



# Occupational inhalant allergy in food handling occupations

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## Purpose of review

Review article on recent developments on inhalant food allergens associated with occupational respiratory allergy and asthma.

## Recent findings

This review has found that occupational inhalant allergy in food handling occupations is a common and recognisable clinical entity (class 3 food allergy) in high-risk food occupations such as bakeries and seafood processing. Aerosolised food proteins from plant or animal food sources, additives and biological food contaminants cause occupational sensitization, rhinitis and asthma. The risk of allergy may be enhanced across the food value chain as a result of food processing techniques including the introduction of new food allergens in the food matrix. Occupational food allergy and asthma can be prevented by improved health-based exposure standards, workplace control measures, education and training activities, and early diagnosis accompanied with exposure reduction.

## Summary

Future studies need to focus on exposure-response studies to establish improved exposure limits especially for flour dust, the relevance of cooked vs raw foods in influencing risk, identifying and characterising major inhalant food allergens accompanied with component resolved diagnostic approaches, and evaluating the effectiveness of interventions for common high-risk food sensitizers causing occupational rhinitis and asthma.

## Keywords

food handling and processing, inhalant food allergens, occupational asthma, occupational food allergy

## INTRODUCTION

Occupational sensitisation due to inhalant food allergens during food handling, classified by the European Academy of Allergy and Clinical Immunology (EAACI) Consensus Statement as a class 3 food allergy (Table 1), is estimated to account for up to 25% of occupational asthma (OA) and occupational rhinitis (OR) [1<sup>■</sup>]. The main allergen sources include high molecular weight (HMW) food proteins in plant or animal food sources, additives (enzymes, flavourants, colourants, thickening agents, sulphites) and biological food contaminants (insects, mites, parasites and fungi) in food storage, preparation and processing facilities [1<sup>■</sup>,2]. The predominant mechanism of sensitisation is through aerosolisation of allergens during workplace handling and their subsequent inhalation.

## METHODS

Published studies were identified from PubMed and MEDLINE for the period 2018–2021, as an update to the comprehensive review published in 2019 by the

EAACI FORA Taskforce [1<sup>■</sup>]. The following keywords were used in the search strategy: (occupational allergy) or (inhalant food allergy) or (work-related allergy) AND (occupational allergic respiratory disease) or (respiratory allergy or asthma or rhinitis) AND (food processing) or (food handling) or (food industry). Specific searches also included (wheat allergen) or (flour dust or wheat allergens) or (baker's asthma or rhinitis) AND occupational exposure),

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## KEY POINTS

- Occupational inhalant food allergy is caused by high molecular weight food proteins in plant or animal food sources, additives and biological food contaminants in food storage, preparation and processing facilities.
- The predominant mechanism of sensitization is through aerosolization of allergens during workplace handling resulting in occupational rhinitis and asthma.
- Occupational food allergy and asthma can be prevented by improved health-based exposure standards, workplace control measures, education and training activities and early diagnosis accompanied with exposure reduction.

(seafood processing or manufacturing or handling or industry) or (seafood allergy or asthma or occupational seafood allergy) or (seafood allergens) or (work-related exposure or occupational seafood exposure or bioaerosol exposure or enzyme exposure), given these two entities are the most commonly studied. References published within the timeframe not otherwise identified in the initial search were added to provide appropriate continuity and context.

## OCCUPATIONS AND POPULATIONS AT RISK

### Causative agents

There are few prospective studies that follow the development of adult respiratory disease with exposure to occupational asthmagenic agents. In a population-based study, Tagiyeva *et al.* reported an increased risk of adult onset wheezing illness, lung function impairment and excess Forced expiratory volume in

one second (FEV<sub>1</sub>) decline with occupational exposure to food-related agents in adults without childhood wheeze [3].

A comprehensive list of agents causing occupational allergy, OR or OA is listed in the EAACI Consensus Statement [1<sup>¶</sup>]. Additional agents that have been reported in this review period are listed in Table 2 [4–19]. Notable newly reported plant agents include an additional allergen *Prunus persica* 9 in peach tree pollen, causing allergic sensitization in peach orchard farm workers [5]. Another is quinoa flour causing wheeze in a mill worker as seeds become popular in wheat allergic or gluten-intolerant individuals [6]. Occupational allergy to donkey milk was reported in a food laboratory analyst that handled both liquid and powdered lyophilized forms [12]. It is rare since it is not widely consumed and is considered to be hypoallergenic.

An unusual allergen in a butcher involved in sausage production, when adding binding agents, containing enzyme transglutaminase from *Streptomyces mobaraensis* to catalyze cross-linking of meat proteins to produce a more stable texture [14]. Psyllium has reemerged in bakers due to the increasing popularity of gluten-free and vegan food as a substitute for gluten or eggs [17]. An exotic rare cause of OA due to saponins from soapnuts and quillaja bark (*Quillaja saponaria*), added to beer was also reported [18].

Finally, two new seafood allergens were reported in workers handling dry shrimp *Gammarus* powder (*Pen m* 4) and fish (creatine kinase) [7,8].

### Epidemiology and risk factors

It is estimated that OA occurs in 3–10% of green coffee bean workers, 4–13% of bakers, 2–8% of bony fish processors and 4–36% of shellfish processors [1<sup>¶</sup>,20,21]. Occupational risk factors for OA include

**Table 1.** Classification of food allergy

|         | Primary route of sensitization                                       | Population affected                                                                                | Symptoms with food ingestion | Symptoms with food inhalation |
|---------|----------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|------------------------------|-------------------------------|
| Class 1 | Gastrointestinal tract, transcutaneous (with disrupted skin barrier) | Commonly children but can also occur in adults                                                     | Always                       | Occasional                    |
| Class 2 | Cross-reactive allergens present in inhaled sources <sup>a</sup>     | Commonly adults but can also occur in children/adolescents                                         | Always                       | Seldom                        |
| Class 3 | Respiratory tract, transcutaneous (with disrupted skin barrier)      | Commonly adults in the workplace, but can also occur in the domestic setting with food preparation | Seldom                       | Always                        |

<sup>a</sup>Example: pollen food syndromes.

