



# Novel approaches in occupational asthma diagnosis and management

Santiago Quirce<sup>a,b</sup>, Javier Domínguez-Ortega<sup>a,b</sup>, and Juan A. Luna<sup>a,b</sup>

## Purpose of review

To describe the recent findings of the last 2 years on the epidemiology and phenotypes of occupational asthma, as well as new developments in its diagnosis and management.

## Recent findings

Data from nine longitudinal studies showed a population attributable fraction for the occupational contribution to incident asthma of 16%. The main phenotypes of occupational asthma are: occupational asthma caused by high-molecular-weight (HMW) or low-molecular-weight (LMW) agents, irritant-induced asthma and occupational asthma-chronic obstructive pulmonary disease overlap. Among the variety of causative agents of occupational asthma, food-derived components are increasingly being reported, accounting for up to 25% cases of occupational asthma and/or occupational rhinitis. Recently, a specific inhalation challenge (SIC)-independent model has been developed to calculate the probability of occupational asthma diagnosis in workers exposed to HMW agents. In this model, work-specific sensitization, bronchial hyperresponsiveness, inhaled corticosteroid use, rhinoconjunctivitis and age 40 years or less were the most relevant predictive factors. Specific IgE measurements showed a pooled sensitivity of 0.74 and a specificity of 0.71 in the diagnosis of occupational asthma for HMW agents, while a lower sensitivity (0.28) and a higher specificity (0.89) was shown for LMW agents. Cessation of exposure to workplace sensitizers is the cornerstone of management of work-related conditions.

## Summary

An early and precise diagnosis of occupational asthma is crucial, allowing appropriate management and implementation of preventive strategies.

## Keywords

high-molecular-weight agents, irritant-induced asthma, low-molecular-weight agents, occupational asthma, specific inhalation challenge, work-related asthma

## INTRODUCTION

Work-related asthma (WRA) is any type of asthma that is associated with work, and encompasses two subtypes: occupational asthma and work-exacerbated asthma (WEA). Occupational asthma is defined as a type of asthma induced by workplace exposures (sensitizers or irritants), whereas WEA refers to asthma triggered by irritants or exercise in workers who are known to have concurrent or preexisting asthma [1]. Sensitizer-induced occupational asthma is due to an allergic response to high-molecular-weight (HMW) ( $\geq 10$  kDa) or low-molecular-weight (LMW) agents ( $< 10$  kDa), either through the interaction with specific IgE antibodies or by other immune (usually cellular) mechanisms [1]. This review deals with recent findings and new developments in occupational asthma.

## Epidemiology

A recent American Thoracic Society (ATS)/European Respiratory Society (ERS) statement on the occupational burden of nonmalignant respiratory diseases, using pooled data from nine longitudinal studies, reported a population attributable fraction for the occupational contribution to incident asthma of 16% [95% confidence interval (CI), 10–22%] [2].

<sup>a</sup>Department of Allergy, La Paz University Hospital, IdiPAZ and <sup>b</sup>CIBER of Respiratory Diseases CIBERES, Madrid, Spain

Correspondence to Santiago Quirce, Department of Allergy, La Paz University Hospital, IdiPAZ, P. La Castellana, 261, 28046 Madrid, Spain. E-mail: squirce@gmail.com

**Curr Opin Pulm Med** 2021, 27:9–14

DOI:10.1097/MCP.0000000000000737

## KEY POINTS

- The population attributable fraction for incident asthma from occupation has been recently estimated to be 16% (95% confidence interval 10–22%). The prevalence of occupational asthma among males and females varies significantly depending on occupation, workplace exposures and job categories.
- The main occupational asthma clinical phenotypes include: occupational asthma caused by HMW or LMW agents, irritant-induced asthma and occupational asthma-chronic obstructive pulmonary disease overlap.
- Demonstration of specific IgE-mediated sensitization is a very important step in the diagnosis of sensitizer-induced occupational asthma. However, this test has a sensitivity of 0.74 and a specificity of 0.71 for HMW agents, and a much lower sensitivity but a higher specificity for LMW agents.
- SIC is the reference test for the diagnosis occupational asthma, however it is time consuming, safety precautions are mandatory, and it is only available in a few specialized centres worldwide. To overcome these problems, a non-SIC-based model for occupational asthma induced by HMW agents has been developed with a good diagnostic performance.
- Management of sensitizer-induced occupational asthma requires cessation of exposure to the causative agent. If not feasible, adjustments in the work processes and occupational hygiene measures including the use of protective equipment, can be tried and their effectiveness monitored objectively.

