Curr Otorhinolaryngol Rep (2017) 5:220–228
DOI 10.1007/s40136-017-0170-4

SPECIAL TOPICS IN OTORHINOLARYNGOLOGY: OTOLARYNGIC ALLERGY (E TOSKALA, SECTION EDITOR)

Occupational Allergic Airway Disease

Gianna Moscato [1]

Published online: 29 November 2017
© Springer Science+Business Media, LLC 2017

Abstract
Purpose of Review The purpose of this paper was to review recent advances on causal agents, diagnosis and management of occupational allergic airway diseases.
Recent Findings Food-derived products are a major cause of occupational asthma (OA) and occupational rhinitis (OR), and flour and seafood are the most important allergen sources. In recent years, farmers, cleaners, veterinarians, swimming pool workers and waste workers have been shown as novel categories at higher risk. Molecular diagnosis may greatly improve the diagnostic workup of allergic OA and OR. The use of immunotherapy and biologics may ameliorate the treatment of allergic OA.
Summary Occupational allergies are a burden for society and surveillance of exposed workers may identify new categories at risk. Cessation of exposure is the best treatment option for OA and OR. An accurate environmental control is needed to reduce asthma exacerbations in work-exacerbated asthma. The management of occupational allergic airway diseases should include a follow-up programme providing close collaboration between health care providers and patients, and ad hoc educational tools aimed at ameliorating patient's knowledge should be developed.

Keywords Work-related asthma · Occupational asthma · Work-related rhinitis · Occupational rhinitis · Diagnosis · Management

Introduction

The burden of occupational respiratory diseases is a global health problem. It is estimated that up to 25% of all adult asthma cases in the general population are related to work [1]. The term 'work-related asthma' (WRA) encompasses two nosological entities: *occupational asthma* (OA), namely asthma 'caused' by workplace exposure, and *work-exacerbated asthma* (WEA), i.e. personal asthma that 'worsens' at work, triggered by various work-related factors (e.g. irritants, aeroallergens, exercise) [2]. WRA also includes variants such as occupational eosinophil bronchitis or potroom asthma (Fig. 1).

Work-related rhinitis (WRR) is also commonly found in workers and is frequently associated to asthma, with which it shares same mechanisms and agents [3].

The purposes of this paper are to summarize the current scientific evidence on causal agents, diagnosis and management of WRA and WRR, and to review the specific literature published within the years 2014–2017.

Data Sources, Search Strategy and Study Selection

A literature search was conducted using PubMed Medline. Published studies in English from January 1, 2014 through June 30, 2017 were identified having key words as 'work-related' OR 'occupational' AND 'asthma' OR 'rhinitis' OR 'respiratory' AND 'diagnosis' OR 'management'. Reference citations published within the 2014–2017 timeframe that had

This article is part of the Topical Collection on *Special Topics in Otorhinolaryngology: Otolaryngic Allergy*

✉ Gianna Moscato
giannamoscato12@gmail.com

[1] Specialization School in Occupational Medicine, Department of Public Health, Forensic and Experimental Medicine, University of Pavia, Via San Felice 2, 27100 Pavia, Italy

