sequence homology between crustacean and mollusk tropomyosins is only 50 – 60%, crustacean-sensitized patients are not necessarily reactive to mollusks and vice versa [24, 32, 67]. In patients with shellfish allergies, cross-reactions to mites and cockroaches have also been described, the so-called "mite-shellfish syndrome", and explained by the involvement of cross-reactive tropomyosins [17, 29, 33, 53, 67, 100]. Also, de-novo sensitizations to shrimp allergens have been reported in patients under specific immunotherapy for house dust mite allergy [93]. A homologous tropomyosin allergen (Ani s 3) has been discovered in the parasitic nematode *Anisakis simplex*. This parasite resides in the crustacean muscle, and even more commonly in the fish muscle, and thus can be ingested together with the infested host animal [82, 100].

Sensitization

Allergies to seafood often develop in childhood, although the prevalence is higher in adulthood [29, 86, 87]. Sensitization occurs mainly via the gastrointestinal tract through ingestion [29, 54, 67, 75]. Secondary sensitization to shellfish seems to be due to cross-reactivity in the context of the "mite-shellfish syndrome", meaning via primary sensitization to mite and cockroach allergens occurring through respiratory exposure [24, 33, 54, 55, 89].

Primary sensitization in the workplace is mainly via the respiratory tract by inhalation of aerosolized seafood particles (e.g., vapors from boiling or drying seafood) [29, 34, 52, 67, 84, 87]. Finally, sensitization may also be caused by direct skin contact, for example in cases of pre-existing skin barrier damage [35], and/or fish preparation without protective gloves [4, 26, 28, 29, 34, 67, 71, 84].

Special remarks on seafood allergenicity

Quite a number of allergic persons report clinical symptoms to seafood exclusively depending on its method of preparation [4]. Cooking, frying, grilling, salting, drying, or freezing can reduce or increase the allergenicity to seafood. For example, fish that is kept on ice for several days seems to contain intact high-molecular-weight allergens and a higher IgE-binding capacity than fresh fish [52]. On the other hand, it was shown in the mouse model that cooked fish extract was more allergenic than raw fish extract and also capable of triggering a parvalbumin-specific antibody response [92]. Furthermore, the heating of seafood proteins in the presence of sugars leads to the formation of advanced glycation end products (Maillard reaction), the so-called advanced glycation end products (AGEs) [17, 32, 75]. These AGEs are able to stimulate the absorption of allergens by antigen-presenting cells so that heated seafood allergens may be more potent than their non-heated counterparts [24, 33].

Diagnostics

The diagnosis of a seafood allergy is based on medical history, allergy tests and, if necessary, challenge tests (oral or by inhalation) (double-blind, placebo-controlled if possible) [10, 29, 67]. Based on the patient's history, specific IgE serum antibodies are determined in vitro, and rubbing and/or prick tests are performed in vivo [42, 86, 87]. The basophil activation test can be useful as an additional in vitro test [80]. However, this test has not yet been established in clinical routine because of lack of clinical validation [10, 33]. Challenge testing is not necessary if medical history, medical documentation, and allergy test results are clearly correlated, and the patient is symptom-free during seafood avoidance (e.g., diagnostic elimination diet [100]), [11, 66]. Important to note, none of the allergy tests can reliably predict the risk of life-threatening anaphylaxis to seafood.

Since the allergens of closely related seafood are extremely similar, it is generally useful to test selected representatives of different taxonomic families. For some seafood allergic persons, it is also of great interest to know to which taxonomic species they are allergic to and which ones they tolerate in order to adjust their allergen avoidance and, if necessary, dietary habits accordingly [42].

Specific IgE determination

Allergen extracts and components from different kinds of seafood are commercially available for specific IgE determination in serum [42]. The allergen extracts are a complex protein mixture of allergenic and non-allergenic seafood components, with variable composition [27, 38, 48]. Some seafood allergens may even be completely absent from the difficult-to-standardize extracts, causing a diagnostic gap, i.e., false negative test results [27, 86, 87].

Modern approaches to improving the diagnosis of seafood allergies aim to use the actual allergenic components instead of allergen extracts [2, 33, 42, 86, 87]. Using recombinant DNA technology, it is possible to produce recombinant allergens that are pure, precisely defined, and characterized. Individual allergen components are already commercially available such as the fish parvalbumins of carp rCyp c 1 and cod rGad c 1 and the shrimp tropomyosin rPen a 1 [36, 42, 100]. Nevertheless, the use of allergen extracts remains indispensable for the time being, since quite a few (up to 1/3 [87]) of those persons allergic to seafood are sensitized to other, mostly minor allergens [38, 45, 100]. The commercial availability of further, not only major but also minor, allergen components for specific IgE determination therefore represents an important perspective for a more accurate in vitro diagnosis. Based on clinical studies, a diagnostic test consisting of a combination of seafood allergen components will have to be defined [38, 86].

Prick test

Since allergy test solutions have to be approved as pharmaceuticals due to European legislation, the panel of commercially available seafood allergen extracts for prick testing is limited. Mostly only the prick-to-prick test with fresh or processed native material remains [15, 20, 33, 42, 82, 100]. The prick-to-prick test with native seafood is considered more sensitive than the prick test with commercially available allergen extracts [61], especially if the seafood is prepared with the same processing method as when the allergic reaction was triggered [97]. In addition, commercially available extracts from different manufacturers are characterized by very variable allergen contents, which is mainly due to the different preparation methods of the test solutions [68].

