Current Allergy and Asthma Reports (2025) 25:22
https://doi.org/10.1007/s11882-025-01204-x

REVIEW

Occupational Respiratory Allergy to Flour in the Modern Era

Olivier Vandenplas[1] · **Virginie Doyen**[1] · **Monika Raulf**[2]

Accepted: 22 April 2025

Abstract

Purpose of the Review A comprehensive literature review was conducted in order to identify and summarize recent research on IgE-mediated occupational respiratory allergy to flour, focusing on the impact of modern developments in the baking industry characterized by industrialization of production processes and a growing use of baking "improvers".

Recent Findings Although respiratory allergy to flour is a potentially preventable condition through effective workplace control measures, available data indicate that exposure to flour dust has not decreased in the last decade and flour remains the most prevalent cause of occupational respiratory allergy. The development of the baking industry has led to the introduction of new allergen sources, although their contribution to the development of clinical respiratory allergy remains largely uncertain. In recent years, the diagnostic performance of serum-specific IgE antibody determination against wheat/rye flour and α-amylase compared with specific inhalation challenge with flour as the reference standard has been clarified, making these tests a first-line component of diagnostic algorithms.

Summary Available information on the prevalence and incidence of respiratory allergy to flour in recent decades indicates that this condition still imposes a substantial health and socioeconomic burden worldwide. Available data highlight the need to reinforce workplace health-related policies and regulations.

Keywords Flour allergy · Occupational asthma · Occupational rhinitis · Rye flour · Specific IgE antibodies · Wheat flour

Introduction

The allergic nature of occupational asthma (OA) — often referred to as baker's asthma — and rhinitis (OR) caused by cereal flour was recognized almost a century ago [1]. Since then, a considerable amount of research has been conducted and progress has been made in identifying the causal allergens, the determinants of the disease, and the development of preventive strategies [2–5].

Nevertheless, the baking industry has experienced important developments during recent decades due to the industrialization of production processes, technological innovations, and changing nutritional habits of consumers. As a result of the modern developments in the bakery industry, flour may now contain a wide variety of potential allergens, which include not only wheat and rye flour, but also flour derived from other cereals (e.g., barley, oats rice, corn, einkorn), non-cereal flours (buckwheat, soybean, lupine), "improvers" (mainly enzymes), seeds (e.g., sesame, sunflower), and various other ingredients (e.g., gluten, malt flour, egg powder, whey protein powder, emulsifiers).

This document aims to critically analyze and synthesize the available literature on occupational respiratory allergy to flour (ORAF) with a special focus on studies published during the last five years. We conducted a scoping review of the evidence pertaining to the impact of recent developments in baking processes on causal allergens, epidemiology, and diagnostic approaches to flour-induced OA and OR.

Methods

A PubMed search was performed using the keywords ("Flour"[Mesh] OR "Baker") AND ["Asthma, Occupational"[Mesh] OR"Rhinitis, Allergic"[Mesh])"]. This

✉ Olivier Vandenplas
olivier.vandenplas@chuuclnamur.uclouvain.be

[1] Centre Hospitalier Universitaire UCL Namur, Department of Chest Medicine, Université Catholique de Louvain, Yvoir, Namur, Belgium

[2] Institute of Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr-University Bochum (IPA), Bochum, Germany

Published online: 28 April 2025

literature search identified 16 potentially relevant original studies and case series published between January 2020 and December 2024. The bibliographic search was extended to the period 2000–2024 to identify cross-sectional studies assessing the prevalence of work-related asthma (WRA) and rhinitis (WRR) symptoms and/or IgE-mediated sensitization to bakery allergens in exposed workforces. The publications cited in the reference lists of the retrieved studies and review articles were scrutinized in order to identify other potentially relevant reports to contextualize recent data.

The Modern Bakery Environment

Since the seventies, technical innovations in bakery processes have introduced a variety of additives. These "improver" additives include mainly enzymes (i.e., α-amylase, glucoamylase, cellulase, xylanase, β-xylosidase, and proteases) that are potential allergen sources, the best known of which is fungal α-amylase. These enzymes are incorporated into flour to improve the processability of dough and enhance the softness and shelf life of end products [6, 7]. Currently, flour is usually delivered to bakeries as premixed, ready-to-use flour products whose composition has been developed to obtain specific characteristics of the final product.

On the other hand, increasing awareness of the impact of food on health in affluent countries has led to changes in nutrition habits and a demand for a greater variety of breads, especially gluten-free alternatives (e.g., made from buckwheat, soybean, and lupine flours).

Industrialization and urbanization have led to a shift from traditional small-sized "craft" bakeries to highly mechanized and almost fully automated "industrial" bakeries. In some countries, the production of bread products has been relocated from large-scale industrial to small-scale "in-store" supermarket bakeries. The impact of these changes in production sites on workplace exposure to flour dust remains largely unknown. A meta-analysis of 21 studies evaluating flour dust exposure published up to 2017 confirmed that weighing/mixing and dough forming produced the highest inhalable dust (3.1–4.9 mg/m^3) and wheat allergen levels (37–40 µg/m^3) [8]. Multivariate models identified these specific tasks and small bakery size as predictors of higher inhalable dust and wheat allergen concentrations. Overall, the models showed a slight decline in inhalable flour dust levels over the years since 1990, while both wheat allergen and α-amylase increased from 1990 to 1996, then decreased.

Flour Allergens

Cereal Flour Allergens

Wheat flour is composed of starch (about 70–75%) and proteins classified into three fractions according to their solubility: 1) the water/salt-soluble fraction, which includes albumins and globulins; 2) the water/ethanol soluble gliadins; and 3) the glutenins which are extractable in dilute acetic acid [9, 10]. Wheat is a complex allergenic mixture containing more than 100 different IgE-binding protein spots [9, 10]. To date, 28 wheat allergens have been characterized and listed in the World Health Organization/International Union of Immunological Societies allergen nomenclature database (www.allergen.org, last accessed March 23, 2025). Wheat allergens involved in ORAF are described in Table 1 [11].

Sander and coworkers [11] found a great inter-individual variability in the pattern of sIgE reactivity to 19 recombinant wheat flour proteins. The highest rates of sIgE reactivity were found for dimeric α-amylase inhibitors 0.19 (Tri a 28) and Tri a 29.01 and a thiol reductase homologue (Tri a 27), but none of the single wheat allergens tested so far have fulfilled the criteria for being a major allergen involved in ORAF. Receiver operating characteristics analysis revealed that a combination of sIgE against five components (Tri a 27, Tri a 28, Tri a 29.02, Tri a 39, and Tri a 32) produced the highest area under the curve (0.84) for identifying ORAF, but this was still lower than the values (0.89 and 0.88) provided by the determination of sIgE against whole wheat (ImmunoCAP f4) and rye (ImmunoCAP f5) flour extracts, respectively.

The vast majority of subjects with ORAF show sIgE against both wheat and rye flours [12]. Several allergens of cereals other than wheat and rye (barley, oat, and maize) have been identified using sera from subjects with ORAF (Table 1). However, their role in the development of ORAF remains uncertain because most subjects (89%) with a positive specific inhalation challenge (SIC) with flour and positive sIgE against wheat and/or rye flour also show sIgE reactivity to at least one of the other cereals [12].