EAACI consensus statement on food processing and occupational respiratory allergy [1<sup>¶</sup>].

**Table 2.** Recent case reports of food handling workers with occupational rhinitis or asthma due to inhalant food allergens

| Agent                                                                                      | Occupation                                 | Other Symptoms                             | Skin prick or intradermal test     | Other immunologic evidence            | Specific bronchial provocation | Other evidence                                                |
|--------------------------------------------------------------------------------------------|--------------------------------------------|--------------------------------------------|------------------------------------|---------------------------------------|--------------------------------|---------------------------------------------------------------|
| Plants/vegetables/fruits/spices                                                            |                                            |                                            |                                    |                                       |                                |                                                               |
| Carrot [4]                                                                                 | Cook                                       | Sneezing, rhinorrhoea, conjunctivitis      | Positive to carrot                 | IgE positive                          | ND                             | ND                                                            |
| Peach tree pollen ( <i>Prunus persica</i> 9) [5]                                           | Peach orchard farm workers (n = 21)        | Rhinitis, asthma                           | Positive to peach tree pollen      | Immunoblot                            | ND                             | Nasal provocation                                             |
| Seeds                                                                                      |                                            |                                            |                                    |                                       |                                |                                                               |
| Quinoa flour [6]                                                                           | Mill worker                                | Wheeze                                     | Positive to quinoa                 | ND                                    | ND                             | FeNO, methacholine challenge                                  |
| Buckwheat [7]                                                                              | Cooks, baker, Grocery store worker (n = 6) | Recurrent watery rhinitis, cough, dyspnoea | Positive to buckwheat              | Specific IgE                          | ND                             | Spirometry, FeNO, serial PEF                                  |
| Mushrooms                                                                                  |                                            |                                            |                                    |                                       |                                |                                                               |
| Mushroom sp. [8] ( <i>L shimeji</i> , <i>F velutipes</i> , <i>A bisporus/brunnescens</i> ) | Farmer                                     | Nasal, wheezing                            | Positive for mushroom              | Immunoblot positive                   | ND                             | Serial FEV <sub>1</sub> , PEF                                 |
| Farm products                                                                              |                                            |                                            |                                    |                                       |                                |                                                               |
| Pork [9]                                                                                   | Slaughterhouse Workers (n = 4)             | Recurrent cough, dyspnoea, watery rhinitis | Positive pork meat                 | Immunoblot positive                   | Positive (pork meat and liver) | Nasal provocation, FeNO, spirometry                           |
| Shrimp Gammarus Powder [10]                                                                | Manufacturing/packaging animal feed worker | Rhinorrhea, dyspnoea, cough, wheezing      | Positive to shrimp Gammarus        | IgE to shrimp                         | Positive (shrimp Gammarus)     | Spirometry, bronchodilator challenge                          |
| Fish Creatine Kinase [11]                                                                  | Fishmonger                                 | Dyspnoea, pruritis                         | Positive to raw hake, sole, tuna   | IgE to sole, hake Immunoblot Positive | ND                             | Spirometry, FeNO mass spectrometry for protein identification |
| Milk derivatives                                                                           |                                            |                                            |                                    |                                       |                                |                                                               |
| Donkey milk [12]                                                                           | Food analyst                               | Rhinitis                                   | Positive for donkey milk           | Immunoblot positive                   | ND                             | ND                                                            |
| Rennet (chymosin) [13]                                                                     | Cheese maker                               | Dry cough, wheezing, sneezing              | Positive to rennet                 | IgE to rennet                         | ND                             | Bronchodilator challenge, FeNO                                |
| Additives and preservatives                                                                |                                            |                                            |                                    |                                       |                                |                                                               |
| Trans-Glutaminase [14] ( <i>Streptomyces mobaraensis</i> )                                 | Butcher                                    | Cough, sneezing                            | Positive to transglutaminase       | Immunoblot positive                   | ND                             | Spirometry (FEV <sub>i</sub> )                                |
| Gum Arabic [15]                                                                            | Candy factory                              | Rhinitis                                   | Negative                           | Positive to Gum Arabic                | ND                             | Nasal provocation                                             |
| Locust (carob) Bean Gum [16]                                                               | Cheese maker                               | Rhinitis, wheezing                         | ND                                 | IgE positive                          | ND                             | Serial PEF                                                    |
| Psyllium [17]                                                                              | Baker                                      | Itchy eyes/nose wheeze, cough              | Positive to psyllium               | IgE positive                          | ND                             | FeNO                                                          |
| Soapnut and quillaja bark [18]                                                             | Processing worker                          | Rhino-conjunctivitis, asthma               | Positive to quillaja bark, soapnut | Specific IgE                          | Positive (soapnut extract)     | FeNO, Serial FEV <sub>1</sub>                                 |
| Sodium metabisulphite (SMBS) [19]                                                          | Coffee factory worker                      | Rhinitis                                   | Positive SMBS                      | Oral provocation                      | ND                             | Nasal provocation                                             |

FeNO, fractional exhaled nitric oxide; IgE, Immunoglobulin E; ND, not done; PEF, peak expiratory flow.

the allergenicity of food proteins, nature of work processes and allergen exposure levels, whereas atopy, OR and ingestion-related allergy are important host risk factors.

Recent epidemiological studies have focussed mainly on workers in flour mills baking industries and the seafood industry (Tables 3 and 4). OA in these two food sectors have been reviewed in greater detail elsewhere [20,21].