Occupational occurrence

In Germany, allergologically relevant contact with seafood allergens has to be considered for professionals in each of the following occupational groups and subgroups (quarterly number of employees as of September 30, 2019; Statistics of the Federal Employment Agency, Nuremberg, Germany, April 2020 [81]):

- Fishing industry (2,954 employees) including fish farming and fishing
- Fish processing (2,781 employees) in the area of food and luxury food production
- Food preparation (741,078 employees) including cooks
- Food control (4,557 employees)
- Food sale (487,597 employees).

According to the employment statistics of the Federal Employment Agency, a total of 41,742,042 people in Germany were registered for social security and marginal part-time employment as of September 30, 2019 [81], which indicates a 2.9% share of potentially work-related seafood exposure in Germany.

Occupational seafood allergies are of great importance in the fishing and fish-processing industries [21, 82]. Inhalation is the most common route of exposure. The allergens enter the respiratory tract as aerosolized particles, vapors, or dust during work processes such as cleaning, cutting, cooking, or drying of seafood [33]. For example, 30 ng/m^3 aerosolized fish antigen is sufficient to cause sensitization and workplace-related asthmatic reactions [75, 82]. Respiratory allergies among (deep-sea) fishers, fish, crab and shrimp processors, mussel openers, seafood vendors, and fish traders/sellers have been documented [31, 33].

In the field of food preparation, cooks are among the most exposed professional subgroups. For instance, their tasks include filleting fresh fish. During preparation, they may inhale aerosolized seafood particles [56, 84]. Finally, they have to season dishes containing seafood. In addition to a case series [12], there are several case reports on allergies caused by seafood in professional chefs [1, 31, 33, 62, 64, 71].

Therapy

Up to now, there is no causal therapy for seafood allergy [29, 42, 67]. Patients with seafood allergy suffer from their symptoms for the rest of their lives [11, 19, 29, 53, 54, 67, 100], even after the end of work-related exposure [34]. They must therefore be informed in detail about the possible consequences of continuous exposure to seafood [55], especially because of a constant threat of life-threatening anaphylaxis [73, 74]. Since the severity of a previous systemic allergic reaction cannot predict the severity of a subsequent one, they should be provided with an emergency kit – containing dimetindene maleate drops, betamethasone solution, and two epinephrine auto-injectors as well as for asthmatics, possibly also salbutamol aerosol – and information and training on their use [7, 10, 11, 12, 19, 37, 40, 69, 74, 79, 82, 99].

Specific immunotherapy as a causal therapy approach with mutated, recombinant, low-allergenic seafood proteins [29, 49, 67, 82, 84, 87, 89, 92], or specific oral tolerance induction with seafood [40] cannot be recommended at present due to the lack of standardized clinical protocols and the inherent risk of anaphylaxis [65, 67, 86, 87]. Therefore, only strict and lifelong allergen elimination diet remains. This means avoidance of the corresponding allergenic proteins – and thus, all seafood members of the same taxonomic group – which is to be followed not only at the workplace but also in private life [10, 11, 40, 42, 54, 65, 82, 83, 84, 86, 87, 89].

Prevention measures

In clinical routine, it is important to ask insured persons with work-related skin complaints on seafood exposure about respiratory complaints and vice versa. Results suggest that allergic respiratory disorders are common in those with occupational allergic contact urticaria and protein contact dermatitis, and that effective preventive measures should include skin and respiratory protection [12, 26]. In all cases, workplace/environmental as well as dietary allergen elimination strategies should be implemented [33, 42].

In view of the lack of generally applicable allergen workplace thresholds, the experts of the European Academy of Allergy and Clinical Immunology (EAACI; https://www.eaaci.org/, last access: 11/July/2020) consider reducing the level of allergens in the air as much as possible as the best protection [33]. For example, high exposure to aerosolized fish proteins (up to 986 ng/m^3) including allergens has been measured during fish processing [9]. Preventive measures depend on the industry and include, for example, changes in the production process, improved room ventilation, or respiratory protection devices.

The European Regulation on the provision of food information to consumers (Regulation (EU) No. 1169/2011 of the European Parliament and of the Council, latest consolidated version dated 12/12/2011; http://data.europa.eu/eli/reg/2011/1169/2011-12-12, last accessed: 11/July/2020) states that every packaged or bulk food product containing fish, crustaceans and mollusks, or products derived thereof must be labelled with an appropriate reference to this allergenic component. The clear intention is to support the allergic patient in everyday life [11, 42, 100]. Thus, the allergic consumer shall consult the list of ingredients at every purchase [82] so that, as far as possible, allergic reactions [95] upon unintentional consumption of seafood allergens can be prevented [75, 83]. International dishes in which fish is used as a seasoning are a good example for “hidden” allergens in food [11]. Seafood allergens can even be part of poultry or pork meat or other animal products (e.g., eggs) as a result of fattening the animals with fishmeal feed [22, 56, 83]. Increasingly, fish gelatin is being used instead of beef or pork gelatin [3, 44].

Special remarks

At the workplace of a cook, complete absence of seafood allergens must include avoiding 1) skin contact, 2) inhalation, for example during cooking, and 3) ingestion, for example during seasoning [28, 51, 69]. Bystander effects (i.e., reactions of uninvolved persons in the vicinity), which are not uncommon in the catering industry [11], should also be avoided. Hidden sources of allergens (cross-contamination during food preparation or when clearing and rinsing cookware contaminated with seafood remains [8, 95], seafood allergens in kitchen dust [51], etc.) additionally complicate the implementation.