The proportion of women in the labour market has increased significantly in the past 25 years, and sex issues in occupational health are becoming more relevant. Moscato *et al.* [3<sup>¶</sup>] wrote a systematic review on sex differences in occupational (respiratory and skin) allergic diseases, including asthma. The prevalence of occupational asthma among males and females varies significantly depending on the occupations, workplace exposures, industries and job categories. Overall, the sex distribution of work-related asthma varies across countries without clear global difference. Notwithstanding, occupational rhinitis and contact dermatitis are higher in women, although it is unclear if this is due to a sex effect or to differences in work exposure.

Jeebhay *et al.* [4] conducted a thorough review on the role of food processing in occupational respiratory allergy, and they concluded that food components are responsible for up to 25% of occupational rhinitis and/or occupational asthma. Raw and processed animal and plant products, additives and preservatives, microbes, insect and mite contaminants are the main allergen sources. The

allergenicity of the food proteins, exposure levels and atopy are important risk factors. A new type of food allergy, namely class 3 food allergy [4] was proposed, that is characterized by respiratory symptoms from dust particulate or aerosols derived from food that are readily inhaled and can act as primary sensitizers in the airways, usually without any symptoms upon ingestion. Although most food agents typically cause IgE-mediated allergic reactions, other mixed IgE-mediated and non-IgE-mediated reactions have also been described [4].

## Clinical aspects and phenotypes

Over the last few years, efforts are being made to better identify the different phenotypes of work-related asthma and specifically of occupational asthma [5]. The traditional classification of occupational asthma in immunologic (sensitizer-induced) and nonimmunologic (irritant-induced) subtypes is helpful for diagnostic purposes and to implement the most adequate management and prevention strategies. A recent article [6<sup>¶¶</sup>] discusses the main occupational asthma clinical phenotypes: occupational asthma caused by HMW or LMW agents, irritant-induced asthma and occupational asthma chronic obstructive pulmonary disease (COPD) overlap. This clinical classification, which is based on pathophysiological mechanisms, is practical, easy to perform and with relevant implications for management and prevention.

The assessment of the inflammatory profile (eosinophilic and noneosinophilic) within the airways is useful to define the inflammatory phenotypes of occupational asthma, as well as to confirm the diagnosis and to prescribe anti-inflammatory and/or biological therapy [5]. Given the marked overlap between the inflammatory and the aforementioned clinical phenotypes of occupational asthma, both classification approaches are necessary for a better characterization of the patients.

In this regard, Vandenplas *et al.* [7] have studied a large European multicenter cohort (E-PHOCAS) of 1180 individuals with occupational asthma diagnosis based on a positive-specific inhalation challenge (SIC) result. LMW agents were involved in 635 (53.8%) and HMW agents in 544 (46.1%) of the SICs, while in 13 individuals the causal agent was not identified. Individuals with occupational asthma caused by HMW agents, as compared with LMW agents, were slightly younger, more often atopic, never smokers and more frequently had work-related rhinitis, conjunctivitis and wheezing at work, but less often experienced chest tightness and sputum production (Table 1). Individuals with occupational asthma caused by HMW agents more

**Table 1.** Clinical and laboratory features in occupational asthma induced by high-molecular-weight and low-molecular-weight agents