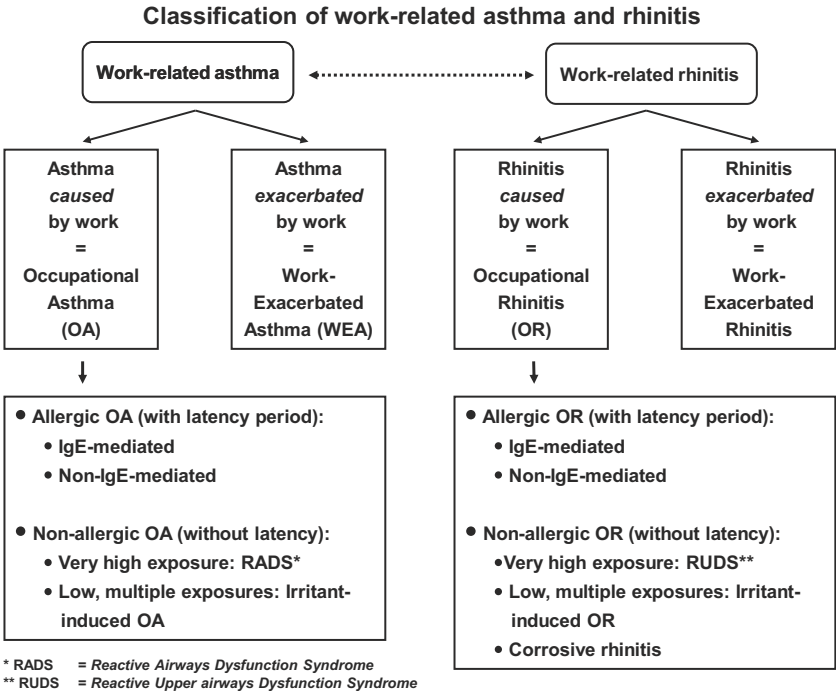

Fig. 1 Classification of work-related asthma and work-related rhinitis (from Ref. 3)

not been otherwise identified in the initial search were added where relevant. One hundred twenty-five papers, including case reports, original articles, reviews, position papers and consensus documents of scientific societies, were found for WRA, and 25 for WRR. The most relevant were included in the article and reviewed by the author.

Work-Related Asthma

Excellent comprehensive reviews on WRA have been published in the last years [4••, 5••].

OA is the most frequent type of WRA and is currently one of the most common occupational lung disease reported in countries with surveillance schemes all around the world [4••, 6••]. Two subtypes are recognized:

1. *Allergic* OA, consequent to exposure to a sensitizing high-molecular weight (HMW) agent (> 10 kDa), or to a low-molecular weight (LMW) agent acting through an immunological IgE- or non-IgE-mediated mechanism. It is characterized by the presence of a latency period between beginning of exposure and symptom onset. It is associated to rhinitis in a high proportion of cases.
2. *Non-allergic* OA, induced by irritants through non-immunological mechanism (*IIA*). A new classification of IIA has recently been proposed based on clinical and exposure characteristics, as well as on the level of available evidence that supports a causal relationship between workplace exposure to irritants and the inception of asthma on an individual basis (Fig. 2) [7••]. The most definite form of IIA is the acute-onset reactive airway dysfunction syndrome (RADS), in which a close temporal relationship between exposure to a single or multiple exposure to very high doses of an irritant may be identified. Subacute IIA, i.e. asthma that develops more insidiously in subjects with a history of multiple symptomatic high-level exposures, should be considered as 'probable' IIA. IIA that develops after chronic 'moderate' irritant exposures at work can only be considered as 'possible' IIA, since the causal relationship cannot be confirmed with certainty on an individual basis. Evidence of a causal effect of chronic workplace irritant exposure in new-onset asthma remains limited, and further research is needed to improve assessment of irritant exposures and identify biomarkers [8]. The chronic type of IIA may be difficult to differentiate from immunological LMW agent-induced asthma [7••, 8] and from WEA [2].

WEA has recently been reviewed [9••]: it may occur in up to 21% of working asthmatics, but it seems to be frequently unrecognized. Workers with WEA appear to have features of greater asthma severity than workers with OA [10]. WEA severity may range from a unique mild exacerbation to daily or severe exacerbations that may require a change of work. Both OA and WEA are associated with greater health care use and tenfold higher direct costs than non-work-related asthma. An accurate control of work exposures and asthma management may improve outcome and prevent exacerbations.