Impact of an allergy

In the case of occupational, especially systemic allergic reactions to seafood, it is difficult to safely avoid exposure to the potent allergens. In many cases, occupational reorientation is inevitable [12, 20, 33, 71].

As far as skin and mucosal are involved, seafood allergy with its various manifestations is defined by the clinical severity classification of the contact urticaria syndrome according to von Krogh and Maibach (Table 1) [12, 98]. The assessment procedure may include a contextual review primarily on the question of the presence of an occupational disease (BK (German für Berufskrankheit)) according to No. 5101 of the Annex to the German Ordinance on Occupational Diseases. In individual cases, the presence of a BK No. 4301 can also be determined. This is the case when the respiratory tract is involved. However, this corresponds to a uniform allergic phenotype with reactions in multiple organ systems. As such, the constellation is to be treated as a systemic disease in the case of an insured event – based on BK No. 5101 and BK No. 4301 – leading to an overall reduction in earning capacity (MdE (German for Minderung der Erwerbstätigkeit)) with respect to the impact of the allergic disorder [72, 78]. Due to the observed course of manifestation, however, respiratory diseases, such as allergic rhinopathy or allergic asthma, will rarely be objectively justified in occupational dermatology groups, since “respiratory in-

Table 1. Contact urticaria syndrome, according to von Krogh and Maibach [98].

Stage	Cutaneous reactions	Extracutaneous reactions
Localized reactions		
I	– Contact urticaria – Dermatitis/Eczema – Nonspecific reactions: itching, prickling, burning	Ø
Systemic reactions		
II	– Generalized urticaria – Angioedema	Ø
III	– Urticaria in combination with	• rhinitis, conjunctivitis • asthma • orolaryngeal reactions • gastrointestinal reactions
IV	– Urticaria in combination with	• anaphylactic reactions

volvement" appears to be caused primarily by swelling of the mucous membranes in the upper mouth and throat and by swelling of the tongue [12, 26].

The restriction to gaining employment in the general labor market due to the occupational disease is pivotal for the assessment of the MdE [14]. In addition to the proportion of closed jobs in the general labor market, the severity of the clinical manifestations of the allergic reactions is also taken into account in the assessment of the MdE. The occurrence of seafood in the general labor market provides the basis for creating or sustaining a work-related disease [14, 60]. Thus, although the occupational exposure to seafood is extremely limited and can be well defined, an allergy acquired during this occupational exposure may manifest itself not only onto the skin but also onto other organ systems as a systemic disease.

Impact of an allergy to seafood: mild, in justified individual cases moderate to severe

Based on the clinical severity classification of the contact urticaria syndrome (Table 1), the following case considerations arise, which also take into account the hazard of allergen contacts outside the given work area:

1. In the case of allergic reactions manifesting on the skin and the directly adjacent mucous membranes exclusively upon work-related exposure, the *effect of an allergy* is to be assessed as "mild" due to the infrequent occurrence of seafood in allergenic form in the general labor market. If also in the case in other work areas by unexpected exposure aforementioned symptomatology occurs, then a higher estimate as "moderate" *effect of an allergy* can be justified in individual cases due to a barely foreseeable increase in the sensitization grade.
2. In the case of manifestation of a multi-organ involvement, i.e., with allergic reactions that exceed the skin organ, and which so far have only occurred in the proximate working environment, the *effect of an allergy* shall be assessed as "moderate", considering the latent danger of a system reaction also in working areas without expected allergen contact.
3. With manifestation of a multi-organ involvement also outside of the given work area by unexpected job-related allergen exposure, the allocation of the *effect of an allergy* as "severe" is justified.

From multi-organ involvement onwards, the involvement of skin and respiratory tract organs can result in the combined presence of a BK No. 5101 and BK No. 4301 that are to be considered as a single insurance case under the aspect of a systemic disease [72, 77, 78].

A clinically relevant immunological cross-reaction between fish and chicken meat can have an effect on everyday life and therefore may become MdE-relevant in well-founded individual cases with otherwise often overlapping occurrence as occupational substances in the general job market. The other possible immunological cross-reactions between fish and frog or crocodile meat as well as between shellfish and mites or cockroaches are usually not relevant for MdE, but should be recorded as indirect occupational disease consequences by experts and treated at the expense of the accident insurer in individual cases of clinical relevance [77]. Since house dust mite sensitization is widespread in the general population [23], it is not usually recognized as an indirect occupational disease, unless the pre-occupational absence of corresponding clinical symptoms is comprehensible on the basis of previous medical findings. In that case, the component-specific sensitization profile can be analyzed with the currently commercially available major allergens rDer p 1, rDer p 2, and rDer p 23 as specific markers for primary sensitization as well as the minor allergen rDer p 10 as a marker for cross-reactivity between tropomyosins of invertebrates, such as crustaceans, mollusks and insects, and it shows a sole or leading sensitization to house dust mite tropomyosin (rDer p 10) [70, 88].

Funding

None.

Conflict of interest

The authors state that they have no conflicts of interest with regard to the topic of this paper.