Non-Cereal Flours

A recent case series further highlighted the potential respiratory sensitizing potential of buckwheat (*Fagopyrum esculentum*), an herbaceous plant of the *Polygonaceae* family [13]. Occupational exposure to buckwheat flour is likely to increase since this seed has a high protein content and is used to produce gluten-free bread and cookies, and traditional "ethnic" foods such as noodles, blinis, and crepes.

Soybean (*Glycine max*) and lupine (*Lupinus angustifolius/albus*) flours, both legumes of the *Fabaceae* family, are also increasingly used because of their high protein content and absence of gluten. The soybean allergens involved in flour-induced OA are predominantly

Table 1 Cereal flour allergens

Allergen[a]	Biochemical name	Clinical relevance
Wheat (*Triticum aestivum*)		
Tri a 15	Wheat monomeric α-amylase inhibitor 0.28 (WMA-1–0.28)	sIgE-reactivity in 9% of ORAF, but not in controls[b]
Tri a 25	Thioredoxin	sIgE-reactivity in 18% of ORAF and 17% of controls[b] [11]
Tri a 27	Thiol reductase homologue	sIgE-reactivity in 27% of ORAF, but not in controls[b] [11]
Tri a 28	Dimeric α-amylase inhibitor 0.19	sIgE-reactivity in 24% of ORAF, but not in controls[b] [11]
Tri a 29	Tetrameric α-amylase inhibitor	
- Tri a 29.0201	CM2	sIgE-reactivity to Tri a 29.0201 in 14% of ORAF, but not in controls[b] [11]
- Tri a 29.0101	CM1	sIgE reactivity to Tri a 29.0101 in 21% of ORAF and 7% of controls[b] [11]
Tri a 30	Tetrameric α-amylase inhibitor CM3	sIgE-reactivity in 10% of ORAF, but not in controls[b] [11]
Tri a 31	Triosephosphate-isomerase (TPIS)	Not exclusively recognized by specific IgE from bakers [11]
Tri a 32	1-cys-peroxiredoxin	sIgE-reactivity in 14% of ORAF, but not in controls[b] [11]
Tri a 33	Serpin	sIgE-reactivity in 8% of ORAF, but not in controls[b] [11]
Tri a 34	Glyceraldehyde- 3-phosphate-dehydrogenase (GAPDH)	sIgE-reactivity in 5% of ORAF, but not in controls[b] [11]
Tri a 35	Dehydrin	sIgE-reactivity in 2% of ORAF, but not in controls[b] [11]
Tri a 39	Serine protease inhibitor-like protein (SPILA)	sIgE-reactivity in 18% of ORAF, but not in controls[b] [11]
Tri a 40	Wheat tetrameric α-amylase inhibitor-CM17 protein	sIgE-reactivity in 8% of ORAF and 15% of controls[b]; Tri a 40.0101 has minimal effect on sensitivity and specificity [11]
Na	Glucose/ribitol dehydrogenase as novel wheat allergens in	Identified in pooled sera from Italian bakers [75], but not assessed in individual sera
Na	Class I heat shock protein 1	
Rye (*Secale cereale*)		
Sec c 38	Dimeric α-amylase/trypsin inhibitor (formerly designated as Sec c 1)	sIgE reactivity in 15 of 21 subjects with ORAF patients [76]
Barley (*Hordeum vulgare*)		
Hor v 15	Salt-soluble α-amylase inhibitor BMAI- 1 precursor	Major IgE-binding component in sera from subjects with ORAF [77]
Maize (*Zea mays*)		
Zea m 25	Thioredoxin-*h*1	Shares 74% identity with Tri a 25 [78]

CM Chloroform/methanol-soluble, *ORAF* occupational respiratory allergy to flour, *sIgE* specific IgE antibody

[a]World Health Organization/International Union of Immunological Societies allergen nomenclature (http://www.allergen.org)

[b]Control subjects in reference [11] include individuals with pollen allergy and wheat sIgE

high-molecular-weight proteins present in both soybean hulls and flour Interestingly, whereas allergens involved in asthma outbreaks during soybean unloading, are mainly low-molecular-weight proteins (Gly m 1 and Gly m 2) concentrated in the hull [14]. Gly m 4, 5, and 6 are available as recombinant soy allergens, but further validation is needed to determine if these allergens are relevant in ORAF and whether they should be implemented in the diagnosis evaluation of this condition.

Up to now, lupine flour has been documented as inducing OA and OR in food processing workers, but not in bakers [15]. Among 116 bakers without known food allergy who were evaluated for WRA and/or WRR symptoms, 33% exhibited sIgE to lupine and 23% to soybean [16]. Among the lupine-sensitized subjects, sIgE to peanut was detected in 92% and to soy in 61%. Only three out of the 38 subjects with lupine sIgE failed to show sensitization to wheat or rye, but the clinical relevance of lupine sensitization was not substantiated through SICs in these subjects. In addition, inhibition experiments suggested IgE cross-reactivity between wheat flour and lupine.

Enzymes

The role of "improver" enzymes in the development of flour-induced OA and OR is still uncertain. The most frequently used enzyme is fungal α-amylase derived from *Aspergillus oryzae*, which is listed as Asp o 21 and available for sIgE assay (ImmunoCAP k87, Thermo Fisher Scientific, Uppsala, Sweden). Analysis of the E-PHOCAS cohort showed that 15% of 179 subjects with a positive flour SIC showed sIgE against α-amylase, but only one of these subjects was not sensitized to wheat or rye [12]. These data suggest a minor direct role of sensitization to α-amylase in the development of clinical ORAF.

Substantial rates (6%–13%) of sensitization to enzymes other than α-amylase, including glucoamylase, cellulase, and xylanase have been reported among bakers [17–19]. Simonis et al. [19] compared the sensitization profiles of bakers evaluated for ORAF during the periods 1999–2001 and 2009–2011 together with their personal exposure to inhalable dust. They found a decline in the rate of sensitization to fungal α-amylase from 26 to 13% and a decrease in α-amylase exposure while overall dust exposure remained unchanged. During the period 2009–2011, the rate of sensitization to glucoamylase derived from *Aspergillus niger* (38%) was higher than those observed for cellulase (16%) and α-amylase (13%). Overall, 30% of bakers were sensitized to at least one of these three baking enzymes. Nevertheless, the clinical relevance and the contributions of baking enzymes separate from those of flour and α-amylase have been documented only in occasional case reports. In addition, a study of UK supermarket bakers experiencing work-related respiratory symptoms provided evidence that only a small proportion of bakers (5%) is sensitized to "improver" enzymes without co-sensitization to either flour or α-amylase [20].

Burden of the Disease

Prevalence and Incidence among Exposed Workforces

Cross-sectional studies conducted among workers exposed to flour before 1998 provided prevalence estimates of 5%–28% for sensitization to wheat and 2%–16% for sensitization to α-amylase either by skin-prick tests (SPT) or sIgE tests [2]. The rate of work-related asthma (WRA) and work-related rhinitis (WRR) symptoms ranged from 3 to 21% and from 7 to 30%, respectively [2]. Of note, WRR symptoms were 1.3 to 10 times more frequent than WRA symptoms.