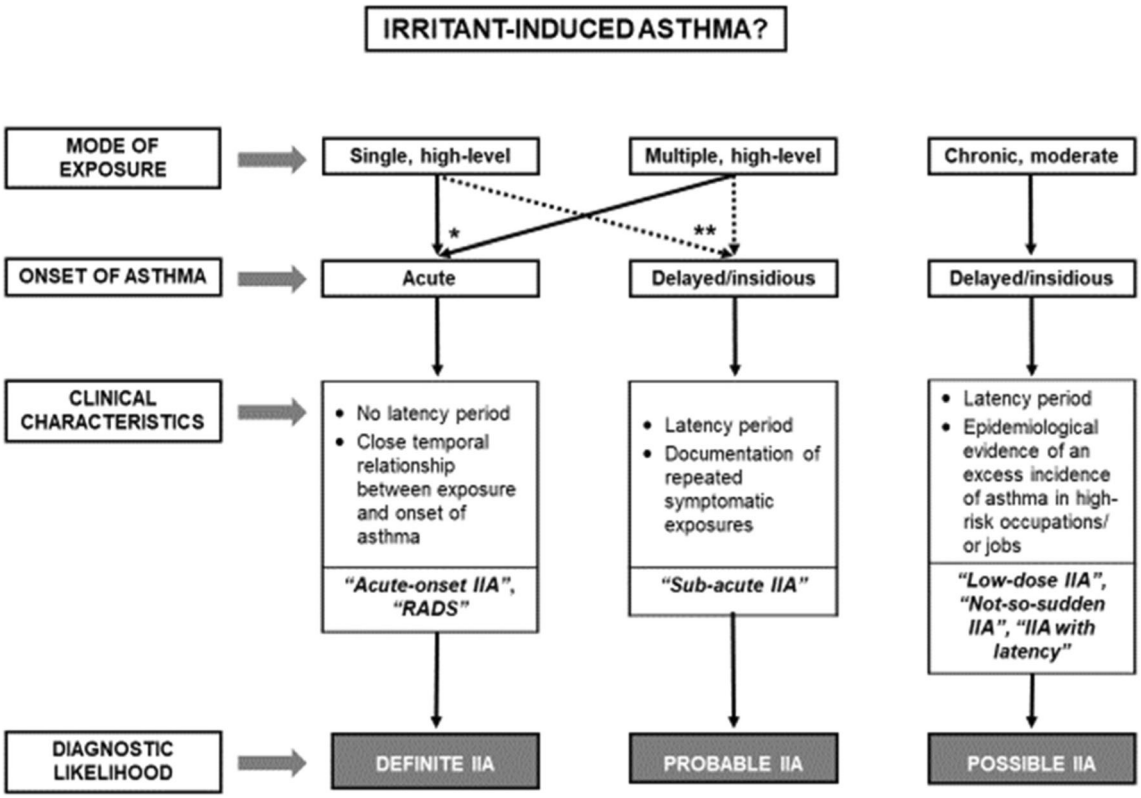

Fig. 2 Classification of irritant-induced asthma (adapted from Ref. 7) (see enclosed file)

More than 300 causal agents of OA have been associated with WRA [5••]. The Association of Occupational and Environmental Clinics has elaborated a web-based listing of agents associated with new-onset WRA, categorising substances as sensitizing agent or irritant [11]. Among a total of 327 substances identified as causative agents of OA, 52.9% were coded as sensitizers, 10.7% as generally recognized as an asthma-causing agent, 1.2% as irritants and 0.6% as both a sensitizer and an irritant, and 34.6% agents were pending of revision. Table 1 reports common causal agents of sensitizer-induced OA and categories of workers at major risk. However, every year, new agents and categories at risk are reported in the literature.

Occupational exposure to foods by inhalation is a major cause of respiratory occupational allergy, asthma, rhinitis and hypersensitivity pneumonitis [12–14]. The International Labour Organisation estimates that the food industry comprises about 10% of the global working population, including a broad spectrum of occupations, from farmers to food processing industry workers. Food-derived hazardous substances include biological agents containing HMW proteins derived from plant or animal sources, additives and enzymes, and food contaminants [13].

Baker's asthma is an allergic, IgE-mediated OA and is a leading cause of OA all around the world [15–18, 19•, 20]. Bakers and pastry makers employed in small enterprises or in supermarket bakeries are the workers most frequently affected [15, 21]. Wheat and rye flour proteins, and the enzyme alpha-amylase used as bread improver are the most frequently involved allergens [15, 16, 22••]. However, recent papers highlight the importance of sensitization to other enzymes [23, 24, 25•].

Seafood processing industry workers and those employed in maritime environment are also at higher risk for allergic asthma and rhinitis [26, 27, 28•]. OA is more commonly associated with shellfish (4–36%), which include crustaceans and molluscs, than with bony fish (2–8%) [27, 29].

Exposure to animal allergens is the greatest risk factor for developing OA and OR in laboratory workers. In addition to IgE-related mechanisms, others, such as innate immune responses, possibly related to endotoxin, may be involved [30•].

Respiratory allergies due to storage mites have been reported in people with various occupations (farmers, grain workers, bakers, laboratory researchers). A recent interesting Italian paper also provides strong evidence that storage mites play a role in the onset of allergic respiratory disorders in ham production worker [31•].