References

[1] *Abeck D, Korting HC, Ring J.* [Contact urticaria with transition to protein contact dermatitis in a cook with atopic diathesis]. Derm Beruf Umwelt. 1990; *38:* 24-26. PubMed
[2] *Agabriel C, Robert P, Bongrand P, Sarles J, Vitte J.* Fish allergy: in Cyp c1 we trust. Allergy. 2010; *65:* 1483-1484. CrossRef PubMed
[3] *André F, Cavagna S, André C.* Gelatin prepared from tuna skin: a risk factor for fish allergy or sensitization? Int Arch Allergy Immunol. 2003; *130:* 17-24. CrossRef PubMed
[4] *Bahna SL.* You can have fish allergy and eat it too! J Allergy Clin Immunol. 2004; *114:* 125-126. CrossRef PubMed
[5] *Baur X, Bakehe P.* Allergens causing occupational asthma: an evidence-based evaluation of the literature. Int Arch Occup Environ Health. 2014; *87:* 339-363. CrossRef PubMed
[6] *Bischoff SC, Herrmann A, Manns MP.* Prevalence of adverse reactions to food in patients with gastrointestinal disease. Allergy. 1996; *51:* 811-818. CrossRef PubMed
[7] *Bock SA, Muñoz-Furlong A, Sampson HA.* Fatalities due to anaphylactic reactions to foods. J Allergy Clin Immunol. 2001; *107:* 191-193. CrossRef PubMed
[8] *Boehncke WH, Pillekamp H, Gass S, Gall H.* Occupational protein contact dermatitis caused by meat and fish. Int J Dermatol. 1998; *37:* 358-360. CrossRef PubMed
[9] *Dahlman-Höglund A, Renström A, Acevedo F, Andersson E.* Exposure to parvalbumin allergen and aerosols among herring processing workers. Ann Occup Hyg. 2013; *57:* 1020-1029. PubMed
[10] *Davis CM, Gupta RS, Aktas ON, Diaz V, Kamath SD, Lopata AL.* Clinical management of seafood allergy. J Allergy Clin Immunol Pract. 2020; *8:* 37-44. CrossRef PubMed
[11] *Deutscher Allergie- und Asthmabund e.V. (DAAB).* Was hilft bei Fisch-Allergie? Allergie konkret. 2017; *3:* 6-8.
[12] *Dickel H, Bruckner T, Altmeyer P, Künzlberger B.* [Seafood allergy in cooks: a case series and review of the literature]. J Dtsch Dermatol Ges. 2014; *12:* 891-902. CrossRef PubMed
[13] *Dickel H, Kuss O, Schmidt A, Kretz J, Diepgen TL.* Importance of irritant contact dermatitis in occupational skin disease. Am J Clin Dermatol. 2002; *3:* 283-289. CrossRef PubMed
[14] *Diepgen TL, Krohn S, Bauer A, Bernhard-Klimt C, Brandenburg S, Drexler H, Elsner P, Fartasch M, John SM, Kleesz P, Köllner A, Letzel S, Merk HF, Mohr P, Münch H, Palsherm K, Pappai W, Palfner S, Römer W, Sacher J, et al.* Empfehlung zur Begutachtung von arbeitsbedingten Hauterkrankungen und Hautkrebserkrankungen – Bamberger Empfehlung. Dermatol Beruf Umw. 2016; *64:* 89-136. CrossRef
[15] *Doutre M-S.* Occupational contact urticaria and protein contact dermatitis. Eur J Dermatol. 2005; *15:* 419-424. PubMed
[16] *Ebo DG, Kuehn A, Bridts CH, Hilger C, Hentges F, Stevens WJ.* Monosensitivity to pangasius and tilapia caused by allergens other than parvalbumin. J Investig Allergol Clin Immunol. 2010; *20:* 84-88. PubMed
[17] *Faber MA, Pascal M, El Kharbouchi O, Sabato V, Hagendorens MM, Decuyper II, Bridts CH, Ebo DG.* Shellfish allergens: tropomyosin and beyond. Allergy. 2017; *72:* 842-848. CrossRef PubMed
[18] *Flais MJ, Kim SS, Harris KE, Greenberger PA.* Salmon caviar-induced anaphylactic shock. Allergy Asthma Proc. 2004; *25:* 233-236. PubMed
[19] *Fogg MI, Spergel JM.* Management of food allergies. Expert Opin Pharmacother. 2003; *4:* 1025-1037. CrossRef PubMed
[20] *Freeman S, Rosen RH.* Urticarial contact dermatitis in food handlers. Med J Aust. 1991; *155:* 91-94. CrossRef PubMed
[21] *Gautrin D, Cartier A, Howse D, Horth-Susin L, Jong M, Swanson M, Lehrer S, Fox G, Neis B.* Occupational asthma and allergy in snow crab processing in Newfoundland and Labrador. Occup Environ Med. 2010; *67:* 17-23. CrossRef PubMed
[22] *González Galán I, García Menaya JM, Jiménez Ferrera G, González Mateos G.* Anaphylactic shock to oysters and white fish with generalized urticaria to prawns and white fish. Allergol Immunopathol (Madr). 2002; *30:* 300-303. CrossRef PubMed
[23] *Haftenberger M, Laußmann D, Ellert U, Kalcklösch M, Langen U, Schlaud M, Schmitz R, Thamm M.* [Prevalence of sensitisation to aeraoallergens and food allergens: results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2013; *56:* 687-697. CrossRef PubMed
[24] *Hajeb P, Selamat J.* A contemporary review of seafood allergy. Clin Rev Allergy Immunol. 2012; *42:* 365-385. CrossRef PubMed
[25] *Halkier-Sørensen L, Thestrup-Pedersen K.* Skin irritancy from fish is related to its postmortem age. Contact Dermat. 1989; *21:* 172-178. CrossRef PubMed
[26] *Helaskoski E, Suojalehto H, Kuuliala O, Aalto-Korte K.* Occupational contact urticaria and protein contact dermatitis: causes and concomitant airway diseases. Contact Dermat. 2017; *77:* 390-396. CrossRef PubMed