Pooled estimates of the prevalence of WRR, WRA, and positive SPT and sIgE against wheat and α-amylase derived from 14 cross-sectional studies of bakery workers published between 2000 and 2024 are summarized in Table 2 [21–34]. These data further demonstrate that substantial proportions of reported WRR and WRA symptoms are not mediated by IgE-sensitization to flour allergens. On the other hand, IgE-mediated sensitization to wheat may not be associated with respiratory symptoms in approximately 60% of bakery workers [23, 25, 28, 32]. In addition, SPT to flour may be positive in 1.5% to 5% of subjects nonoccupationally exposed to flour, probably resulting from cross-reactivity with grass pollen allergens [35, 36]. The association of WRR/WRA symptoms with IgE-mediated sensitization to wheat, considered as a proxy for probable OR and OA, was available in only four studies [23, 25, 28, 32] (Table 2). These studies provided pooled estimates of 12% (95% confidence interval [CI], 4–19%) for probable OR and 6% (95% CI, 2–11%) for probable OA.

Table 2 Pooled prevalence estimates of work-related respiratory symptoms and IgE-mediated sensitization to flour allergens reported by cross-sectional studies of exposed workers (2000–2024)

Outcome	Pooled prevalence estimate % (95% CI)	No. of studies (no. of subjects)	References
Work-related rhinitis symptoms	28 (21–35)	11 (3,857)	[23–30, 32–34]
Work-related asthma symptoms	11 (8–15)	11 (3,798)	[23–28, 30–34]
Positive SPT to wheat	13 (9–16)	6 (1,468)	[21, 22, 26, 29, 30, 32]
Positive SPT to α-amylase	5 (0–10)	3 (867)	[22, 26, 29]
Positive sIgE to wheat	12 (6–18)	7 (2,463)	[23–28, 32]
Positive sIgE to α-amylase	3 (1–4)	6 (1,623)	[23, 24, 26–28, 32]
Probable occupational rhinitis[a]	12 (4–19)	4 (1,685)	[23, 25, 28, 32]
Probable occupational asthma[b]	6 (2–11)	4 (1,685)	[23, 25, 28, 32]

95% *CI* 95% confidence interval, *sIgE* specific IgE antibodies, *SPT* skin-prick test. Pooled estimates were obtained using the restricted maximum likelihood estimator method.

[a]Probable occupational rhinitis defined by work-related rhinitis symptoms associated with sIgE against wheat.

[b]Probable occupational asthma defined by work-related asthma symptoms associated with sIgE against wheat.

The few studies that relied on measurement of nonspecific bronchial hyperresponsiveness (NSBH) to methacholine or histamine or reversible airflow obstruction [28, 31, 32] and/or monitoring of peak expiratory flow rates at work and away from work [33], and/or SIC [21] provided prevalence estimates of OA ranging from 2.0% to 6.4%.

Epidemiological studies investigating the incidence of ORAF among exposed workers are far less common than studies assessing its prevalence. Only two prospective studies of newly exposed bakery workers [37] or baker apprentices [38] combined objective tests (i.e., assessment of IgE-mediated sensitization or SIC) in addition to the results obtained from questionnaires for defining probable OA due to flour. These older studies provided estimates of 1 [37] to 3 [38] incident cases of probable OA per 100 person-years. A recent survey conducted among bakery students in Alberta, Canada during the period 2015–2018 found an incidence of positive SPT to flour of 2.5 per 100 person-years, indicating an ongoing sensitizing effect of exposure to the bakery environment [39]. Estimates of the incidence of probable OR, defined by WRR associated with sensitization to bakery allergens, ranged between 1.3 and 6.3 new cases per 100 person-years [40].

Prevalence and Incidence in Population-Based Studies

Limited information is available on the burden of ORAF in the general population. The Occupational Disease Surveillance System in the Province of Ontario, Canada (2002–2013), documented an increased risk of new-onset asthma among male bakers and confectionery workers (hazard ratio, 2.3 [95% confidence interval [CI], 1.5–3.6]) [41]. A population-based case–control study of incident asthma among adults in Southern Finland found an increased risk of atopic asthma in bakers and food processors (odds ratio, 4.7, 95% CI 1.2–18.7) [42]

National voluntary notification programs and medicolegal statistics of OA indicated that flour was the most frequent cause of OA between 1989 and 2002 in almost all industrialized countries [43]. More recent data from surveillance programs in the UK (1992–2006) [44] and France (2001–2018) [45] suggest a downward trend in the numbers of incident cases of OA, including flour-induced OA. Nevertheless, flour remained the most prevalent cause of OA in France, accounting for 10% of notified cases [45] and the second commonest reported cause (8.5%) in Korea [46]. In the retrospective E-PHOCAS cohort of 1,167 subjects with OA ascertained through an SIC completed during the 2006–2015 in 20 European tertiary centers, flour was still identified as the most prevalent cause of OA, accounting for 30% of all OA cases [47].

Risk Factors

A recent systematic review of the current evidence on the role of environmental and host factors in the initiation of OA concluded that the level of workplace exposure to wheat and α-amylase and atopy are the major risk factors for the development of IgE-mediated sensitization to these allergens and probable OA among exposed workers [48]. There is moderate evidence that allergic rhinitis and NSBH before entering exposure to flour are associated with an increased risk of acquiring IgE-mediated sensitization to work-related HMW allergens, including flour [49]. Although WRR precedes the occurrence of WRA in approximately 60% of the subjects with flour-induced OA [12], the likelihood of developing flour-induced OA among workers affected with OR induced by flour has never been formally quantified.

There is only weak evidence supporting a role of smoking [24], skin exposure to flour [34, 50], and genetic factors (i.e., Toll-like receptor 4 variants and beta$_2$-adrenergic receptor polymorphisms) [51, 52] in the development of ORAF.

Pathophysiological Mechanisms

Although flour-induced OA is deemed to be mediated by an IgE-mediated type I hypersensitivity mechanism, a substantial proportion (12%–38%) of subjects who develop an asthmatic reaction after challenge exposure to flour fail to demonstrate sIgE reactivity to currently available bakery allergens (Table 3). Doyen et al. [12] found that those subjects with undetectable sIgE against wheat and rye and a positive SIC with flour required a significantly longer duration of challenge exposure to flour to elicit an asthmatic reaction and exhibited a significantly smaller increase in post-challenge fractional exhaled nitric oxide (FeNO). They also showed lower levels of baseline blood and sputum eosinophil counts, although sputum eosinophils significantly increased after asthmatic reactions induced by flour exposure. These findings suggest an attenuated degree of specific bronchial responsiveness to flour allergens and a low baseline T2 status. Another potential explanation for the absence of detectable sIgE against wheat and rye is that some relevant allergens might be missing in the wheat or rye extracts currently used to assess sIgE [53].