Farmers employed in different occupations, but especially those who grow and harvest crops, are considered at increased risk for developing food-induced OA and OR [13]. The results of a survey conducted on 2011 Farm and Ranch Safety Survey data suggest that the proportion of US farm operators with current asthma that may have farm WRA is higher than the proportion of US ever-employed adults with current asthma who have WRA [32•].

Table 1 Common causal agents and occupations at risk for occupational asthma and occupational rhinitis

Agents	Occupation
HMW agents	
Cereal flours, enzymes	Bakers, food industry workers, farmers
Shellfish, bony fish	Seafood workers, maritime workers
Laboratory animals (rat, mouse)	Laboratory workers
Latex	Health care workers
Animal-derived allergens, plant allergens, moulds	Farmers, greenhouse workers
Biological enzymes	Pharmaceutical and detergent industry workers
LMW agents	
Cleaning products	Cleaners
Persulfates	Hairdressers
Isocyanates	Plastic industry workers, spray painters,
Acid anhydrides	Plastic industry workers
Wood dust	Carpenters, furniture makers
Drugs	Pharmaceutical workers, health care workers
Mixture of irritants	Chemical factory workers

A study carried out in Champagne vineyard workers in France found a prevalence of work-related respiratory symptoms of 11%, which was associated with sensitization to grass pollens and with activities performed close to vine in late spring [33].

Healthcare workers remain a category at high risk for occupational respiratory diseases, being exposed to a bulk of HMW and LMW agents, i.e. allergic sensitizers or irritants, including natural rubber latex, various medications, disinfectants (mainly alcohol bleach and sprays) and cleaning products [34–38].

There is evidence that cleaning products, including cleaning sprays, bleach, ammonia and disinfectants (e.g., chloramine-T, quaternary ammonium compounds and ethanolamine), can aggravate asthma and also give rise to OA [35]. Women are most of workers exposed at risk and have a higher frequency than men of work-related respiratory symptoms and diseases [39•, 40]. An irritant mechanism seems more common, although several case reports show an immunologic mechanism, especially in healthcare workers exposed to disinfectants [39•].

Interestingly, recent papers have shown an excess risk for asthma and respiratory symptoms in novel categories of workers, like swimming pool workers, and regulations to require air monitoring and improvements in ventilation are recommended to reduce exposure levels of chloramines, the presumed etiologic agents [41, 42].

Diagnosis of WRA

Since up to 25% of cases of adult asthma are related to work, an occupational origin should be sought for every new-onset asthma in an adult. The possibility of a WEA should also be considered in any asthmatic patient with repeated asthma exacerbations.

Notwithstanding, WRA is still underdiagnosed and underdetected worldwide [6••, 43, 44]. One reason may be the scarce awareness of the disease among specialists, as shown by a recent study performed among Italian allergists, and another, the complexity of the diagnostic workup [19•]. An operative protocol addressed to allergists and physicians dealing with asthma useful for identifying the subjects suspected of having WRA has been developed by an ad hoc EAACI task force [2]. A correct diagnosis is extremely important to reduce or limit the consequences of the disease. Missing a diagnosis of OA may lead to continued exposure of the worker to the culprit agent, with progressive deterioration of asthma; conversely, a diagnosis of OA when it is not present may lead to inappropriate removal from exposure and unnecessary financial disruption and unemployment [4••]. Diagnosing and differentiating WEA from OA is of utmost importance because their treatment, prognosis, and medical and social impact greatly differ [45].

The clinical investigation of OA is a stepwise process with a two-sided objective: the first is to demonstrate the presence of asthma and the second to confirm its relationship to work [2]. The starting point is a detailed clinical and occupational history, aimed to investigate type of symptoms and work-relatedness, and to collect information on occupational exposure. The presence of comorbidities should be investigated, especially rhinitis, which is associated to allergic OA in up to 92% of cases and may affect its severity [46•]. Documentation on noxious compounds (sensitizers and irritants) present at the workplace to which the worker is more directly exposed should be obtained by the employer (material safety data sheets etc.) [2].

History has a low specificity for diagnosis and must be confirmed by objective tests, which partially differ for allergic and non-allergic OA (Table 2).

The presence of asthma may be confirmed by means of spirometry, bronchodilator test and/or measurement of non-specific bronchial hyperresponsiveness (NSBH). Afterwards, a first confirmation of work-relatedness of asthma may be obtained through serial measurement of peak expiratory flow (PEF) in periods at work and away from work. To increase PEF sensibility and specificity, serial measurements of NSBH to methacholine may be associated [2].