[27] *Hilger C, van Hage M, Kuehn A.* Diagnosis of allergy to mammals and fish: Cross-reactive vs. specific markers. Curr Allergy Asthma Rep. 2017; *17:* 64. CrossRef PubMed

[28] *James JM, Crespo JF.* Allergic reactions to foods by inhalation. Curr Allergy Asthma Rep. 2007; *7:* 167-174. CrossRef PubMed

[29] *Jappe U, Kuehn A.* Neues zu diagnostisch relevanten Einzelallergenen aus pflanzlichen und tierischen Nahrungsmittelallergenquellen. Allergologie. 2016; *39:* 425-438. CrossRef

[30] *Jarisch R.* Histaminintoleranz – Histamin und Seekrankheit. (3. neu bearbeitete und erweiterte Auflage ed.) In: Georg Thieme Verlag KG, Stuttgart New York (2013)

[31] *Jeebhay MF, Cartier A.* Seafood workers and respiratory disease: an update. Curr Opin Allergy Clin Immunol. 2010; *10:* 104-113. CrossRef PubMed

[32] *Jeebhay MF, Lopata AL.* Occupational allergies in seafood-processing workers. Adv Food Nutr Res. 2012; *66:* 47-73. CrossRef PubMed

[33] *Jeebhay MF, Moscato G, Bang BE, Folletti I, Lipińska-Ojrzanowska A, Lopata AL, Pala G, Quirce S, Raulf M, Sastre J, Swoboda I, Walusiak-Skorupa J, Siracusa A.* Food processing and occupational respiratory allergy- An EAACI position paper. Allergy. 2019; *74:* 1852-1871. A corrigendum can be found at: https://doi.org/10.1111/all.14232. CrossRef PubMed

[34] *Jeebhay MF, Robins TG, Lehrer SB, Lopata AL.* Occupational seafood allergy: a review. Occup Environ Med. 2001; *58:* 553-562. CrossRef PubMed

[35] *Kaae J, Menné T, Thyssen JP.* Severe occupational protein contact dermatitis caused by fish in 2 patients with filaggrin mutations. Contact Dermat. 2013; *68:* 319-320. CrossRef PubMed

[36] *Kleine-Tebbe J, Jakob T.* Molecular Allergy Diagnostics: Innovation for a Better Patient Management. 1st ed. Switzerland: Springer International Publishing; 2017.

[37] *Klimek L.* Von harmlos bis letal: Nahrungsmittelallergien. HAUT. 2012; *23:* 60-62.

[38] *Klueber J, Schrama D, Rodrigues P, Dickel H, Kuehn A.* Fish allergy management: From component-resolved diagnosis to unmet diagnostic needs. Curr Treat Options Allergy. 2019; *6:* 322-337. CrossRef

[39] *Kobayashi Y, Akiyama H, Huge J, Kubota H, Chikazawa S, Satoh T, Miyake T, Uhara H, Okuyama R, Nakagawara R, Aihara M, Hamada-Sato N.* Fish collagen is an important panallergen in the Japanese population. Allergy. 2016; *71:* 720-723. CrossRef PubMed

[40] *Kourani E, Corazza F, Michel O, Doyen V.* What do we know about fish allergy at the end of the decade? J Investig Allergol Clin Immunol. 2019; *29:* 414-421. CrossRef PubMed

[41] *Kuehn A, Codreanu-Morel F, Lehners-Weber C, Doyen V, Gomez-André SA, Bienvenu F, Fischer J, Ballardini N, van Hage M, Perotin JM, Silcret-Grieu S, Chabane H, Hentges F, Ollert M, Hilger C, Morisset M.* Cross-reactivity to fish and chicken meat – a new clinical syndrome. Allergy. 2016; *71:* 1772-1781. CrossRef PubMed

[42] *Kuehn A, Dickel H.* Allergien auf Meerestiere. Allergologie. 2016; *39:* 274-284. CrossRef

[43] *Kuehn A, Hilger C, Graf T, Hentges F.* Protein- und DNS-basierte Methoden als komplementäre Methoden zum Nachweis von Fischallergenen in Nahrungsmitteln. Allergologie. 2012; *35:* 343-350. CrossRef

[44] *Kuehn A, Hilger C, Hentges F.* Anaphylaxis provoked by ingestion of marshmallows containing fish gelatin. J Allergy Clin Immunol. 2009; *123:* 708-709. CrossRef PubMed

[45] *Kuehn A, Hilger C, Lehners-Weber C, Codreanu-Morel F, Morisset M, Metz-Favre C, Pauli G, de Blay F, Revets D, Muller CP, Vogel L, Vieths S, Hentges F.* Identification of enolases and aldolases as important fish allergens in cod, salmon and tuna: component resolved diagnosis using parvalbumin and the new allergens. Clin Exp Allergy. 2013; *43:* 811-822. CrossRef PubMed