The majority (71%) of asthmatic reactions induced by flour are associated with a ≥ 2% increase in sputum eosinophils [54], which is consistent with what has been described in individuals exposed to common inhalant allergens [55]. In 60% of the subjects with flour-induced OA, the asthmatic reaction is associated with an increase in FeNO (≥ 13 ppb), reflecting T2-derived inflammation [54], Nevertheless, 16% of subjects with a positive SIC response to flour show a

Table 3 Sensitivity, specificity, and predictive values of skin-prick tests and sIgE determination compared to specific inhalation challenges with flour

Flour allergen	Threshold	Prevalence of positive SICs (%)	Sensitivity[e] (%)	Specificity[e] (%)	Positive predictive value[e] (%)	Negative predictive value[e] (%)	Reference
Skin-prick tests							
Wheat	≥ 2 mm	37/71 (52)	68	74	74	68	*Van Kampen, 2008* [59]
	≥ 5 mm	37/71 (52)	22	100	100	54	
Rye	≥ 2 mm	63/95 (66)	78	84	91	66	*Van Kampen, 2008* [59]
	≥ 4.5 mm	37/71 (52)	38	100	100	45	
Wheat	≥ 3 mm	151/314 (48)	42	86	73	61	*Wiszniewska 2011* [60]
Wheat[b]	≥ 1.5 mm	77/120 (64)	38–58	89–93	88–92	49–58	*Van Kampen, 2013* [61]
Rye[b]	≥ 1.5 mm	76/119 (64)	21–81	88–98	89–97	40–72	
Specific IgE antibodies[a]							
Wheat	≥ 0.35 KU_A/l	37/71 (52)	87	68	74	82	*Van Kampen, 2008* [59]
	≥ 2.32 KU_A/l[c]	37/71 (52)	51	100	100	65	
Rye	≥ 0.35 KU_A/l	63/95 (66)	87	62	82	71	*Van Kampen, 2008* [59]
	≥ 9.64 KU_A/l[c]	63/95 (66)	30	100	100	42	
Wheat	≥ 0.35 KUA/l	151/314 (48)	62	77	72	68	*Wiszniewska 2011* [60]
Wheat	≥ 0.35 KU_A/l	205/264 (78)	84 (78–89)	71 (58–82)	91 (86–95)	56 (44–67)	*Doyen, 2024* [12]
	≥ 5.10 KU_A/l[d]	205/264 (78)	40 (33–47)	97 (88–100)	98 (92–100)	32 (25–39)	
Rye	≥ 0.35 KU_A/l	205/264 (78)	85 (80–90)	78 (65–88)	93 (88–96)	61 (49–72)	
	≥ 6.20 KU_A/l[d]	205/264 (78)	42 (36–50)	97 (88–100)	98 (92–100)	33 (26–40)	
α-amylase	≥ 0.35 KUA/l	151/314 (48)	17	93	68	54	*Wiszniewska 2011* [60]
α-amylase	≥ 0.35 KU_A/l	179/226 (79)	13 (9–19)	100 (94–100)	100 (87–100)	24 (20–31)	*Doyen, 2024* [12]

SIC Specific inhlation challenge with flour, *SPT* Skin-prick test, *sIgE* Specific IgE antibodies.

[a]ImmunoCAP, Thermo Fischer Scientific—Phadia, Uppsala, Sweden.

[b]SPT performed with four commercial extracts compared with the SIC results.

[c]Threshold sIgE value providing a positive predictive value of 100% compared with the SIC result.

[d]Threshold sIgE value providing a specificity ≥95% compared with the SIC result.

[e]95% confidence interval between parentheses.

post-challenge neutrophilic pattern (i.e., sputum neutrophil count ≥ 76%) [56]. Of note, flour was involved in a substantial proportion (46%) of the subjects with a post-challenge neutrophilic pattern in the E-PHOCAS cohort [56]. These data indicate that a high-molecular-weight protein agent can induce an eosinophilic or neutrophilic pattern of airway inflammation independently from the presence of sIgE.

Diagnostic Approaches

Vailable data indicate that ORAF still remains unrecognized for a long time. In the E-PHOCAS cohort, the median duration of WRA symptoms prior to the diagnosis of OA due to flour was 3 years (25 th–75 th percentiles, 1–6) [12].

The clinical history has a high sensitivity but a low specificity for diagnosing OA in general, indicating a need for further objective assessments to reach a definite diagnosis [57]. The available information on the validity of these procedures is critically reviewed below to provide pragmatic guidance to clinicians who are investigating workers with flour-related asthma symptoms. On the basis of existing evidence, a working diagnostic algorithm is proposed that can be adapted to the purpose of diagnosis and available resources (Fig. 1).

Clinical Features

The vast majority (92%) of workers with flour-induced OA also experience WRR symptoms, but this proportion is not significantly different from that recorded in subjects with WRA symptoms who showed a negative SIC with flour (86%) [12].

Data from the E-PHOCAS cohort [12] showed that a substantial proportion (20%) of the workers with flour-induced OA experience work-related skin symptoms consistent with contact urticaria (7%) and/or protein contact dermatitis (13%). In a recent epidemiological survey of 727 bakery workers, Olivieri et al. [34] found