|                                      | HMW-induced OA                                                                                 | LMW-induced OA                                                              | References                             |
|--------------------------------------|------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|----------------------------------------|
| Atopy                                | Very common                                                                                    | Less common than with HMW                                                   | [5,6 <sup>■</sup> ,7]                  |
| Specific IgE tests (serum)           | Available for several agents<br>Sensitivity 0.74 Specificity 0.71                              | Only for a few agents<br>Sensitivity 0.28 Specificity 0.89                  | [19,20 <sup>■</sup> ]                  |
| Occupational rhinitis/conjunctivitis | Most patients and often precedes OA                                                            | Less frequent than with HMW                                                 | [5,6 <sup>■</sup> ,7]                  |
| Type of asthmatic response on SIC    | Most commonly immediate                                                                        | Commonly isolated late                                                      | [7,14]                                 |
| Non-SIC-based model for diagnosis    | Available                                                                                      | Not available                                                               | [15 <sup>■</sup> ,16]                  |
| Blood and sputum eosinophilia        | Common and more pronounced than with LMW                                                       | Less common and usually not so elevated as with HMW (except with acrylates) | [5,6 <sup>■</sup> ,7,10 <sup>■</sup> ] |
| FeNO levels                          | Frequently elevated and increase after SIC                                                     | Not so elevated as with HMW                                                 | [5,7]                                  |
| Airflow limitation                   | In a minority but more frequent than with LMW                                                  | Uncommon                                                                    | [7]                                    |
| Severe asthma exacerbations          | Relatively frequent                                                                            | More frequent than with HMW                                                 | [7]                                    |
| Implications for further exposure    | Removal, or alternatively marked reduction of exposure and use of RPE (only in selected cases) | Removal                                                                     | [6 <sup>■</sup> ,26 <sup>■</sup> ,29]  |

FeNO, fractional exhaled nitric oxide; HMW, high-molecular-weight; LMW, low-molecular-weight; OA, occupational asthma; RPE, respiratory protective equipment; SIC, specific inhalation challenge.

frequently showed peripheral blood eosinophilia ( $>300$  cells/ $\mu$ l), and a higher increase in post-SIC fractional exhaled nitric oxide (FeNO) levels, than individuals with occupational asthma due to LMW agents. However, no differences in sputum eosinophil counts were found between both groups at baseline nor post-SIC. Individuals with occupational asthma caused by LMW agents had a significantly higher rate (26%) of severe asthma exacerbations while exposed at work than individuals sensitized to HMW agents (19%), but the latter individuals showed a higher risk of airway inflammation. This study found phenotypic differences between occupational asthma induced by HMW and LMW agents in their clinical, inflammatory and functional characteristics, supporting the need to correctly identify the occupational asthma phenotype, which should lead to a more personalized management approach.

In the same cohort, Vandenplas *et al.* [8] found that 16.2% (95% CI, 14.0–18.7%) individuals had severe occupational asthma defined by ERS/ATS criteria [9]. Multivariable logistic regression analysis revealed that severe occupational asthma was associated with persistent exposure to the causal agent at work; a longer duration of the disease; a low level of education; childhood asthma; and sputum production. This study indicates that a substantial proportion of individuals with occupational asthma manifests with severe asthma and identifies potentially modifiable risk factors for severe occupational asthma that should be targeted to reduce the adverse impacts of the disease.

Suojalehto *et al.* [10<sup>■</sup>] assessed the characteristics of acrylate-induced occupational asthma also in this European multicenter cohort study of individuals with occupational asthma. A total of 55 individuals with occupational asthma induced by acrylates confirmed by SIC were recruited and compared with individuals with occupational asthma due to other LMW agents ( $n=418$ ) and isocyanates ( $n=125$ ). When compared with occupational asthma caused by other LMW agents, acrylate-induced occupational asthma was associated with female sex, younger age, lower BMI, more frequent work-related urticaria and lower treatment level. Work-related rhinitis was more frequent in acrylate-induced than isocyanate-induced occupational asthma and the increase in post-SIC FeNO was greater than in occupational asthma induced by other LMW agents or isocyanates. All individuals with acrylate-induced occupational asthma showed sputum eosinophilia post-SIC, while this inflammatory pattern was less frequently observed in occupational asthma caused by other LMW agents (61%) or isocyanates (67%). These phenotypic features of acrylate-induced occupational asthma resembles more occupational asthma caused by HMW agents, suggesting that acrylates may induce occupational asthma through immunological mechanisms that are different from other LMW agents.

The prevalence and clinical features of asthma-chronic obstructive pulmonary disease overlap (ACO) among individuals with WRA has been scarcely investigated. A recent study carried out in

USA by telephone interview found that 51.9% of adults with WRA and 25.6% of adults with non-WRA had ever been diagnosed with COPD. Individuals with concomitant WRA and COPD had more severe exacerbations and worse asthma outcomes than those without the combination of both conditions [11].