[46] *Kuehn A, Hutt-Kempf E, Hilger C, Hentges F.* Clinical monosensitivity to salmonid fish linked to specific IgE-epitopes on salmon and trout beta-parvalbumins. Allergy. 2011; *66:* 299-301. CrossRef PubMed

[47] *Kuehn A, Lehners C, Hilger C, Hentges F.* Food allergy to chicken meat with IgE reactivity to muscle alpha-parvalbumin. Allergy. 2009; *64:* 1557-1558. CrossRef PubMed

[48] *Kuehn A, Scheuermann T, Hilger C, Hentges F.* Important variations in parvalbumin content in common fish species: a factor possibly contributing to variable allergenicity. Int Arch Allergy Immunol. 2010; *153:* 359-366. CrossRef PubMed

[49] *Kuehn A, Radauer C, Swoboda I, et al.* Fischallergie: Parvalbumine und andere Allergene. Allergo J. 2012; *21:* 16-18. CrossRef

[50] *Leung NYH, Wai CYY, Shu S, Wang J, Kenny TP, Chu KH, Leung PS.* Current immunological and molecular biological perspectives on seafood allergy: a comprehensive review. Clin Rev Allergy Immunol. 2014; *46:* 180-197. CrossRef PubMed

[51] *Lin H-Y, Shyur S-D, Fu J-L, Lai YC, Lin JS.* Fish induced anaphylactic reaction: report of one case. Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi. 1998; *39:* 200-202. PubMed

[52] *Lopata AL, Jeebhay MF.* Airborne seafood allergens as a cause of occupational allergy and asthma. Curr Allergy Asthma Rep. 2013; *13:* 288-297. CrossRef PubMed

[53] *Lopata AL, Kleine-Tebbe J, Kamath SD.* Allergens and molecular diagnostics of shellfish allergy: Part 22 of the Series Molecular Allergology. Allergo J Int. 2016; *25:* 210-218. A corrigendum can be found at: https://link.springer.com/article/10.1007/s40629-017-0016-0. CrossRef PubMed

[54] *Lopata AL, Lehrer SB.* New insights into seafood allergy. Curr Opin Allergy Clin Immunol. 2009; *9:* 270-277. CrossRef PubMed

[55] *Lopata AL, O'Hehir RE, Lehrer SB.* Shellfish allergy. Clin Exp Allergy. 2010; *40:* 850-858. CrossRef PubMed

[56] *Lucas D, Lucas R, Boniface K, Jegaden D, Lodde B, Dewitte JA.* Occupational asthma in the commercial fishing industry: a case series and review of the literature. Int Marit Health. 2010; *61:* 13-16. PubMed

[57] *Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, Aalberse RC, Agache I, Asero R, Ballmer-Weber B, Barber D, Beyer K, Biedermann T, Bilò MB, Blank S, Bohle*

B, Bosshard PP, Breiteneder H, Brough HA, Caraballo L, et al. EAACI Molecular Allergology User's Guide. Pediatr Allergy Immunol. 2016; *27 (Suppl 23):* 1-250. CrossRef PubMed

[58] *Moonesinghe H, Mackenzie H, Venter C, Kilburn S, Turner P, Weir K, Dean T.* Prevalence of fish and shellfish allergy: A systematic review. Ann Allergy Asthma Immunol. 2016; *117:* 264-272.e4. CrossRef PubMed

[59] *Morishima R, Motojima S, Tsuneishi D, Kimura T, Nakashita T, Fudouji J, Ichikawa S, Ito H, Nishino H.* Anisakis is a major cause of anaphylaxis in seaside areas: An epidemiological study in Japan. Allergy. 2020; *75:* 441-444. CrossRef PubMed

[60] *Nowak D, Diepgen TL, Drexler H; Consensus of the Germn Society of Pneumology, the Working Group of Dermatology in the German Dermatologic Society and the German ociety for Occupational and Environmental Medicine.* [Reduced earning capacity due to IgE-mediated skin and airway allergy. Consensus paper]. Pneumologie. 2004; *58:* 365-366. CrossRef PubMed

[61] *Onesimo R, Giorgio V, Pill S, Monaco S, Sopo SM.* Isolated contact urticaria caused by immunoglobulin E-mediated fish allergy. Isr Med Assoc J. 2012; *14:* 11-13. PubMed

[62] *Pala G, Pignatti P, Perfetti L, Gentile E, Moscato G.* Occupational allergic contact urticaria to crustacean in a cook. J Investig Allergol Clin Immunol. 2012; *22:* 142-143. PubMed

[63] *Pascual CY, Reche M, Fiandor A, Valbuena T, Cuevas T, Esteban MM.* Fish allergy in childhood. Pediatr Allergy Immunol. 2008; *19:* 573-579. CrossRef PubMed

[64] *Patel PC, Cockcroft DW.* Occupational asthma caused by exposure to cooking lobster in the work environment: a case report. Ann Allergy. 1992; *68:* 360-361. PubMed

[65] *Pite H, Prates S, Borrego LM, Matos V, Loureiro V, Leiria-Pinto P.* Resolution of IgE-mediated fish allergy. Allergol Immunopathol (Madr). 2012; *40:* 195-197. CrossRef PubMed

[66] *Reese I, Schäfer C, Werfel T, Worm M.* Diätetik in der Allergologie: Diätvorschläge, Positionspapiere und Leitlinien zu Nahrungsmittelallergie und anderen Nahrungsmittelunverträglichkeiten. 5. überarbeitete und erweiterte Auflage. München – Orlando: Dustri-Verlag Dr. Karl Feistle GmbH & Co. KG; 2017.