Olivieri *et al.* reported a higher prevalence of work-related nasal (25.7%) than asthma-like symptoms (9.5%) in bakers using only wheat flour in traditional Italian bakeries (Table 3) [22]. The risk of work-related asthma-like symptoms was higher in bakers compared to shop assistants, with higher odds when multigrain flour was used (OR=3.4, 95% CI 1.1–10.8). In a sub-study, fractional exhaled nitric oxide (FeNO) levels were higher in sensitized bakers with work-related lower airway symptoms compared to nonsensitized bakers as has been reported previously by Baatjies *et al.* [23<sup>•</sup>,24]. In another Italian study of bakers, a significant correlation was observed between increasing duration or flour dust exposures >2 mg/m<sup>3</sup> and declining FEV<sub>1</sub>/Forced vital capacity (FVC) ratio [25].

In Ethiopian flour mill workers, significant risk factors for work-related respiratory symptoms included employment duration >5 years, flour mixing operations, inadequate workplace ventilation, lack of respiratory protective equipment and bakers having no safety training [26–28]. Two studies of bakeries in the DR Congo and Benin reported the prevalence of OA as 3.6% and 10% respectively [29,30].

Epidemiological studies were reported from Norwegian crab processing workers and Swedish fishers and processors (Table 4). In the former group, atopy was significantly associated with positive Skin prick test (SPT) or raised IgE to king- and edible crab. Workers exhibited differential IgE binding patterns to various forms of crab extracts (raw and cooked meat, intestines, shell) frequently to tropomyosin and arginine kinase as well as to two novel proteins, hemocyanin and enolase [31<sup>•</sup>]. More studies are needed to determine their relevance for occupational sensitization through inhalation. In the latter study, the risk of asthma among fish filleting workers increased with employment duration in fish processing and the use of pressured sprayers. Filleters were also more likely to change their work tasks due to respiratory symptoms than other fish processing workers [32]. Mason *et al.* used data from the Surveillance of Work-related and Occupational Respiratory Disease reporting system for 1992–2017 showing an excess incidence of annual OA for UK land-based seafood processors of 70 per

100 000 workers compared to 2.9 in 'all other industries', implicating prawns and salmon/trout processing [33]. These findings are consistent with others, highlighting the need to reduce bioaerosol exposures [34].

In an isolated study of poultry farm workers, Ngajilo *et al.* reported a 3% prevalence of OA [35]. Workers sensitized to chicken-specific allergens (8%) were more likely to be atopic or employed as casual-workers, whereas those with work-related chest symptoms were more likely to work in the rearing-department (OR=3.2, 95% CI: 1.2–8.4).

## EXPOSURE ASSESSMENT

Exposure assessment is important in identifying high-risk exposures and evaluating the effectiveness of interventions. El-Zaemey *et al.* used data from the Australian Work Exposure Study-Asthma, found that among the 4,878 respondents, 12.4% reported occupational exposure to asthmagens derived from animals, fish and/or shellfish, whilst 12.8% reported occupational exposure to asthmagens derived from plants [36,37]. Furthermore, farmers/food handling workers were the most common occupational group exposed to animals/seafood (33%) and plants, mainly to flour (66%).

Exposure studies have been reported mainly for flour dust, since it continues to be associated with a higher incidence of OA and OR. Recent studies have been reviewed in a separate communication [38<sup>•</sup>]. Notable is the systematic review of 21 studies, which demonstrated that weighing/mixing and dough forming tasks were associated with the highest inhalable dust (3.078–4.930 mg/m<sup>3</sup>) and wheat allergen levels (37–40 µg/m<sup>3</sup>) [39]. Furthermore, small bakery size was also associated with higher exposures.

Noncompliance with exposure limits continues to be highlighted. Zamani *et al.* reported high mean dust levels of 11.06 mg/m<sup>3</sup> in Iranian flour mill workers, with 45% of samples exceeding the American Conference of Governmental Industrial Hygienists (ACGIH) standard of 0.5 mg/m<sup>3</sup> [40]. Irish bakeries had 70% of measurements exceeding 1 mg/m<sup>3</sup> whereas Norwegian bakeries had 29% of samples exceeding 3 mg/m<sup>3</sup> [41,42]. Similarly, dust levels in Canadian bakeries were on average, double the exposure standard [39].

Furthermore, mycotoxin exposures have also been reported in Portuguese fresh bread dough companies [43], documenting exposures to deoxynivalenol (DON) as high as 58.2 ng/g, whilst a study in the Norwegian grain industry reported 1,3-β-glucan concentrations of 32 µg/m<sup>3</sup> [44]. A study of Irish bakeries and pizzerias reported fungi including *Penicillium* and mycotoxin exposures dominated by

**Table 3.** Summary of recent epidemiological studies of work-related symptoms, rhinitis and asthma in plant food handling workplaces