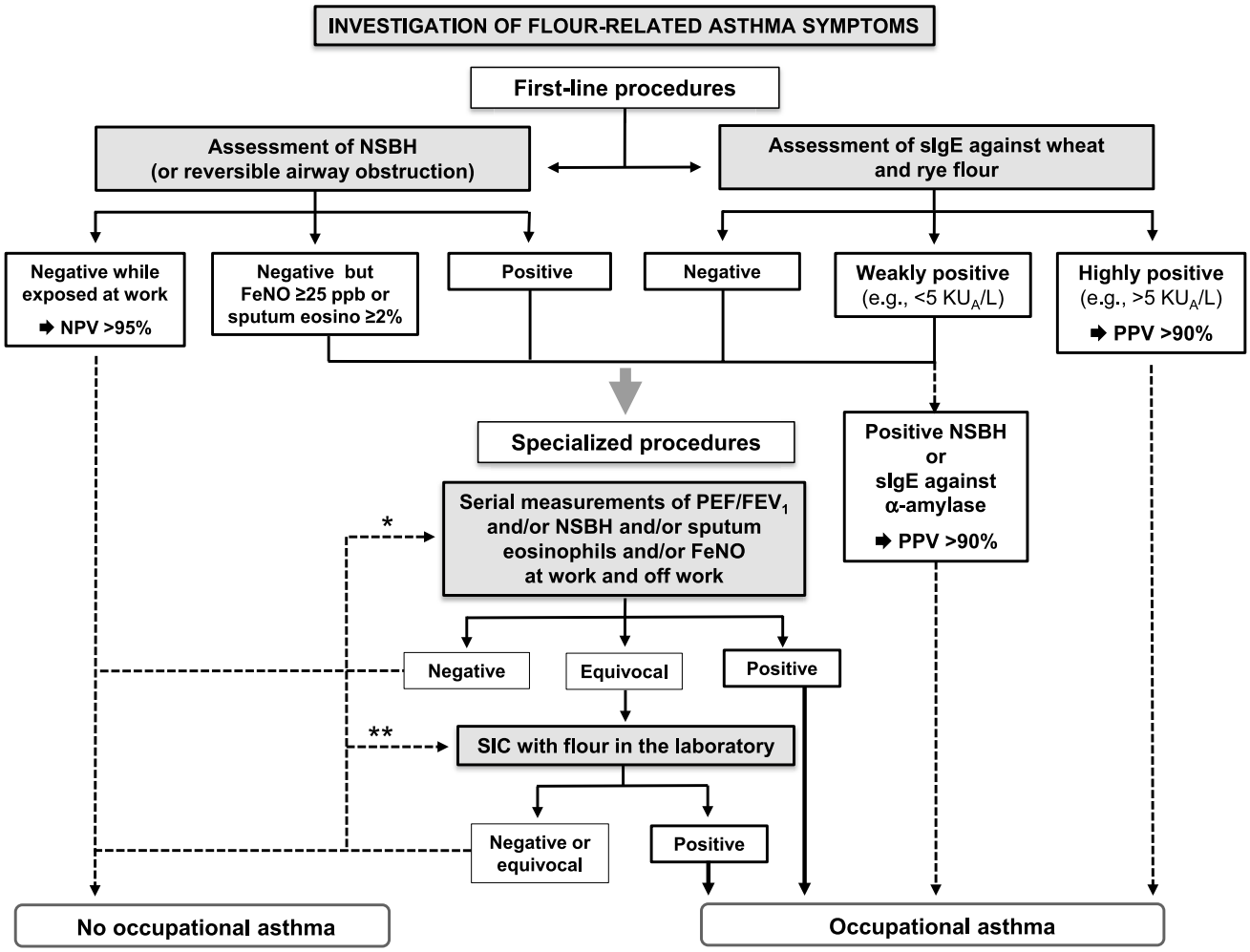

Fig. 1 A pragmatic, evidence-based algorithm for diagnosing flour-induced occupational asthma. Specialized procedures should be considered when establishing or excluding a diagnosis of flour-induced occupational asthma is required for the most appropriate management of patients. *FeNO*, fractional exhaled nitric oxide; *NPV*, negative predictive value; *NSBH*, nonspecific bronchial hyperresponsiveness; *OA*, occupational asthma; *PEF*, peak expiratory flow; *PPV*, positive predictive value; *sIgE*, specific IgE antibodies; *SIC*, specific inhalation challenge with flour. * If the SIC with flour is negative/equivocal, but the clinical history is highly suggestive of OA, consider serial measurements of PEF and/or NSBH and/or airway inflammatory markers at work and away from work. ** If assessment at work is negative/equivocal while the clinical history is highly suggestive of OA, consider an SIC with the flour(s) used at work in the laboratory

that work-related dermatitis symptoms were significantly more frequent in workers who experienced WRR (28%) and WRA (44%) than in those without airway symptoms (6%) but they did not assess IgE-mediated sensitization to bakery allergens. In a review of 291 cases of occupational contact urticaria or protein contact dermatitis, flour was the most prevalent cause, accounting for 15% of all cases [58]. Among these subjects with skin allergy to flour, 25% and 67% were diagnosed with concomitant OA or OR due to flour, respectively.

Intriguingly, food allergy to flour is an extremely rare occurrence in subjects with ORAF [16], with the notable exception of OA caused by buckwheat flour [13].

Immunological Tests

The major limitation of SPT is the lack of quality and availability of commercial flour extracts. The sensitivity of commercial extracts of wheat and rye is generally low, ranging from 38 to 81% compared with the result of SIC with flour (Table 3) [12, 59–61] and is largely affected by their highly variable protein and antigen content [61]. In addition, SPT with flour extracts was less sensitive than the assessment of sIgE against wheat and rye (Table 3).

Among 264 subjects who completed an SIC with flour in the E-PHOCAS study, sIgE levels ≥ 0.35 kUA/L against wheat and rye flours provided similarly high

sensitivities of ~ 85%, moderate specificities (71%–78%), high positive predictive values (PPVs) (91%–93%), and low negative predictive values (NPVs) (56%–61%) [12]. Increasing the threshold sIgE value to 5.10 kU_A/L for wheat and to 6.20 kU_A/L for rye flour provided a specificity ≥ 95% and further enhanced the PPV to 98%, strongly supporting a diagnosis of flour-induced OA without the need to perform an SIC (Table 3).

Remarkably, an sIgE level ≥ 0.35 kU_A/L against fungal α-amylase was detected in 15% of subjects with a positive SIC to flour but in none of the subjects with a negative SIC, providing a specificity and a PPV of 100% in identifying flour-induced OA (Table 3) [12]. Accordingly, the identification of sIgE against α-amylase could provide further evidence supporting a diagnosis of flour-induced OA, especially in subjects who demonstrate a "low" titer of sIgE against wheat or rye (e.g., 0.35–5 KU_A/L).

Nonspecific Bronchial Hyperresponsiveness Testing

Although the presence of NSBH has a low specificity and PPV, the absence of NSBH has a high NPV, making the diagnosis of OA highly unlikely in the absence of NSBH [57, 62]. However, cessation of exposure to the offending agent is often associated with an improvement in NSBH that may even fully resolve within a few days of being off work. Pralong et al. [63] demonstrated that the sensitivity and NPV of NSBH decreased from 98% when NSBH is measured while the subjects are exposed at work to 67% and 82%, respectively, when they are off work at the time of assessment.

In the cohort of subjects challenged with flour in the E-PHOCAS cohort, the presence of NSBH at baseline assessment yielded a low sensitivity (74%) [12], but 44% of the subjects were removed from exposure at the time of evaluation. Nevertheless, using the presence of either baseline NSBH or a positive sIgE assay against wheat or rye in identifying a positive SIC response increased the sensitivity from 84% with sIgE alone to 98% and the NPV from 61 to 80%. On the other hand, combining the presence of NSBH and a positive sIgE result to wheat or rye flour increased the specificity of sIgE assessment alone from 71% up to 85% and the PPV from 91 to 93%. Accordingly, the presence of NSBH in subjects with a "low" level of sIgE could support a diagnosis of OA.

Assessment of Exposure-Related Changes in Functional and Inflammatory Indices

Although SIC is still regarded as the "reference" method for diagnosing OA [64, 65], this specialized technique is unavailable in most countries. Alternatively, the causal relationship between WRA symptoms and exposure to flour can be investigated using serial assessments of changes in functional indices (peak expiratory flow rate, forced expiratory volume in 1 s, NSBH) and/or inflammatory markers (FeNO, sputum eosinophils) related to workplace exposure [57]. In addition, a recent study showed that exposure-related changes in FeNO (≥ 13 ppb) and sputum eosinophils (≥ 1.25%) each achieve a ≥ 95% specificity in identifying asthmatic reactions and strongly support a diagnosis of OA [54].

Outcome and Management

Systematic reviews of OA due to various agents agreed that complete cessation of exposure to agents causing OA is associated with the highest probability of improvement [66, 67]. However, patients should be aware that removal from exposure results in symptom recovery and resolution of NSBH in less than one-third of affected workers [66–68]. In addition, complete avoidance of exposure is associated with a substantial psycho-social and financial impact [66]. Accordingly, reduction of exposure to the causal agent may be considered an alternative to complete avoidance in order to minimize adverse socio-economic consequences [66, 67]. Overall, reduction of exposure seems to have a less beneficial effect than complete avoidance [66, 67] and requires careful medical monitoring in order to ensure an early identification of asthma worsening. However, there is scarce information on the outcome and management options of ORAF [69].

The management of flour-induced OR aims not only to minimize nasal symptoms and their impact on patients' quality of life, but may also offer the opportunity to prevent the subsequent development of OA. Nevertheless, quantitative estimates of the long-term risk of developing OA among workers with flour-induced OR are lacking [40]. The clinical benefits resulting from complete avoidance of exposure to the offending agent should therefore be weighed against the potential adverse socio-economic impact of removal from exposure on an individual basis [40].

Although some improvement in asthma control and FeNO level during sublingual specific immunotherapy with wheat flour extracts has been reported [70], it remains unknown whether this approach has a beneficial effect on the long-term course of the disease in workers who remain exposed to the causal agent. Furthermore, this therapeutic option is currently limited by the unavailability of standardized allergen extracts [71].

Prevention

Preventive strategies and their effectiveness in reducing flour dust exposures and ORAF have been comprehensively reviewed by Jeebhay and Baatjies [5]. Reducing exposure to flour dust is the most rational primary prevention approach for minimizing the burden of the disease. Although improved exhaust ventilation at highly exposed job sites, enclosure or automation of parts of the baking process, and substitution of traditional wheat flour used for dusting surfaces with "low dust" flours [72] can substantially reduce exposure, compliance with occupational exposure limits seems to remain suboptimal. A recent survey of Italian facilities found that a substantial proportion (83%) of personal exposure samples were still above the Threshold Limit Value-Time Weighted Average of 0.5 mg/m^3 of flour dust recommended by the American Conference of Governmental Industrial Hygienists, especially during dough making and forming [73].