Ojanguren *et al.* [12] carried out a retrospective study to evaluate the presence of ACO in individuals with occupational asthma and to compare the clinical characteristics of occupational asthma patients with or without ACO. Of the 304 study individuals, 86.2% were diagnosed with occupational asthma and 13.8% with occupational ACO. Individuals with occupational ACO were older, received higher doses of inhaled corticosteroids (ICS), had been exposed to the culprit agent for a longer period of time, were more frequently exposed to LMW agents (70 vs. 52%) and were less atopic than individuals with occupational asthma. No statistically significant differences were observed between both groups in the inflammatory pattern in sputum. Jaakkola *et al.* [13] reported that the risk of ACO among Finish workers was significantly related to the presence of mold odour in the workplace, but not to other dampness indicators.

## Diagnosis

Occupational asthma is usually diagnosed following a stepwise approach [1,5]. The first step is a focused and complete history taking, aimed at correlating symptoms and exposure to potential sensitizers in the workplace. Occupational asthma diagnosis requires the demonstration of bronchial hyperresponsiveness (BHR) while the patient is still in the workplace. Whenever possible, it is important to evaluate immunological reactivity to the occupational asthma eliciting agent by immunological tests [skin prick testing or specific immunoglobulin E (sIgE) measurements]. SIC with the suspected agent is still considered the reference test to confirm occupational asthma. However, SIC is not always accessible, particularly in a nonspecialized setting. Furthermore, the pattern of bronchial response may be different according to the molecular weight of the implicated agent. Lipińska-Ojzanowska *et al.* [14] have evaluated SIC with workplace allergens and nonspecific BHR in 200 patients with occupational asthma. A single early asthmatic response was more frequently associated with HMW agents exposure (86.2%) than with LMW agents (20%), while an isolated late response was more often observed with LMW agents (45.7%) than with HMW allergens (3.8%), confirming previous reports [7]. Significantly, baseline nonspecific BHR before SIC was more often

detected in LMW-induced occupational asthma than in HMW-induced occupational asthma (81.4 vs. 54.6%). Moreover, the median value of the provocative concentration of methacholine causing a drop in FEV<sub>1</sub> of 20% was significantly lower in LMW-induced occupational asthma pre and post-SIC. Individuals with HMW-induced occupational asthma were older and showed lower levels of BHR than LMW-induced occupational asthma individuals.

Although SIC is the reference test for the diagnosis of occupational asthma, it is a semi-invasive time-consuming procedure which has several limitations: that is, the requirement of sophisticated equipment and space, trained personnel, close supervision and monitoring, while there are scarce referral centres. To overcome these problems, using data from Canadian workers exposed to HMW agents a non-SIC-based model has been proposed to calculate an individuals' probability of occupational asthma diagnosis [15<sup>■</sup>]. In the 160 patients who underwent BHR tests to methacholine while still exposed at workplace 1 month before SIC, the inclusion of different outcomes in the model, such as age 40 years or less, agent type, inhaled corticosteroid use, rhinoconjunctivitis, BHR and specific sensitization to workplace agents, showed a significant higher sensitivity than the combination of work-specific sensitization and BHR alone. This was particularly the case in those patients who were at the top 70% of the clinical scores (96.4 vs. 86.9%), and a better negative predictive value (93.6 vs. 84.1%) ( $P < 0.001$ ) as well. Although with the limitation of being retrospective and derived from data in a highly selected population, this model could offer a simple guidance to physicians to refer suspected cases of occupational asthma caused by HMW agents to specialized centres, where SIC can be performed. However, the model is not applicable to LMW-induced occupational asthma patients (not tested in this population). More recently, this model has been validated using databases from five different specialized centres in Belgium, Finland, Poland and Spain, with a high accuracy in European data for HMW-agents [16]. Similarly to the situation in Canada, this model is not suitable for individuals exposed to LMW-induced agents and those patients who were no longer exposed to the offending workplace agents [16].