| Author/<br>Country                  | Study design    | Subjects (n)                       | Participation<br>rate (%) | Age (yrs.)<br>mean (range)                       | Workplace            | Diagnostic<br>methods for<br>defining<br>rhinitis | Diagnostic<br>methods<br>for defining<br>asthma | Atopy<br>assessment | Risk factors<br>(host and<br>occupational)                                                                         | Predictors of WRS/rhinitis symptoms/<br>asthma symptoms/OA: OR (95% CI)<br>(unless otherwise stated)                                                                                                                                                                                                                                                                                                                       |
|-------------------------------------|-----------------|------------------------------------|---------------------------|--------------------------------------------------|----------------------|---------------------------------------------------|-------------------------------------------------|---------------------|--------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Olivieri, 2021,<br>Italy [22]       | Cross-sectional | 727                                | 92                        | 40.7 ± 11.6                                      | Traditional bakeries | Q                                                 | Q                                               | Q                   | WR rhinitis: gender,<br>atopy, job task WR<br>asthma: gender,<br>atopy, job years, job                             | WR nasal sx:<br>- males 2 (1.4–2.8)<br>- atopy 6.2 (4.1–9.3)<br>- task using wheat only 1.9 (1.2–3.1)<br>- using wheat and additives 2.6 (1.7–4.1)<br>- using wheat, additives and multigrain 2.7 (1.4–5)<br>WR asthma-like sx:<br>- gender 2.4 (1.4–4.2)<br>- atopy 4.5 (2.7–7.6)<br>- working ≥5yrs 1.9 (1.1–3.4)<br>- using wheat and additives 3.5 (1.7–7.3)<br>- using wheat, additives and multigrain 5.1 (2.1–12.1) |
| Olivieri, 2021,<br>Italy [23*]      | Cross-sectional | 174                                | 92                        | 40.2 ± 11.3                                      | Bakery               | Q                                                 | Q, BHR, SPT                                     | SPT                 | Sensitization to<br>occupational<br>allergens, WR nasal,<br>WR lower airway sx,<br>WR asthma                       | FeNO higher in sensitized vs nonsensitized –<br>22.8 vs 12.0 ppb<br>FeNO higher in WR nasal and sensitized vs<br>WR nasal and nonsensitized – 25.4 vs<br>13.4 ppb<br>FeNO higher in WR lower airway sx and<br>sensitized vs WRLA and nonsensitized –<br>31.2 vs 13.3 ppb                                                                                                                                                   |
| Mekonnen,<br>2021,<br>Ethiopia [26] | Cross-sectional | 560 (280 exp,<br>280 nonexp)       | 100                       | Exposed 28 (IQR<br>20) Nonexposed<br>31 (IQR 15) | Flour mill           | Q                                                 | Q                                               | ND                  | Flour mill workers: age,<br>educational status,<br>inadequate<br>ventilation, work<br>years, no safety<br>training | Flour mill workers:<br>- age >35yrs 2.0 (1.3 – 5.5)<br>- No education 1.5 (1.3 – 3.1)<br>- inadequate ventilation 2 (1.2–3.6)<br>- >5yrs work yrs 1.9 (1.2–4.7)<br>- no safety training 2.5 (1.5–4.8)                                                                                                                                                                                                                      |
| Kitenge, 2021,<br>DR Congo<br>[29]  | Cross-sectional | 389 (276<br>bakers, 113<br>nonexp) | Not stated                | 32 (17–59)                                       | Bakeries             | Q                                                 | Q, PEF                                          | Not stated          | ND                                                                                                                 | bakers vs controls: WR rhinitis –31% vs 2%,<br>WR asthma –5% vs 0%                                                                                                                                                                                                                                                                                                                                                         |
| Ade, 2020,<br>Benin [30]            | Cross-sectional | 210                                | 91                        | 25.5 (22–32)                                     | Bakeries             | Q                                                 | BHR                                             | Q                   | Rhino-conjunctivitis                                                                                               | Probable OA<br>- rhino-conjunctivitis ( $P < 0.05$ )                                                                                                                                                                                                                                                                                                                                                                       |
| Lagiso, 2020,<br>Ethiopia [27]      | Cross-sectional | 406 (196 mill,<br>260 nonexp)      | 97                        | NR                                               | Flour mill           | Not reported                                      | Q                                               | Not stated          | Mixing dept, work<br>years,<br>working >8hrs,                                                                      | Flour mill workers: with respiratory sx<br>- mixing dept 5.3 (1.7–16.6)<br>- work years 6–9 yrs 5.1 (2.1–12.5)<br>- work years ≥ 10 yrs 2.5 (1.0–6.1)<br>- working >8hrs 2.4 (1.2–5.1)                                                                                                                                                                                                                                     |

Table 3 (Continued)

| Author/<br>Country                   | Study design    | Subjects (n) | Participation<br>rate (%) | Age (yrs.)<br>mean (range) | Workplace   | Diagnostic<br>methods for defining<br>rhinitis | Diagnostic<br>methods for defining<br>asthma | Atopy<br>assessment | Risk factors<br>(host and<br>occupational)                                                                       | Predictors of WRS/rhinitis symptoms/<br>asthma symptoms/OA: OR (95% CI)<br>(unless otherwise stated)                                                                                                                                                  |
|--------------------------------------|-----------------|--------------|---------------------------|----------------------------|-------------|------------------------------------------------|----------------------------------------------|---------------------|------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Crivellaro,<br>2020, Italy<br>[25]   | Cross-sectional | 142          | Not stated                | 39.9 ± 11.3                | Bakeries    | Q                                              | Q                                            | SPT                 | Flour dust, duration of<br>employment;                                                                           | - FEV <sub>1</sub> /FVC declined with increasing dust<br>>2mg/m <sup>3</sup> (P < 0.017), duration of<br>exposure in yrs (P = 0.02)                                                                                                                   |
| Alemseged,<br>2019,<br>Ethiopia [28] | Cross-sectional | 424          | 97.8                      | 29.7 ± 8.5                 | Flour mills | Q                                              | Q                                            | Not stated          | Age group, monthly<br>income, work<br>experience, past<br>exposure use of<br>respiratory protective<br>equipment | Respiratory sx:<br>- age 24–45 yrs 1.9 (1.2–3.2)<br>- age >45 yrs 12.3 (4.4–36.6)<br>- monthly income 1.7 (1–2.8)<br>- work experience >10 yrs 2.6 (1–6.6)<br>- past exposure 1.9 (1.1–3.2)<br>- no respiratory protective equipment 2.3<br>(1.3–4.1) |

BHR, bronchial hyperresponsiveness; FeNO, fractional exhaled nitric oxide; HR, hazard ratio; IQR, interquartile range; ND, not done; NR, not reported; OA, occupational asthma; PEF, peak expiratory flow; Q, questionnaire; sIgE, serum-specific immunoglobulin E; SPT, skin prick tests; sx, symptoms; WR, work-related.