[67] *Ruethers T, Taki AC, Johnston EB, Nugraha R, Le TTK, Kalic T, McLean TR, Kamath SD, Lopata AL.* Seafood allergy: A comprehensive review of fish and shellfish allergens. Mol Immunol. 2018; *100:* 28-57. CrossRef PubMed

[68] *Ruethers T, Taki AC, Nugraha R, Cao TT, Koeberl M, Kamath SD, Williamson NA, O'Callaghan S, Nie S, Mehr SS, Campbell DE, Lopata AL.* Variability of allergens in commercial fish extracts for skin prick testing. Allergy. 2019; *74:* 1352-1363. CrossRef PubMed

[69] *Sackesen C, Adalioglu G.* Hidden fish substance triggers allergy. J Investig Allergol Clin Immunol. 2003; *13:* 216-217. PubMed

[70] *Sánchez-Borges M, Fernandez-Caldas E, Thomas WR, Chapman MD, Lee BW, Caraballo L, Acevedo N, Chew FT, Ansotegui IJ, Behrooz L, Phipatanakul W, Gerth van Wijk R, Pascal D, Rosario N, Ebisawa M, Geller M, Quirce S, Vrtala S, Valenta R, Ollert M, et al.* International consensus (ICON) on: clinical consequences of mite hypersensitivity, a global problem. World Allergy Organ J. 2017; *10:* 14. CrossRef PubMed

[71] *Sano A, Yagami A, Suzuki K, Iwata Y, Kobayashi T, Arima M, Kondo Y, Yoshikawa T, Matsunaga K.* Two cases of occupational contact urticaria caused by percutaneous sensitization to parvalbumin. Case Rep Dermatol. 2015; *7:* 227-232. CrossRef PubMed

[72] *Schönberger A, Mehrtens G, Valentin H.* Arbeitsunfall und Berufskrankheit – Rechtliche und medizinische Grundlagen für Gutachter, Sozialverwaltung, Berater und Gerichte. 9., völlig neu bearbeitete Auflage. Berlin: Erich Schmidt Verlag GmbH & Co. KG; 2017.

[73] *Seitz CS, Bröcker EB, Trautmann A.* Occupational allergy due to seafood delivery: Case report. J Occup Med Toxicol. 2008; *3:* 11. CrossRef PubMed

[74] *Shah E, Pongracic J.* Food-induced anaphylaxis: who, what, why, and where? Pediatr Ann. 2008; *37:* 536-541. CrossRef PubMed

[75] *Sharp MF, Lopata AL.* Fish allergy: in review. Clin Rev Allergy Immunol. 2014; *46:* 258-271. CrossRef PubMed

[76] *Sicherer SH, Muñoz-Furlong A, Sampson HA.* Prevalence of seafood allergy in the United States determined by a random telephone survey. J Allergy Clin Immunol. 2004; *114:* 159-165. CrossRef PubMed

[77] *Skudlik C, Allmers H, John SM, Becker D, Dickel H, Geier J, Häberle M, Lessmann H, Mahler V, Wagner E, Weisshaar E, Wehrmann W, Werfel T, Zagrodnik F, Diepgen TL.* Beurteilung der Auswirkungen einer Allergie gegenüber Naturgummilatex bei der Minderung der Erwerbsfähigkeit im Rahmen der BK 5101. Dermatol Beruf Umw. 2010; *58:* 54-60. CrossRef

[78] *Skudlik C, John SM, Schwanitz HJ.* Vergleich von Begutachtungsempfehlungen für die BK-Ziffern 4301 und 5101: Brauchen wir eine neue BK-Ziffer für berufsbedingte Typ-I-Allergien mit Multiorgan-Manifestation? Dermatol Beruf Umw. 2000; *48:* 13-18.

[79] *Song TT, Worm M, Lieberman P.* Anaphylaxis treatment: current barriers to adrenaline auto-injector use. Allergy. 2014; *69:* 983-991. CrossRef PubMed

[80] *Sørensen M, Kuehn A, Mills ENC, Costello CA, Ollert M, Småbrekke L, Primicerio R, Wickman M, Klingenberg C.* Cross-reactivity in fish allergy: A double-blind, placebo-controlled food-challenge trial. J Allergy Clin Immunol. 2017; *140:* 1170-1172. CrossRef PubMed

[81] Statistik der Bundesagentur für Arbeit. Tabellen, Beschäftigte nach Berufen (Klassifikation der Berufe 2010) (Quartalszahlen). In: Bundesagentur für Arbeit, Nürnberg (April 2020).