Regarding the use of such models, in which sensitization needs to be properly demonstrated, it is well known that sIgE test performance is rather satisfactory for a broad spectrum of HMW agents, whereas this is considerably lower for LMW agents [5,6<sup>■</sup>]. Nonetheless, the number of available and well standardized occupational allergens is limited [17]. Moreover, there is a lack of evidence and

validation for allergen components in most of the HMW-allergens, with the exception of wheat flour, some animal danders and natural rubber latex [18].

Lux *et al.* [19] have systematically reviewed the performance of sIgE measurements in the diagnosis of occupational asthma using data from 62 studies. They confirmed that sIgE detection tests exhibited a pooled sensitivity of 0.74 and a specificity of 0.71 for HMW agents, while showing a lower sensitivity (0.28) and a higher specificity (0.89) for LMW agents. Like in other studies, they found a broad spectrum in the ability to detect sIgE for LMW agents, ranging from the acid anhydrides with relatively high detection rates (sensitivity 81%) to diisocyanates (sensitivity 27%) and a much lower sensitivity for plicatic acid (9.6%) [19,20<sup>■</sup>]. Moreover, negative results for LMW allergens did not exclude sensitization [19,20<sup>■</sup>]. In their systematic review and meta-analysis, Baur *et al.* [20<sup>■</sup>] concluded that there is an urgent need for an international consensus on standardization in the manufacture of extracts and quality control standards and for full transparency of the content of allergen preparations, as previously recommended [21].

## Management and prevention of occupational asthma

All patients with occupational asthma should be managed as other asthmatics with regard to asthma education, appropriate pharmacotherapy as per guidelines, and control of exposure to environmental triggers. In the management of sensitizer-induced occupational asthma, cessation of exposure to the causative agent is of paramount importance; but if not feasible, this may require changes in the work process, occupational hygiene measures such as use of respiratory protective equipment (RPE) or ultimately, removal of the worker from the workplace [22]. In the future, immunomodulation through specific allergen immunotherapy or with biological agents might potentially allow safe ongoing exposure to the workplace, but further studies are needed [1]. A study showed that an air-fed RPE with charcoal filters reduces, but rarely eliminates, the fall in peak expiratory flow in workers with occupational asthma due to metal-working fluids [23]. The efficacy of RPE in the management of workers with sensitizer-induced occupational asthma should be monitored objectively.

In the management of irritant-induced occupational asthma, unlike sensitizer-induced occupational asthma, the exposure would not need to be completely eliminated. Reduction of exposure to irritants in the workplace may require better ventilation, use of RPE, job modification and measures to

reduce the chance of accidental spill or breakdown in industrial processes [22].

Primary prevention for sensitizer-induced occupational asthma focuses on exposure control measures, avoiding the use of agents that are known to induce occupational asthma, and substituting them by safer substances. When this is not possible, reduced exposure to respiratory sensitizers can be effective, with measures such as using encapsulated enzymes, avoiding sprayed products, mechanization and robotization, improving general and local ventilation, using of effective RPE for short potential exposure [22], and keeping environmental exposures to workplace agents below permissible exposure limits. Larsen *et al.* [24], studying a retrospective cohort (1970–2017) of 5024 industrial enzyme production workers, found a dose–response relationship between exposure to industrial enzymes and the risk of developing IgE-mediated allergy, smoking being identified as a major risk factor.

In this context, it has been recently proposed to restrict the use of diisocyanates in the European Union. Scholten *et al.* [25] have systematically reviewed biomarkers for biomonitoring diisocyanates exposure and the need for a harmonized approach is highlighted. Preventive measures have been associated with substantial reductions in the incidence of occupational asthma from natural rubber latex and from diisocyanates [26<sup>■</sup>,27]. Cleaning products remain an unresolved problem at present with respect to asthma risk in janitors, professional cleaners and healthcare workers [26<sup>■</sup>]. Primary prevention for irritant-induced asthma would consist of preventing workers' exposure, accidental or not, to high-level irritant vapour, gases, dusts and fumes.

Secondary prevention comprises medical surveillance programmes (MSP) and other measures for early detection of affected workers allowing early intervention. MSPs usually include a preplacement respiratory questionnaire, spirometry, and if feasible, the performance of specific immunologic tests, FeNO, induced sputum and exhaled breath condensate. There are relatively few studies that have assessed the specific effectiveness of MSP and optimal frequency [22]. The other measures include reducing fear of loss of job and a consequently reduced income for affected workers, screening of coworkers [28], improving knowledge of occupational asthma and the appropriate steps to obtain a correct diagnosis among at-risk workers, their primary care providers, physicians and other healthcare providers [26<sup>■</sup>,27].