It is increasingly acknowledged that effective prevention strategies should be multifaceted, combining engineering measures aimed at reducing flour dust exposure with education and worker training to improve work and cleaning practices, exposure monitoring to ensure compliance, and medical surveillance for the early identification of high-risk workers [5]. However, there are few well-designed intervention studies with quantified exposure data that have assessed the impact of prevention strategies on the incidence of ORAF over time. Al Badri et al. [74] conducted a controlled randomized trial evaluating the long-term health outcomes of workplace interventions in bakers in South Africa. This study found that FeNO decline at the one-year follow-up assessment was greater in the intervention group (i.e., enclosed mixer or training), especially among participants with baseline FeNO > 25 ppb, compared with the control group.

Conclusions

The key lesson from recent data is that flour-induced OA and OR are still major contributors to the global burden of occupational respiratory allergies. Although substantial progress has been made in characterizing bakery allergens and delineating preventive strategies, a number of unanswered questions should be further addressed.

Refinement of diagnostic testing should focus on characterizing sIgE reactivity to cereal allergen components and "improver" enzymes in the subset of subjects who develop a positive bronchial response to flour without detectable sIgE using currently available assays. In addition, tools for detecting sIgE sensitization to new flour ingredients used for the production of gluten-free and vegan products, should be developed and made available to clinicians.

Prospective workplace intervention studies coupled with exposure monitoring should be implemented in order to evaluate the impact of prevention strategies on the incidence of ORAF and their effectiveness in individuals with flour-induced OA and/or OR who remain at work. To improve personalized disease management, further research is required to quantify the risk and identify the determinants of the development of flour-induced OA among workers with OR who remain exposed to flour.

Exploring serial measurements of airway inflammatory markers such as FeNO is warranted for improving the early identification of flour-induced OA and assessing the long-term impact of workplace interventions.

Key References

- M.F. Jeebhay and R. Baatjies. "Prevention of baker's asthma." *Curr Opin Allergy Clin Immunol,* vol. 20, no. 2, pp. 96–102, Apr 2020, https://doi.org/10.1097/ACI.0000000000000804.

  A comprehensive review of preventive strategies aimed at reducing exposure to flour dust and available evidence pertaining to their effectiveness.

- J. Pyana Kitenge J 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*, vol 95, no. 1, pp. 293–301, Jan 2022, https://doi.org/10.1007/s00420-021-01698-8.

  A unique survey using serial measurements of peak expiratory flow rates at and off work rather than immunological tests in order to investigate the causal relationship between work and respiratory symptoms.

- J. Beach et al. "Flour exposure, sensitization and respiratory health among Alberta trainee bakers." *Occup Med (Lond)*, vol. 72, no. 8, pp. 559–65, Dec 2022, https://doi.org/10.1093/occmed/kqac101.

  This longitudinal study of trainee bakers over a 3-year period found an incidence of new sensitization to bakery allergens of 2.5/100 person-years, thereby providing evidence for an ongoing sensitization risk from exposure to bakery environments.

- V. Doyen et al. "Diagnostic accuracy of specific IgE against wheat and rye in flour-induced occupational asthma." *J Allergy Clin Immunol Pract*, vol. 12, no. 8, pp. 2017–2025.e5, Aug 2024, https://doi.org/10.1016/j.jaip.2024.05.014.

This multicenter study assessed the diagnostic accuracy of sIgE against wheat and rye flour, and fungal alpha-amylase compared with the results of specific inhalation challenge with flour as the reference standard in a large multicenter cohort of subjects evaluated for flour-related asthma symptoms. In addition, the E-PHOCAS cohort is the first that comprehensively characterizes the clinical and inflammatory characteristics of flour-induced occupational asthma.

Acknowledgements The authors wish to thank Raphaël Georis, PhD (Scientific Support Unit, Centre Hospitalier Universitaire UCL Namur) for computing pooled prevalence estimates

Authors Contribution All authors contributed equally to the design, literature review, and production of this manuscript. They provided input and critical feedback into the drafting of the manuscript. All authors read and approved the final manuscript.

Funding This work was funded in part by the *Fondation Mont-Godinne*.

Data Availability No datasets were generated or analysed during the current study.

Declarations

Human and Animal Rights and Informed Consent All reported studies with human subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Declaration of Helsinki and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

Competing Interests The authors declare no competing interests.