DON [41]. A study of swine production workers, also reported high levels (272 ng/g) of exposure to DON [45].

Exposure to bioaerosols in fish processing areas on board Norwegian fishing trawlers were reported to have high levels of proteins, trypsin, parvalbumin and endotoxin [46]. Exposures varied depending on the age and type of fish processed and high endotoxin levels were associated with high-pressure water cleaning of machines and floors. Sauvé *et al.* also reported higher endotoxin levels during bedding work, hog handling and working in barn/confinement buildings, grain bins and grain elevators among farmers in Iowa [47]. Increased exposures to 1,3-β-glucan were also observed for bedding work, cleaning and feed/grain storage work.

## DIAGNOSIS AND MANAGEMENT

The diagnostic approach for suspected occupational allergy in food handling workers is no different to other occupational exposure contexts [1<sup>¶</sup>]. Raulf reviewed allergen component analysis and concluded that despite various efforts to characterize occupationally relevant wheat allergens, no major allergen in wheat is identifiable [48]. A whole-wheat extract remains the best option to determine IgE sensitization due to its higher diagnostic sensitivity for baker's asthma. However, single wheat allergens may assist in differentiating between different classes of food allergy viz. wheat-induced food allergy (class 1), grass pollen allergy (class 2) and baker's asthma (class 3).

Taghiakbari *et al.* using clinical scores developed a model to predict OA due to HMW agents (53% exposed to flour and associated agents). Significant variables included those ≤40 years of age, rhino-conjunctivitis, inhaled corticosteroid use, agent type, nonspecific BHR and occupational-specific sensitization. This is a useful approach for clinics without access to specific inhalation challenge tests [49].

A systematic review of 26 nonrandomized controlled studies of workplace interventions for the management of OA by Henneberger *et al.* concluded that both removal and reduction of exposure had better clinical outcomes than continued exposure [50]. However, only removal from exposure was associated with improved lung function. The potential benefits of this approach need to be considered within the context of potential job loss.

## PREVENTION

Various strategies are aimed at either reducing exposures, the risk of sensitization or the development of OR and OA to food agents.

**Table 4.** Summary of recent epidemiological studies of work-related symptoms, rhinitis and asthma in animal food handling workplaces

| Author/<br>Country                    | Study design              | Subjects (n)                                             | Participation<br>rate (%) | Age (yrs.)<br>mean (range)                                     | Workplace                     | Diagnostic<br>methods for<br>defining rhinitis | Diagnostic<br>methods for<br>defining asthma | Atopy<br>assessment | Risk factors<br>(host and<br>occupational)                            | Predictors of<br>WRS/rhinitis symptoms/<br>asthma symptoms/<br>OA: OR (95% CI) (unless otherwise stated)                                                                                                                                             |
|---------------------------------------|---------------------------|----------------------------------------------------------|---------------------------|----------------------------------------------------------------|-------------------------------|------------------------------------------------|----------------------------------------------|---------------------|-----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Thomassen 2021,<br>Norway [31]        | Cross-sectional           | 184                                                      | Not stated                | 37.25<br>(35.6–38.9)                                           | Crab workers                  | Q                                              | Q                                            | Phadiatop           | Atopy, self-reported allergy                                          | Positive SPT to crab<br>- atopy ( $P=0.001$ )<br>IgE to crab<br>- atopy ( $P<0.001$ )<br>Respiratory sx<br>- atopy ( $P<0.001$ )<br>- self-reported allergy ( $P<0.001$ )                                                                            |
| Dahlman-Högland,<br>2020, Sweden [32] | Cross-sectional<br>survey | 4717 (1836 fishers,<br>916 processors,<br>1965 controls) | ~51                       | Fishermen/Filleling/<br>Processing 46<br>± 11 Controls 45 ± 13 | Fishermen,<br>fish processing | Q                                              | Q                                            | Q                   | Duration in filleting work,<br>atopy, female gender                   | Adult-onset asthma during work in fishing industry<br>- filleting work HR: 3.6 (1.6–8.1)<br>- atopy 3.4 (1.8–6.7)<br>- female 2.6 (1.2–5.6)                                                                                                          |
| Ngijilo, 2018,<br>South Africa [35]   | Cross-sectional           | 230                                                      | 78                        | 37 ± 9                                                         | Poultry farm                  | Q                                              | Q, BHR, sIgE                                 | Phadiatop           | Atopy, casual work, department,<br>exposure to high<br>gas/dust/fumes | Sensitisation to poultry allergens:<br>- atopy 20.9 (4.7–93.2)<br>- casual worker 6.0 (1.1–35.9)<br>WR chest sx:<br>- rearing department 3.2 (1.2–8.4)<br>- exposure to high gas/dust/fumes 4.8 (2.4–9.5)<br>BHR:<br>- casual worker 10.9 (2.0–60.3) |

BHR, bronchial hyperresponsiveness; FeNO, fractional exhaled nitric oxide; HR, hazard ratio; IQR, interquartile range; ND, not done; NR, not reported; OA, occupational asthma; PEF, peak expiratory flow; Q, questionnaire; sIgE, serum-specific Immunoglobulin E; SPT, skin prick tests; sx, symptoms; WR, work-related.