[82] *Stephen JN, Sharp MF, Ruethers T, Taki A, Campbell DE, Lopata AL.* Allergenicity of bony and cartilaginous fish – molecular and immunological properties. Clin Exp Allergy. 2017; *47:* 300-312. CrossRef PubMed

[83] *Stiller D.* Allergien durch Tiere des Meeres. Allergologie. 2008; *31:* 366-370. CrossRef

[84] *Swoboda I.* Fischallergie: Neue Ansätze zur Verbesserung von Diagnose und Therapie. Allergologie. 2011; *34:* 388-397. CrossRef

[85] *Swoboda I, Bugajska-Schretter A, Valenta R, Spitzauer S.* Recombinant fish parvalbumins: Candidates for diagnosis and treatment of fish allergy. Allergy. 2002; *57 (Suppl 72):* 94-96. CrossRef PubMed

[86] *Swoboda I, Kühn A.* Fischallergie – neue Ansätze zur Verbesserung von Diagnose und Therapie. In: Stiller D (ed). Allergien durch tierische Lebewesen. Munich-Orlando: Dustri-Verlag Dr. Karl Feistle GmbH & Co. KG; 2014. p. 17-32.

[87] *Swoboda I, Kühn A.* Das Fischhauptallergen Parvalbumin – vom diagnostischen Marker zur allergenspezifischen Immuntherapie. In: A. Kühn, C. Hilger (eds). Tierallergien. Dustri-Verlag Dr. Karl Feistle GmbH & Co. KG, 2017. p. 107-124.

[88] Thermo Fisher Diagnostics. ImmunoCAP Allergenkomponenten für die In-vitro-Allergiediagnostik. In: Thermo Fisher Scientific Inc. Freiburg (D) Wien (A) Steinhausen (CH): 2018.

[89] *Tsabouri S, Triga M, Makris M, Kalogeromitros D, Church MK, Priftis KN.* Fish and shellfish allergy in children: review of a persistent food allergy. Pediatr Allergy Immunol. 2012; *23:* 608-615. CrossRef PubMed

[90] *Turner P, Ng I, Kemp A, Campbell D.* Seafood allergy in children: a descriptive study. Ann Allergy Asthma Immunol. 2011; *106:* 494-501. CrossRef PubMed

[91] *Untersmayr E, Vestergaard H, Malling H-J, Jensen LB, Platzer MH, Boltz-Nitulescu G, Scheiner O, Skov PS, Jensen-Jarolim E, Poulsen LK.* Incomplete digestion of codfish represents a risk factor for anaphylaxis in patients with allergy. J Allergy Clin Immunol. 2007; *119:* 711-717. CrossRef PubMed

[92] *van der Ventel ML, Nieuwenhuizen NE, Kirstein F, Hikuam C, Jeebhay MF, Swoboda I, Brombacher F, Lopata AL.* Differential responses to natural and recombinant allergens in a murine model of fish allergy. Mol Immunol. 2011; *48:* 637-646. CrossRef PubMed

[93] *van Ree R, Antonicelli L, Akkerdaas JH, Garritani MS, Aalberse RC, Bonifazi F.* Possible induction of food allergy during mite immunotherapy. Allergy. 1996; *51:* 108-113. CrossRef PubMed

[94] *Venter C, Arshad SH.* Epidemiology of food allergy. Pediatr Clin North Am. 2011; *58:* 327-349., ix CrossRef PubMed

[95] *Versluis A, Knulst AC, Kruizinga AG, Michelsen A, Houben GF, Baumert JL, van Os-Medendorp H.* Frequency, severity and causes of unexpected allergic reactions to food: a systematic literature review. Clin Exp Allergy. 2015; *45:* 347-367. CrossRef PubMed

[96] *Vester L, Thyssen JP, Menné T, Johansen JD.* Consequences of occupational food-related hand dermatoses with a focus on protein contact dermatitis. Contact Dermat. 2012; *67:* 328-333. CrossRef PubMed

[97] *Vester L, Thyssen JP, Menné T, Johansen JD.* Occupational food-related hand dermatoses seen over a 10-year period. Contact Dermat. 2012; *66:* 264-270. CrossRef PubMed

[98] *von Krogh G, Maibach HI.* The contact urticaria syndrome – an updated review. J Am Acad Dermatol. 1981; *5:* 328-342. CrossRef PubMed

[99] *Werner-Busse A, Zuberbier T, Worm M.* [The allergic emergency – management of severe allergic reactions]. J Dtsch Dermatol Ges. 2014; *12:* 379-388. PubMed

[100] *Worm M, Reese I, Ballmer-Weber B, Beyer K, Bischoff SC, Classen M, Fischer PJ, Fuchs T, Huttegger I, Jappe U, Klimek L, Koletzko B, Lange L, Lepp U, Mahler V, Niggemann B, Rabe U, Raithel M, Saloga J, Schäfer C, et al.* Guidelines on the management of IgE-mediated food allergies: S2k-Guidelines of the German Society for Allergology and Clinical Immunology (DGAKI) in collaboration with the German Medical Association of Allergologists (AeDA), the German Professional Association of Pediatricians (BVKJ), the German Allergy and Asthma Association (DAAB), German Dermatological Society (DDG), the German Society for Nutrition (DGE), the German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS), the German Society for Oto-Rhino-Laryngology, Head and Neck Surgery, the German Society for Pediatric and Adolescent Medicine (DGKJ), the German Society for Pediatric Allergology and Environmental Medicine (GPA), the German Society for Pneumology (DGP), the German Society for Pediatric Gastroenterology and Nutrition (GPGE), German Contact Allergy Group (DKG), the Austrian Society for Allergology and Immunology (Æ-GAI), German Professional Association of Nutritional Sciences (VDOE) and the Association of the Scientific Medical Societies Germany (AWMF). An erratum can be found at: https://link.springer.com/article/10.1007/s40629-015-0088-7. Allergo J Int. 2015; *24:* 256-293. CrossRef PubMed