When an allergic mechanism is suspected, demonstration of sensitization to an occupational allergen through skin prick tests (SPT) and/or measurement of serum-specific IgE (sIgE) is the further step. The use of these tools is greatly limited by the lack of commercial validated extracts for several allergens. Molecular diagnosis has allowed a better identification of the responsible allergenic proteins at a molecular level at least for some allergens (seafood, latex etc.) [22••, 26, 47•, 48•]. The basophil activation test (BAT) which measures basophil response to allergen-mediated cross-linking of IgE antibodies can be a part of the diagnostic evaluation since it may be helpful in determining the clinically relevant allergen [49, 50]. However, it is not yet available for routine testing.

The specific inhalation challenge (SIC) in the laboratory is considered a reference standard for the diagnosis of OA induced by sensitizers. A consensus statement on SIC, including methodological aspects and the indications for performing the test, has recently been published by the European Respiratory Society [51••]. SIC may also be useful to differentiate between allergic OA and subacute IIA, and between OA and WEA, although the possibility of false negative results, e.g. if tests do not include the relevant sensitizer, should be taken into account [7••, 9••, 45, 52•].

The assessment of bronchial inflammation by means of sputum analysis and/or measurement of fractional exhaled nitric oxide (FeNO) levels is an important supplemental investigation in the diagnosis of OA and should be incorporated in the diagnostic workup, as well as in assessing the SIC response [5••, 51••, 53]. Sputum cell count analysis and a methacholine challenge before and after exposure to the offending agent may represent an effective alternative in diagnosing OA when SICs are unavailable [54•]. Assessment of inflammation is also a key step for diagnosing eosinophilic bronchitis, a variant of WRA, and for characterizing WEA [10, 55].

The diagnosis of irritant OA can usually be established with a reasonable confidence only for the acute-onset type (RADS) based on the retrospective documentation of a close temporal relationship between an inhalation incident and the acute-onset of asthma symptoms, associated to airflow limitation or NSBH. Diagnosis of the other types of IIA is more insidious and difficult [7••].

Two recent comprehensive reviews have discussed the advantages and limitations of each test used in the diagnostic workup of OA, and proposed clinical practice recommendations and a stepwise diagnostic algorithm [56•, 57•].

Management of WRA

The most important measure in management of OA is removing the affected worker from exposure to the sensitizing agent as much as possible, along with timely therapy [4••]. Intervention should be performed as early as possible after symptom onset to prevent permanent asthma; therefore, an early diagnosis is mandatory for a favourable outcome of the disease. Cessation of exposure is the best option for a favourable outcome and is more often obtained through change of work, which may provoke financial disruption for the worker. When exposure cannot be completely avoided, reduction of exposure may be considered as an alternative, although available evidence indicates that reduced exposure is less beneficial than exposure cessation [58].

Pharmacologic therapy should follow the current international asthma guidelines [59]. In IgE-mediated OA, specific allergen immunotherapy (SIT), when validated extracts are available, might be a useful management option able to keep the patient at work [60]. Notwithstanding, due to the lack of commercial standardized extracts, SIT has been scarcely used in occupational allergic diseases, and only for a few HMW sensitizers such as latex, flour, Hymenoptera venom and rodents [61••, 62]. A better identification on a molecular basis of allergens involved in IgE-mediated OA might help in preparing new extracts suitable for immunotherapy.

In selected cases of baker's asthma, the anti-IgE monoclonal antibody omalizumab has been proven to be effective in reducing symptoms [63, 64]. In a recent experimental study performed in a mouse model of OA, using persulfate salts, anti-IgE-treated mice showed a significant improvement in asthma features related to the non-specific bronchial hyperreactivity and airway inflammation, showing that anti-IgE monoclonal antibody has positive effects in murine OA induced by LMW agents [65•].

The management of WEA includes an optimal environmental control and pharmacologic asthma therapy. Usually, a worker with WEA can return to the workplace if measures are taken to limit subsequent exposures to irritants and other non-specific triggers (exercise, etc.) [9••, 43].