## Policy, regulatory frameworks and exposure standards

There are a few occupational exposure limits for food allergens, and these vary between countries as is evident for flour dust with the 8-h-TWA varying between 0.5 and 10 mg/m<sup>3</sup> [1\*,38\*]. Other food agents with exposure standards include grain dust, tea dust, poultry dust, *Penicillium* and proteolytic enzymes. Evidence-based exposure benchmarks to prevent allergic respiratory disease have been used to revise the Dutch exposure standards for flour dust (0.2 mg/m<sup>3</sup>) and fungal  $\alpha$ -amylase (0.9 ng/m<sup>3</sup>) in workers irrespective of atopic status. This represents a major advance for prevention in food handling occupations [51].

## Workplace control measures to reduce exposures

Strategies for reducing exposure are generally specific to the occupation in the food industry and may include modification of food processing, mechanization or automation, use of modified materials, better organization of work, improvement of workplace conditions, improving ventilation and use of respiratory protective devices [52].

In this review period, three studies reported on the effectiveness of control measures to reduce flour dust exposures in bakeries. Martinelli *et al.* evaluated control measures viz. installation of a sleeve to the end of a pipeline, lid on a mixer tub and local exhaust ventilation system, resulting in 16–70% lower dust levels [53\*]. Karjalainen *et al.* focused on changing the working methods used in Finnish bakeries. This included lowering the height when adding ingredients to mixers; careful handling of empty bags to avoid dustiness; emptying bags near the bottom of the mixer; and sprinkling flour from as low a height as possible onto the baking table. Using these methods, mean reductions between 39 and 45% were demonstrated within one year [54].

The effectiveness of a multifaceted intervention (dough mixer lid, training) in South African super-market bakeries in reducing the incidence of allergic sensitization, OR and OA was also reported given the 50% or more reduction in dust and allergen levels previously reported [55,56]. A greater decline in the incidence of wheat sensitization (21% vs 6%) and mean FeNO (16.9 ppb vs 7.7 ppb) among bakers with baseline FeNO  $\geq 25$  ppb was observed in the intervention group, one year after the intervention. The intervention group also showed a decline ( $\geq 10\%$ ) in FeNO at follow-up, particularly in bakers with work-related ocular-nasal symptoms at baseline (OR = 3.73, CI: 1.22–11.42).

Finally, an educational intervention designed to improve the knowledge of preventive measures for allergy and asthma was evaluated in Bavarian farm apprentices [57]. The effect of a short educational video was evaluated 6 months later and reported to improve the knowledge about preventive measures in 20% of apprentices.

## Immunotherapy

In certain settings, workers with OA may choose to continue working in jobs with reduced allergen exposures where it cannot be totally eliminated. A review that included three studies involving foods (all used wheat flour) concluded that there was increasing but modest evidence of beneficial short- and long-term effects of immunotherapy and safety in worker populations [58]. Dubini *et al.* also reported on the success of sublingual specific immunotherapy (SLIT) for baker's asthma and rhinitis [59]. Despite baker's asthma being a common entity, the use of immunotherapy has been limited due to the lack of identifiable major allergenic wheat flour proteins. Given these findings further confirmation is required in larger randomised controlled trials.

## CONCLUSION

In conclusion, this review has highlighted that occupational inhalant allergy in food handling occupations is a common and recognisable clinical entity (class 3 food allergy) in high-risk food occupations such as bakeries and seafood processing. This risk may be enhanced across the food value chain as a result of food being subjected to various food processing techniques. Increasing advances in food technology have also resulted in the introduction of new and unusual allergens as food additives in the food matrix. Future studies need to focus on exposure-response studies to establish improved exposure limits especially for flour dust, the relevance of cooked vs raw food in influencing risk, identifying and characterising major food allergens and evaluating the effectiveness of interventions including immunotherapy for common high-risk food sensitizers causing OR and OA.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES AND RECOMMENDED READING