References

1. van Dishoeck HA, Roux DJ. Sensitization to flour and flour illnesses amongst flour workers. J Hyg (Lond). 1939;39(6):674–9.
2. Houba R, Doekes G, Heederik D. Occupational respiratory allergy in bakery workers: a review of the literature. Am J Ind Med. 1998;34(6):529–46.
3. Brant A. Baker's asthma. Curr Opin Allergy Clin Immunol. 2007;7(2):152–5.
4. Quirce S, Diaz-Perales A. Diagnosis and management of grain-induced asthma. Allergy Asthma Immunol Res. 2013;5(6):348–56.
5. Jeebhay MF, Baatjies R. Prevention of baker's asthma. Curr Opin Allergy Clin Immunol. 2020;20(2):96–102.
6. Goesaert H, Brijs K, Veraverbeke WS, Courtin CM, Gebruers K, Delcour JA. Wheat flour constituents : how they impact bread quality, and how to impact their functionnality. Trends Food Sci Technol. 2005;16:12–30.
7. Park SH, Na Y, Kim J, Kang SD, Park KH. Properties and applications of starch modifying enzymes for use in the baking industry. Food Sci Biotechnol. 2018;27(2):299–312.
8. Aidoo H, Beach J, Elbourne R, Galarneau JF, Straube S, Cherry N. Estimation and validation of flour exposure in bakeries in Alberta. Canada Ann Work Expo Health. 2018;62(9):1096–108.
9. Tatham AS, Shewry PR. Allergens to wheat and related cereals. Clin Exp Allergy. 2008;38(11):1712–26.
10. Salcedo G, Quirce S, Diaz-Perales A. Wheat allergens associated with Baker's asthma. J Investig Allergol Clin Immunol. 2011;21(2):81–92 (**quiz 4**).
11. Sander I, Rihs HP, Doekes G, Quirce S, Krop E, Rozynek P, et al. Component-resolved diagnosis of baker's allergy based on specific IgE to recombinant wheat flour proteins. J Allergy Clin Immunol. 2015;135(6):1529–37.
12. Doyen V, Migueres N, Frere A, Walusiak-Skorupa J, Wiszniewska M, Suojalehto H, et al. Diagnostic accuracy of specific IgE against wheat and rye in flour-induced occupational asthma. J Allergy Clin Immunol Pract. 2024;12(8):2017-25 e5.
13. 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(11):1047–53.
14. Quirce S, Polo F, Figueredo E, Gonzalez R, Sastre J. Occupational asthma caused by soybean flour in bakers–differences with soybean-induced epidemic asthma. Clin Exp Allergy. 2000;30(6):839–46.
15. Campbell CP, Jackson AS, Johnson AR, Thomas PS, Yates DH. Occupational sensitization to lupin in the workplace: occupational asthma, rhinitis, and work-aggravated asthma. J Allergy Clin Immunol. 2007;119(5):1133–9.
16. van Kampen V, Sander I, Quirce S, Bruning T, Merget R, Raulf M. IgE sensitization to lupine in bakers - cross-reactivity or co-sensitization to wheat flour? Int Arch Allergy Immunol. 2015;166(1):63–70.
17. Sander I, Raulf-Heimsoth M, Siethoff C, Lohaus C, Meyer HE, Baur X. Allergy to Aspergillus-derived enzymes in the baking industry: identification of beta-xylosidase from Aspergillus niger as a new allergen (Asp n 14). J Allergy Clin Immunol. 1998;102(2):256–64.
18. Elms J, Fishwick D, Walker J, Rawbone R, Jeffrey P, Griffin P, et al. Prevalence of sensitisation to cellulase and xylanase in bakery workers. Occup Environ Med. 2003;60(10):802–4.
19. Simonis B, Holzel C, Stark U. Glucoamylase: a current allergen in the baking industry. Allergo J Int. 2014;23(8):269–73.
20. Jones M, Welch J, Turvey J, Cannon J, Clark P, Szram J, et al. Prevalence of sensitization to "improver" enzymes in UK supermarket bakers. Allergy. 2016;71(7):997–1000.
21. Talini D, Benvenuti A, Carrara M, Vaghetti E, Martin LB, Paggiaro PL. Diagnosis of flour-induced occupational asthma in a cross-sectional study. Respir Med. 2002;96(4):236–43.
22. Droste J, Myny K, Van Sprundel M, Kusters E, Bulat P, Braeckman L, et al. Allergic sensitization, symptoms, and lung function among bakery workers as compared with a nonexposed work population. J Occup Environ Med. 2003;45(6):648–55.
23. Brant A, Berriman J, Sharp C, Welch J, Zekveld C, Nieuwenhuijsen M, et al. The changing distribution of occupational asthma: a survey of supermarket bakery workers. Eur Respir J. 2005;25(2):303–8.
24. Harris-Roberts J, Robinson E, Waterhouse JC, Billings CG, Proctor AR, Stocks-Greaves M, et al. Sensitization to wheat flour and enzymes and associated respiratory symptoms in British bakers. Am J Ind Med. 2009;52(2):133–40.
25. Jacobs JH, Meijster T, Meijer E, Suarthana E, Heederik D. Wheat allergen exposure and the prevalence of work-related sensitization and allergy in bakery workers. Allergy. 2008;63(12):1597–604.
26. Hur GY, Koh DH, Kim HA, Park HJ, Ye YM, Kim KS, et al. Prevalence of work-related symptoms and serum-specific antibodies to wheat flour in exposed workers in the bakery industry. Respir Med. 2008;102(4):548–55.

27. Page EH, Dowell CH, Mueller CA, Biagini RE, Heederik D. Exposure to flour dust and sensitization among bakery employees. Am J Ind Med. 2010;53(12):1225–32.
28. 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(5):310–6.
29. Mbatchou Ngahane BH, Afane Ze E, Nde F, Ngomo E, Mapoure Njankouo Y, Njock LR. Prevalence and risk factors for allergic rhinitis in bakers in Douala, Cameroon. BMJ Open. 2014;4(8):e005329.
30. Crivellaro MA, Ottaviano G, Maculan P, Pendolino AL, Vianello L, Mason P, et al. Upper and Lower Respiratory Signs and Symptoms in Workers Occupationally Exposed to Flour Dust. Int J Environ Res Publ Health. 2020;17(19):7075.
31. Ade S, Adjobimey M, Agodokpessi G, Kouassi MS, Gounongbe FA, Cisse I, et al. Asthma symptoms in bakeries at Parakou. Benin Pulm Med. 2020;2020:3767382.
32. Aydin O, Sozener ZC, Demirel YS, Secil D, Mungan D. Baker's asthma in bread factory workers. Allergy Asthma Proc. 2021;42(1):72–7.
33. Pyana Kitenge J, Musa Obadia P, Carsi Kuhangana T, Kayembe-Kitenge T, Nkulu Banza P, Nsenga Mukanda L, 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. 2022;95(1):293–301.
34. Olivieri M, Murgia N, Spiteri G, Biscardo CA, Marchetti P, Folletti I, 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(2):112–6.
35. Cullinan P, Lowson D, Nieuwenhuijsen MJ, Sandiford C, Tee RD, Venables KM, et al. Work related symptoms, sensitisation, and estimated exposure in workers not previously exposed to flour. Occup Environ Med. 1994;51(9):579–83.
36. Gautrin D, Infante-Rivard C, Dao TV, Magnan-Larose M, Desjardins D, Malo JL. Specific IgE-dependent sensitization, atopy, and bronchial hyperresponsiveness in apprentices starting exposure to protein-derived agents. Am J Respir Crit Care Med. 1997;155(6):1841–7.
37. Cullinan P, Cook A, Nieuwenhuijsen MJ, Sandiford C, Tee RD, Venables KM, et al. Allergen and dust exposure as determinants of work-related symptoms and sensitization in a cohort of flour-exposed workers; a case-control analysis. Ann Occup Hyg. 2001;45(2):97–103.
38. Walusiak J, Hanke W, Gorski P, Palczynski C. Respiratory allergy in apprentice bakers: do occupational allergies follow the allergic march? Allergy. 2004;59(4):442–50.
39. Beach J, Galarneau JM, Cherry N. Flour exposure, sensitization and respiratory health among Alberta trainee bakers. Occup Med (Lond). 2022;72(8):559–65.
40. Vandenplas O, Hox V, Bernstein D. Occupational Rhinitis. J Allergy Clin Immunol Pract. 2020;8(10):3311–21.
41 Logar-Henderson C, MacLeod JS, Arrandale VH, Holness DL, McLeod CB, Peter A, et al. Adult asthma among workers in Ontario. Results from the occupational disease surveillance system. Ann Am Thoracic Soc. 2019;16(5):563–71.
42. Jaakkola MS, Lajunen TK, Heibati B, Wang YC, Lai CH, Jaakkola JJK. Occupation and subcategories of asthma: a population-based incident case-control study. Occup Environ Med. 2021;78(9):661–8.
43. Vandenplas O. Occupational asthma: etiologies and risk factors. Allergy Asthma Immunol Res. 2011;3(3):157–67.
44. Walters GI, Kirkham A, McGrath EE, Moore VC, Robertson AS, Burge PS. Twenty years of SHIELD: decreasing incidence of occupational asthma in the West Midlands, UK? Occup Environ Med. 2015;72(4):304–10.
45. Lucas D, Robin C, Vongmany N, Dewitte JD, Lodde B, Pougnet R, et al. Main causal agents of occupational asthma in France, reported to the National Network for Occupational Disease Vigilance and Prevention (RNV3P) 2001–2018. Ann Work Expo Health. 2023;67(3):297–302.
46. Kwon SC, Song J, Kim YK, Calvert GM. Work-related asthma in Korea - Findings from the Korea work-related asthma surveillance (KOWAS) program, 2004–2009. Allergy Asthma Immunol Res. 2015;7(1):51–9.
47. Vandenplas O, Godet J, Hurdubaea L, Rifflart C, Suojalehto H, Wiszniewska M, et al. Are high- and low-molecular-weight sensitizing agents associated with different clinical phenotypes of occupational asthma? Allergy. 2019;74:261–72.
48. Doyen V, Gautrin D, Vandenplas O, Malo JL. Comparison of high- and low-molecular-weight sensitizing agents causing occupational asthma: an evidence-based insight. Expert Rev Clin Immunol 2024;1–19.
49. Gautrin D, Ghezzo H, Infante-Rivard C, Magnan M, L'Archeveque J, Suarthana E, et al. Long-term outcomes in a prospective cohort of apprentices exposed to high-molecular-weight agents. Am J Respir Crit Care Med. 2008;177(8):871–9.
50. Arrandale V, Meijster T, Pronk A, Doekes G, Redlich CA, Holness DL, et al. Skin symptoms in bakery and auto body shop workers: associations with exposure and respiratory symptoms. Int Arch Occup Environ Health. 2013;86(2):167–75.
51. Cho HJ, Kim SH, Kim JH, Choi H, Son JK, Hur GY, et al. Effect of Toll-like receptor 4 gene polymorphisms on work-related respiratory symptoms and sensitization to wheat flour in bakery workers. Ann Allergy Asthma Immunol. 2011;107(1):57–64.
52. Hur GY, Park HJ, Lee HY, Koh DH, Lee BJ, Choi GS, et al. Association of beta(2)-adrenergic receptor polymorphism with work-related symptoms in workers exposed to wheat flour. Yonsei Med J. 2011;52(3):488–94.
53. Bittner C, Peters U, Frenzel K, Muesken H, Brettschneider R. New wheat allergens related to baker's asthma. J Allergy Clin Immunol. 2015;136(5):1416-8 e1-2.
54. Doyen V, Migueres N, van Kampen V, Suojalehto H, Mason P, Munoz X, et al. Exhaled nitric oxide and sputum eosinophils are complementary tools for diagnosing occupational asthma. Allergy. 2025;80(4):1115-24.
55. Revez JA, Killian KJ, O'Byrne PM, Boulet LP, Upham JW, Gauvreau GM, et al. Sputum cytology during late-phase responses to inhalation challenge with different allergens. Allergy. 2018;73(7):1470–8.
56. Migueres N, Vandenplas O, Walusiak-Skorupa J, Wiszniewska M, Munoz X, Romero-Mesones C, et al. Sputum inflammatory patterns are associated with distinct clinical characteristics in patients with occupational asthma independently of the causal agent. J Investig Allergol Clin Immunol. 2024;34(2):85–96.
57. Cullinan P, Vandenplas O, Bernstein D. Assessment and management of occupational Asthma. J Allergy Clin Immunol Pract. 2020;8(10):3264–75.
58. Helaskoski E, Suojalehto H, Kuuliala O, Aalto-Korte K. Occupational contact urticaria and protein contact dermatitis: causes and concomitant airway diseases. Contact Dermatitis. 2017;77(6):390–6.
59. van Kampen V, Rabstein S, Sander I, Merget R, Bruening T, Broding HC, et al. Prediction of challenge test results by flour-specific IgE and skin prick test in symptomatic bakers. Allergy. 2008;63(7):897–902.
60. Wiszniewska M, Nowakowska-Swirta E, Palczynski C, Walusiak-Skorupa J. Diagnosing of bakers' respiratory allergy: is specific inhalation challenge test essential? Allergy Asthma Proc. 2011;32(2):111–8.
61. van Kampen V, de Blay F, Folletti I, Kobierski P, Moscato G, Olivieri M, et al. Evaluation of commercial skin prick test solutions for selected occupational allergens. Allergy. 2013;68(5):651–8.