The optimal management of WRA should include a follow-up programme, with periodic assessment of symptoms and lung function, and close collaboration between health care providers and patients, to provide education and skills on the disease. Recent studies indicate that a substantial number of asthma patients have inadequate knowledge of work-related effects on their disease, which may contribute to suboptimal asthma control, and that only a small proportion of patients with asthma might communicate with a health professional about asthma associated with work [66, 67]. The administration of a web-based educational tool on WRA especially developed in Canada to address this knowledge gap in a routine visit at a tertiary care asthma clinic in Toronto showed that the

Table 2 Diagnostic workup of allergic occupational asthma

	Test
1.History suggestive for OA and exposure documentation	
2.Confirmation of bronchial asthma	Typical symptoms, spirometry, bronchodilator test, NSBH to methacholine
3.Confirmation of work-relatedness of asthma	Serial measurements of PEF, alone or associated to serial measurement of NSBH
4.Confirmation of sensitization and of causal role of an occupational agent	SPT and serum sIgE (when available), molecular diagnosis, BAT, SIC with airway inflammation assessment (sputum and/or FeNO)

NSBH non-specific bronchial hyperresponsiveness, *PEF* peak expiratory flow, *SPT* skin prick test, *sIgE* serum-specific IgE, *BAT* basophil activation test, *SIC* specific inhalation challenge

educational tool has a positive effect on WRA knowledge, and that knowledge may be retained in long term [66].

Every patient receiving a diagnosis of OA or WEA should be referred to local authorities for compensation.

Occupational Rhinitis

Occupational rhinitis (OR) is a recognized medical condition which very often presents in association with OA. It is defined as an inflammatory disease of the nose, which is characterized by intermittent or persistent symptoms (i.e. nasal congestion, sneezing, rhinorrhea, itching), and/or variable nasal airflow limitation and/or hypersecretion due to causes and conditions attributable to a particular work environment, and not to stimuli encountered outside the workplace [3, 68]. OR may precede the onset of asthma of 6–12 months; thus, it is considered an early marker of OA. The two conditions share causal agents and the underlying pathogenic mechanisms and inflammation, and can be considered in the broader context of the 'united airway disease' (UAD) mode [68, 69•] (Table 1). The severity of OR may affect the severity of OA [46•].

OR has received increasing interest in the last years, and novel categories of workers at increased risk have been identified. The 2011 Farm and Ranch Safety Survey data were used to investigate the prevalence of lifetime allergic rhinitis and factors associated with allergic rhinitis among US primary farm operators in 2011. An estimated 30.8% of the 2.1 million active farm operators had lifetime allergic rhinitis in 2011. A possible association with pesticide exposure was found [70].

Occupational bioaerosol exposure may induce acute and chronic health effects caused by organic dust in exposed workers, such as compost workers and waste collectors [71]. A cross-sectional study on a total of 69 male waste collectors from the Ruhr area in Germany showed that a high percentage of workers had complaints (eyes 29.0%, nose 39.1% and cough 34.8%) which were strongly work-related, with an association between duration of employment in waste collection (per 10 years) and an increased prevalence of cough (OR = 1.64; 95% CI 0.81, 3.35) and chronic bronchitis (OR = 2.18; 95% CI 0.80, 5.92). An association between rhinitis and cough (OR = 2.62; 95% CI 0.94, 7.27) was also found, supporting the relationships between upper and lower airway disease. Notably, an underlying allergic disease in waste collectors could be suspected more commonly than previously reported [72]. In another study by the same group, aimed to evaluate inflammatory processes in blood and in the respiratory tract in German waste collectors, 63 and 64% of workers reported complaints of the eyes, nose and/or upper airways [73].

Veterinarians are a category of workers at risk for animal-related allergy. In two repeated cross-sectional surveys in 2006 and 2012 in Bavaria, prevalence of allergic symptoms ranged from 5.1 to 5.6% for asthma, 17.0 to 20.2% for rhinitis and 11.4 to 14.3% for wheezing, as well as 7.2 to 11.3% for wheezing without having a cold. The percentage of women in this occupation grew between the first and second survey [74].

A cross-sectional study performed in Italy aimed at investigating the prevalence of work-related upper and lower airway and eye symptoms in 118 workers in polyurethane shoe sole production, exposed to low level of MDI and solvents, found a high prevalence of cough and nasal congestion [75].

Hairdressers are a well-known category at the highest risk for allergic OA and OR, mainly due to persulfate salts [76]. A recent paper has shown an increased risk for OR also in hairdressing apprentices, and bleaching products were found as the main cause of respiratory symptoms [77].