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

- of special interest
- of outstanding interest

1. Jeebhay MF, Moscato G, Bang BE, *et al.* Food processing and occupational ■ respiratory allergy – a EAACI Position Paper. *Allergy* 2019; 74: 1852–1871.
- This overview is a comprehensive expose of the topic and for the first time provides a classification of inhalant food allergy and a detailed list of causative agents.
2. Fukutomi Y. Occupational food allergy. *Curr Opin Allergy Clin Immunol* 2019; 19:243–248.
3. Tagiyeva N, Teo E, Fielding S, *et al.* Occupational exposure to asthmagens and adult onset wheeze and lung function in people who did not have childhood wheeze: a 50-year cohort study. *Environ Int* 2016; 94:60–68.
4. Sánchez-Guerrero IM, Nieto A, Meseguer J, *et al.* Occupational rhinoconjunctivitis induced by unusual allergens of carrot. *J Investig Allergol Clin Immunol* 2020; 30:204–206.
5. Victorio-Puche L, Somoza ML, Martín-Pedraza L, *et al.* Prunus persica 9, a new occupational allergen from peach tree pollen involved in rhinitis and asthma. *Occup Environ Med* 2021; 78:142–144.
6. Guarneri G, Bonadonna P, Olivieri E, Schiappoli M. Occupational asthma induced by exposure to Quinoa. *J Investig Allergol Clin Immunol* 2019; 29:451–452.
7. Jungewelter S, Airaksinen L, Pesonen M. Occupational buckwheat allergy as a cause of allergic rhinitis, asthma, contact urticaria and anaphylaxis – an emerging problem in food-handling occupations? *Am J Ind Med* 2020; 63:1047–1053.
8. Carneiro-Leão L, Carolino F, Pineda F, *et al.* A possible new mushroom allergen in a case of occupational asthma. *J Investig Allergol Clin Immunol* 2019; 29:243–244.
9. Jungewelter S, Airaksinen L, Pesonen M. Occupational rhinitis, asthma, and contact urticaria from IgE-mediated allergy to pork. *Am J Ind Med* 2019; 62:80–84.
10. Sogo A, Cruz MJ, Amengual MJ, Muñoz X. Identification of Pen m 4 as a potential cause of occupational asthma to Gammarus shrimp. *Clin Transl Allergy* 2018; 8:46.
11. Larco-Rojas X, González-Gutiérrez ML, Vázquez-Cortés S, *et al.* Occupational asthma and urticaria in a fishmonger due to creatine kinase, a cross-reactive fish allergen. *Investig Allergol Clin Immunol* 2017; 27:386–388.
12. Giorgis V, Rolla G, Raie A, *et al.* A case of work-related donkey milk allergy. *Investig Allergol Clin Immunol* 2018; 28:197–199.
13. Torrijos EG, Rodríguez CG, Pérez BV, *et al.* Occupational allergic respiratory disease (rhinoconjunctivitis and asthma) in a cheese factory worker. *J Allergy and Clin Immunol Pract* 2018; 6:1416–1417.
14. Sander I, Keller C, Czibor C, *et al.* Unusual allergen in a butcher with respiratory symptoms. *Allergologie select* 2020; 4:105–109.
15. Romita P, Bufano T, Antelmi A, *et al.* Occupational allergic rhinitis and contact urticaria caused by Gum Arabic in a candy factory worker. *Contact Dermatitis* 2018; 78:427–428.
16. Hawley B, Cummings KJ, Mohammed M, *et al.* Allergic sinusitis and severe asthma caused by occupational exposure to locust bean gum: Case report. *Am J Ind Med* 2017; 60:658–663.
17. Jungewelter S, Suomela S, Airaksinen L. Occupational IgE-mediated psyllium allergy in contemporary gluten-free and vegan baking: a case of allergic rhinitis. *Am J Ind Med* 2021; 64:431–434.
18. Merget R, Raulf M, Sander I. Occupational immediate type allergy to soapnut and quillaja bark. *Allergol Select* 2021; 5:77–81.
19. Touati N, Chiriac AM, Bourrain JL, Demoly P. An unusual case of occupational rhinitis. *J Investig Allergol Clin Immunol* 2020; 30:207–208.
20. Cullinan P, Sigsgaard T, Jeebhay MF, *et al.* Occupational asthma in the baking industry. In: Tarlo, Vandenplas, Bernstein, Malo (eds). *Asthma in the Workplace*, 5th edition. CRC Press, Florida, 2021, 12:153–163. ISBN 9780367430092 (hardback), ISBN 9781032043425 (paperback), ISBN 9781003000624 (ebook).
21. Jeebhay MF, Pacheco KA, Lopata AL, Malo JL. Asthma and allergy to animals, fish and shellfish. In: Tarlo, Vandenplas, Bernstein, Malo (eds). *Asthma in the Workplace*, 5th edition. CRC Press, Florida, 2021, 13:165–178. ISBN 9780367430092 (hardback), ISBN 9781032043425 (paperback), ISBN 9781003000624 (ebook).
22. Olivieri M, Murgia N, Spiteri G, *et al.* Exposure to additives or multigrain flour is associated with high risk of work-related allergic symptoms among bakers. *Occup Environ Med* 2021; 78:112–116.