Tertiary prevention comprises optimal treatment to minimize impairment. A systematic review of workplace interventions concludes that asthma symptoms and lung function may improve when people with occupational asthma are removed from

exposure, compared with continuous exposure in the same job [29]. Asthma symptoms but not lung function may improve after reducing exposure, compared with continuous exposure; whereas eliminating exposure can improve symptoms and lung function more than reducing exposure among workers exposed to LMW agents [29].

## CONCLUSION

Occupational asthma represents an important burden to the working population. Our knowledge about this complex disease, that includes several phenotypes and endotypes, has markedly improved in recent years. A critical reappraisal of clinical aspects, etiological agents and diagnostic tests of occupational asthma, as well as of optimal preventive and therapeutic strategies, is necessary to achieve better outcomes in its management and prevention. Current research is aimed at establishing the immunological pathways that determine, not only the phenotypes and endotypes of the disease, but also the presence of risk factors and biomarkers that should allow the implementation of a personalized approach [30].

## Acknowledgements

None.

## Financial support and sponsorship

None.

## 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. Quirce S, Campo P, Dominguez-Ortega J, *et al.* New developments in work-related asthma. *Expert Rev Clin Immunol* 2017; 13:271–281.
2. Blanc PD, Annesi-Maesano I, Balmes JR, *et al.* The occupational burden of nonmalignant respiratory diseases. An Official American Thoracic Society and European Respiratory Society Statement. *Am J Respir Crit Care Med* 2019; 199:1312–1334.
3. Moscato G, Apfelbacher C, Brockow K, *et al.* Gender and occupational allergy: report from the task force of the EAACI Environmental & Occupational Allergy Interest Group. *Allergy* 2020. [Online ahead of print]
- Very interesting review article looking at sex differences in the prevalence of occupational allergic diseases.
4. Jeebhay MF, Moscato G, Bang BE, *et al.* Food processing and occupational respiratory allergy – an EAACI position paper. *Allergy* 2019; 74:1852–1871.
5. Quirce S, Sastre J. Occupational asthma: clinical phenotypes, biomarkers, and management. *Curr Opin Pulm Med* 2019; 25:59–63.
6. Tarlo SM, Quirce S. Impact of identification of clinical phenotypes in occupational asthma. *J Allergy Clin Immunol Pract* 2020; S2213–S2198:30601–30602.
- This up-to-date article performs a critical appraisal of the different clinical phenotypes of occupational asthma, the underlying mechanisms and the clinical implications for diagnosis, management and prevention.
7. Vandenplas O, Godet J, Hurdubaea L, *et al.* European network for the PHenotyping of Occupational Asthma (E-PHOCAS) investigators. Are high- and low-molecular-weight sensitizing agents associated with different clinical phenotypes of occupational asthma? *Allergy* 2019; 74:261–272.
8. Vandenplas O, Godet J, Hurdubaea L, *et al.* European network for the PHenotyping of Occupational Asthma (E-PHOCAS) investigators. Severe occupational asthma: insights from a multicenter European cohort. *J Allergy Clin Immunol Pract* 2019; 7:2309–2318.e4.
9. Chung KF, Wenzel SE, Brozek JL, *et al.* International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014; 43:343–373.
10. Suojalehto H, Suuronen K, Cullinan P, *et al.* Phenotyping occupational asthma caused by acrylates in a multicenter cohort study. *J Allergy Clin Immunol Pract* 2020; 8:971–979.e1.
- Excellent article that provides an in-depth analysis of occupational asthma caused by different acrylates and its distinctive phenotypic features.
11. Dodd KE, Mazurek JM. Prevalence of COPD among workers with work-related asthma. *J Asthma* 2019; 1–9. (published online ahead of print, 2019 Jul 15).