62. Tarlo SM, Balmes J, Balkissoon R, Beach J, Beckett W, Bernstein D, et al. Diagnosis and management of work-related asthma: american college of chest physicians consensus statement. Chest. 2008;134(3 Suppl):1S-41S.
63. Pralong JA, Lemiere C, Rochat T, L'Archeveque J, Labrecque M, Cartier A. Predictive value of nonspecific bronchial responsiveness in occupational asthma. J Allergy Clin Immunol. 2016;137(2):412–6.
64. Beach J, Russell K, Blitz S, Hooton N, Spooner C, Lemiere C, et al. A systematic review of the diagnosis of occupational asthma. Chest. 2007;131(2):569–78.
65. Vandenplas O, Suojalehto H, Aasen TB, Baur X, Burge PS, de Blay F, et al. Specific inhalation challenge in the diagnosis of occupational asthma: Consensus statement. Eur Respir J. 2014;43(6):1573–87.
66. Vandenplas O, Dressel H, Nowak D, Jamart J. What is the optimal management option for occupational asthma? Eur Respir Rev. 2012;21(124):97–104.
67. Henneberger PK, Patel JR, de Groene GJ, Beach J, Tarlo SM, Pal TM, et al. Workplace interventions for treatment of occupational asthma. Cochrane Database Syst Rev (Online). 2019;10:CD006308.
68. Rachiotis G, Savani R, Brant A, MacNeill SJ, Newman Taylor A, Cullinan P. Outcome of occupational asthma after cessation of exposure: a systematic review. Thorax. 2007;62(2):147–52.
69. Bittner C, Garrido MV, Harth V, Preisser AM. IgE reactivity, work related allergic symptoms, asthma severity, and quality of life in bakers with occupational asthma. Adv Exp Med Biol. 2016;921:51–60.
70. Dubini M, Marraccini P, Brass DM, Patrini L, Riboldi L. Occupational asthma and rhinitis due to wheat flour: sublingual specific immunotherapy treatment. Med Lav. 2020;111(3):203–9.
71. Smith AM, Sastre J. The role of immunotherapy and biologic treatments in occupational allergic disease. J Allergy Clin Immunol Pract. 2020;8(10):3322–30.
72. Pocock D, Hall S, Bennett S, Darnton L, Molloy M. Laboratory study of the effectiveness of substituting traditional wheat flour with low dust flour and use of different sieve designs as controls to reduce exposure to inhalable flour dust in commercial bakeries. Ann Work Expo Health. 2023;67(9):1081–7.
73 Martinelli A, Salamon F, Scapellato ML, Trevisan A, Vianello L, Bizzotto R, et al. Occupational exposure to flour dust. Exposure assessment and effectiveness of control measures. Int J Environ Res Publ Health. 2020;17(14):5182.
74. Al Badri FM, 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(5):589–99.
75. Olivieri M, Spiteri G, Brandi J, Cecconi D, Fusi M, Zanoni G, et al. Glucose/Ribitol dehydrogenase and 16.9 kDa class I heat shock protein 1 as novel wheat allergens in baker's respiratory allergy. Molecules. 2022;27(4):1212.
76. Garcia-Casado G, Armentia A, Sanchez-Monge R, Sanchez LM, Lopez-Otin C, Salcedo G. A major baker's asthma allergen from rye flour is considerably more active than its barley counterpart. FEBS Lett. 1995;364(1):36–40.
77. Barber D, Sanchez-Monge R, Gomez L, Carpizo J, Armentia A, Lopez-Otin C, et al. A barley flour inhibitor of insect alpha-amylase is a major allergen associated with baker's asthma disease. FEBS Lett. 1989;248(1–2):119–22.
78. Weichel M, Glaser AG, Ballmer-Weber BK, Schmid-Grendelmeier P, Crameri R. Wheat and maize thioredoxins: a novel cross-reactive cereal allergen family related to baker's asthma. J Allergy Clin Immunol. 2006;117(3):676–81.