23. Olivieri M, Malerba M, Spiteri G, *et al.* Fractional exhaled nitric oxide levels in relation to work related respiratory burden and sensitization to wheat flour and multigrain in bakers. *Clin Transl Allergy* 2021; 11:e12018.  
 This is an extensive study of bakers in traditional bakeries demonstrating the effect of concomitant exposure to enzyme additives and/or multigrain flour among bakers in causing work-related rhinitis and asthma.
24. Baatjies R, Jeebhay MF. Sensitisation to cereal flour allergens is a major determinant of elevated exhaled nitric oxide in bakers. *Occup Environ Med* 2013; 70:310–316.
25. Crivellaro MA, Ottaviano G, Maculan P, Pendolino AL. Upper and lower respiratory signs and symptoms in workers occupationally exposed to flour dust. *Int J Environ Res Public Health* 2020; 17:7075.
26. Mekonnen TH, Dessie A, Tesfaye AH. Respiratory symptoms related to flour dust exposure are significantly high among small and medium scale flour mill workers in Ethiopia: a comparative cross-sectional survey. *Environ Health Prev Med* 2021; 26:96.
27. Lagiso ZA, Mekonnen WT, Abaya SW, *et al.* Chronic respiratory symptoms, lung function and associated factors among flour mill factory workers in Hawassa city, southern Ethiopia: 'comparative cross-sectional study'. *BMC Public Health* 2020; 20:909.
28. Alemseged EA, Takele AK, Zele Y, *et al.* Assessment of chronic respiratory health symptoms and associated factors among flour mill factory workers in Addis Ababa, Ethiopia, 2019: a cross-sectional study. *J Asthma Allergy* 2020; 13:483–492.
29. Kitege JP, Obadia PM, Kuhangana TC, *et al.* Occupational rhinitis and asthma in bakers: a cross-sectional study in the former Katanga province of DR Congo. *Int Arch Occup Environ Health* 2021. doi: 10.1007/s00420-021-01698-8. [Online ahead of print]
30. Ade S, Adjobimey M, Agodokpessi G, *et al.* Asthma Symptoms in Bakeries at Parakou, Benin. *Pulm Med* 2020; 2020:3767382.
31. Thomassen MR, Kamath SD, Bang BE *et al.* Occupational Allergic Sensitization Among Workers Processing King Crab (*Paralithodes camtschaticus*) and Edible Crab (*Cancer pagurus*) in Norway and Identification of Novel Putative Allergenic Proteins. *Front Allergy* 2:718824. doi: 10.3389/falgy.2021.718824.  
 This study has identified two novel proteins, hemocyanin and enolase implicated in occupational allergy associated with crab processing. Future studies need to evaluate the clinical significance using component resolved diagnostic techniques.
32. Dahlman-Högglund A, Andersson E. Work-related symptoms and asthma among fish processing workers. *J Agromed* 2020; 222:1–8.
33. Mason HJ, Carder M, Money A, *et al.* Occupational asthma and its causation in the UK Seafood Processing Industry. *Ann Work Expo Health* 2020; 64:817–825.
34. Bønløkke J, Bang B, Aasmoe L, *et al.* Exposures and health effects of bioaerosols in seafood processing workers - a position statement. *J Agromed* 2019; 24:441–448.
35. Ngajilo D, Singh T, Ratshikhopha E, *et al.* Risk factors associated with allergic sensitization and asthma phenotypes among poultry farm workers. *Am J Ind Med* 2018; 61:515–523.
36. El-Zaemey S, Carey RN, Darcey E, *et al.* Prevalence of occupational exposure to asthmagens derived from animals, fish and/or shellfish among Australian workers. *Occup Environ Med* 2018; 75:310–316.
37. El-Zaemey S, Carey RN, Darcey E, *et al.* The prevalence of exposure to high molecular weight asthmagens derived from plants among workers in Australia. *Am J Ind Med* 2018; 61:824–830.
38. Jeebhay MF, Baatjies R. Prevention of baker's asthma. *Curr Opin Allergy Clin Immunol* 2020; 20:96–102.  
 This overview outlines comprehensive approaches to prevent baker's allergy and asthma in various settings
39. Aidoo H, Beach J, Elbourne R, *et al.* Estimation and validation of flour exposure in bakeries in Alberta, Canada. *Ann Work Expo Health* 2018; 62:1096–1108.
40. Zamani A, Khanjani N, Bagheri Hosseinabadi M, *et al.* The effect of chronic exposure to flour dust on pulmonary functions. *Int J Occup Saf Ergon* 2019; 14:1–7.
41. Viegas C, Fleming GTA, Kadir A, *et al.* Occupational exposures to organic dust in Irish Bakeries and a Pizzeria Restaurant. *Microorganisms* 2020; 8:118.
42. Kirkeleit J, Hollund BE, Riise T, *et al.* Bakers' exposure to flour dust. *J Occup Environ Hyg* 2017; 14:81–91.
43. Viegas S, Assunção R, Nunes C. Exposure assessment to mycotoxins in a Portuguese fresh bread dough company by using a multi-biomarker approach. *Toxins* 2018; 10:342.
44. Straumfors A, Mundra S, Foss OAH. The airborne mycobiome and associations with mycotoxins and inflammatory markers in the Norwegian grain industry. *Sci Rep* 2021; 11:9357.
45. Viegas S, Assunção R, Martins C, *et al.* Occupational exposure to mycotoxins in swine production: environmental and biological monitoring approaches. *Toxins* 2019; 11:78.
46. Heidelberg CT, Bang B, Thomassen MR, *et al.* Exposure to bioaerosols during fish processing on Board Norwegian Fishing Trawlers. *Ann Work Expo Health* 2021; 65:694–702.
47. Sauvé JF, Locke SJ, Josse PR. Characterization of inhalable endotoxin, glucan, and dust exposures in Iowa farmers. *Int J Hyg Environ Health* 2020; 228:113525.
48. Raulf M. Allergen component analysis as a tool in the diagnosis and management of occupational allergy. *Mol Immunol* 2018; 100:21–27.
49. Taghiakbari M, Pralong JA, Lemiere C, *et al.* Novel clinical scores for occupational asthma due to exposure to high-molecular-weight agents. *Occup Environ Med* 2019; 76:1–7.
50. Henneberger PK, Patel JR, de Groene GJ, *et al.* Workplace interventions for treatment of occupational asthma. *Cochrane Database Syst Rev* 2019; 2019:CD006308.
51. Heederik DJJ. Towards evidence-informed occupational exposure limits for enzymes. *Ann Work Expo Health* 2019; 63:371–374.
52. Moscato G, Pala G. Occupational allergy to food-derived allergens. *AIMS Allergy Immunol* 2017; 1:21–30.
53. Martinelli A, Salamon F, Scapellato ML. Occupational exposure to flour dust. ■ Exposure assessment and effectiveness of control measures. *Int J Environ Res Public Health* 2020; 17:5182.  
 This is an important intervention study evaluating simple adjustments in bakeries to substantially reduce flour dust exposure levels
54. Karjalainen A, Leppänen M, Ruokolainen J, *et al.* Controlling flour dust exposure by an intervention focused on working methods in Finnish bakeries: a case study in two bakeries. *Int J Occup Saf Ergon* 2021; 30:1–10.
55. Baatjies R, Meijster T, Heederik D, *et al.* Effectiveness of interventions to reduce flour dust exposures in supermarket bakeries in South Africa. *Occup Env Med* 2014; 71:811–818.
56. Al Badri F, Baatjies R, Jeebhay MF. Assessing the health impact of interventions for baker's allergy and asthma in supermarket bakeries: a group randomised trial. *Int Arch Occup Environ Health* 2020; 93:589–599.
57. Rodríguez-Molina D, Barth S, Herrera, *et al.* An educational intervention to improve knowledge about prevention against occupational asthma and allergies using targeted maximum likelihood estimation. *Int Arch Occup Environ Health* 2019; 92:629–638.
58. Smith AM, Sastre J. The role of immunotherapy and biologic treatments in occupational allergic disease. *J Allergy Clin Immunol Pract* 2020; 8:3322–3330.
59. Dubini M, Marraccini P, Brass DM, *et al.* Occupational asthma and rhinitis due to wheat flour: sublingual specific immunotherapy treatment. *Med Lav* 2020; 111:203–209.