12. Ojangeren I, Moullec G, Hobeika J, *et al.* Clinical and inflammatory characteristics of asthma-COPD overlap in workers with occupational asthma. *PLoS One* 2018; 13:e0193144.
13. Jaakkola MS, Lajunen TK, Jaakkola JJK. Indoor mold odor in the workplace increases the risk of asthma-COPD overlap syndrome: a population-based incident case-control study. *Clin Transl Allergy* 2020; 10:3.
14. Lipińska-Ojzanowska A, Nowakowska-Swirta E, Wiszniewska M, Walusiak-Skorupa J. Bronchial response to high and low molecular weight occupational inhalant allergens. *Allergy Asthma Immunol Res* 2020; 12:164–170.
15. 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; 76:495–501.
- This is a novel score-model for occupational asthma induced by high-molecular-weight (HMW)-agents with excellent discrimination. It could be helpful for secondary-care physicians who have access to pulmonary function test and allergy testing in identifying individuals at a high risk of having occupational asthma and in deciding on appropriate referral to a tertiary centre.
16. Suarathana E, Taghiakbari M, Saha-Chaudhuri P, *et al.* The validity of the Canadian clinical scores for occupational asthma in European populations. *Allergy* 2020. [Online ahead of print]
17. van Kampen V, de Blay F, Folletti I, *et al.* EAACI position paper: skin prick testing in the diagnosis of occupational type I allergies. *Allergy* 2013; 68:580–584.
18. Raulf M, Quirce S, Vandenplas O. Addressing molecular diagnosis of occupational allergies. *Curr Allergy Asthma Rep* 2018; 18:6.
19. Lux H, Lenz K, Budnik LT, Baur X. Performance of specific immunoglobulin E tests for diagnosing occupational asthma: a systematic review and meta-analysis. *Occup Environ Med* 2019; 76:269–278.
20. Baur X, Akdis CA, Budnik LT, *et al.* Immunological methods for diagnosis and monitoring of IgE-mediated allergy caused by industrial sensitizing agents (IMExAllergy). *Allergy* 2019; 74:1885–1897.
- In occupational asthma diagnosis, currently, different immunological tests are in use at various diagnostic centres that often produce considerably divergent results. This review and meta-analysis offers recent information about the performance of specific IgE detection tests and its sensitivity and specificity for HMW and low-molecular-weight-agents.
21. Diamant Z, van Maaren M, van Wijk RG, *et al.* Guidance for the regulatory status of allergen extracts in clinical trials. *Eur Respir J* 2015; 46:1223–1225.
22. Lau A, Tarlo SM. Update on the management of occupational asthma and work-exacerbated asthma. *Allergy Asthma Immunol Res* 2019; 11:188–200.
23. Ilgaz A, Moore VC, Robertson AS, *et al.* Occupational asthma: the limited role of air-fitted respiratory protective equipment. *Occup Med (Lond)* 2019; 69:329–335.
24. Larsen AI, Cederkvist L, Lykke AM, *et al.* Allergy development in adulthood: an occupational cohort study of the manufacturing of industrial enzymes. *J Allergy Clin Immunol Pract* 2020; 8:210–218.e5.
25. Scholten B, Kenny L, Duca RC, *et al.* Biomonitoring for occupational exposure to diisocyanates: a systematic review. *Ann Work Expo Health* 2020; 64:569–585.
26. Tarlo SM, Arif AA, Delclos GL, *et al.* Opportunities and obstacles in translating evidence to policy in occupational asthma. *Ann Epidemiol* 2018; 28:392–400.
- The interesting article describes the different degrees of success in the application of prevention measures with three different causative agents occupational asthma: natural rubber latex, diisocyanates and cleaning products in healthcare work.
27. Tarlo SM. Some progress and direction in the prevention of work-related asthma. *Ann Am Thorac Soc* 2020; 17:274–275.
28. Reilly MJ, Wang L, Rosenman KD. The burden of work-related asthma in Michigan. *Ann Am Thorac Soc* 2020; 17:284–292.
29. Henneberger PK, Patel JR, de Groene GJ, *et al.* Workplace interventions for treatment of occupational asthma. *Cochrane Database Syst Rev* 2019; 10:CD006308.
30. Tarlo SM, Maestrelli P. Precision medicine in the area of work-related asthma. *Curr Opin Allergy Clin Immunol* 2018; 18:277–279.