Diagnosis of OR is a stepwise process [3, 68]. The first step is an accurate clinical and occupational history, followed by nasal examination through anterior rhinoscopy and nasal endoscopy, with assessment of nasal patency and of inflammation in nasal secretions. When an allergic mechanism is suspected, SPT and/or sIgE assessment, when standardized and validated extracts are available, can demonstrate sensitization to an occupational agent. A definite diagnosis can only be established by objective demonstration of the causal relationship between rhinitis and the work environment through nasal provocation test with the suspected agent(s) in the laboratory, which is considered the gold standard for diagnosis [3, 68].

The management of allergic OR includes avoidance or reduction of culprit exposures, and pharmacologic treatment which does not differ from that of non-occupational rhinitis [78]. In allergic OR due to HMW sensitizers, SIT may be proposed when validated extracts are available [3, 68].

Conclusions

In conclusion, occupational allergic airway diseases, WRA and WRR, are still a burden for the society. These diseases are potentially preventable. In OA and OR, elimination of exposure to known sensitizing agents is the most effective measure at a primary, secondary and tertiary levels. When elimination is not possible, reduction of exposure to workplace sensitizers by means of hygiene measures, monitoring airborne allergen levels, is the second best option. An accurate surveillance of workers at the workplace may help in identifying new categories at risk and in preventing adverse health and economic consequences. In WEA, an optimal environmental control may help to reduce asthma exacerbations at the workplace.

The management of WRA and WRR should include a follow-up programme providing close collaboration between health care providers and patients, and ad hoc educational tools aimed at ameliorating WRA and WRR knowledge should be developed. Education of workers on work practices able to reduce exposure and on therapy may help for a favourable outcome and should be implemented especially in high-risk occupations.

Compliance with Ethical Standards

Conflict of Interest The author declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by the author.

References

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. Kogevinas M, Zock JP, Jarvis D, et al. Exposure to substances in the workplace and new-onset asthma: an international prospective population-based study (ECRHS-II). Lancet. 2007;370:336–41.
2. Moscato G, Pala G, Barnig C, et al. EAACI consensus statement for investigation of work-related asthma in non-specialized centres. Allergy. 2012;67(4):491–501. Review
3. Moscato G, Vandenplas O, Gerth Van Wijk R, et al. Occupational rhinitis. EAACI position paper. Allergy. 2008;63:969–80.
4. •• Tarlo SM, Lemiere C. Occupational asthma. N Engl J Med. 2014;370(7):640–9. **An outstanding state of the art review paper on occupational asthma**
5. •• Quirce S, Campo P, Domínguez-Ortega J, et al. New developments in work-related asthma. Expert Rev Clin Immunol. 2017;13(3): 271–81. **A comprehensive and updated review paper on work-related asthma**
6. •• Cullinan P, Muñoz X, Suojalehto H, et al. Occupational lung diseases: from old and novel exposures to effective preventive strategies. Lancet Respir Med. 2017;5(5):445. Review. **An outstanding review paper providing recommendations for research, surveillance and other actions for reducing the burden of occupational lung diseases.**
7. •• Vandenplas O, Wiszniewska M, Raulf M, et al. EAACI position paper: irritant-induced asthma. Allergy. 2014;69:1141–53. **Consensus paper giving new insights into irritant-induced asthma**
8. Dumas O, Le Moual N. Do chronic workplace irritant exposures cause asthma? Curr Opin Allergy Clin Immunol. 2016;16(2):75–85. Review.
9. •• Tarlo SM. Update on work-exacerbated asthma. Int J Occup Med Environ Health. 2016;29(3):36974. Review**. An in-depth review paper on work-exacerbated asthma.**
10. Lemière C, Boulet LP, Chaboillez S, Forget A, Chiry S, Villeneuve H, et al. Work-exacerbated asthma and occupational asthma: do they really differ? J AllergyClin Immunol. 2013;131:704–10.
11. Rosenman KD, Beckett WS. Web based listing of agents associated with new onset work-related asthma. Respir Med. 2015;109:625–31.
12. Cartier A. The role of inhalant food allergens in occupational asthma. Curr Allergy Asthma Rep. 2010;10:349–56.
13. Moscato G, Pala G. Occupational allergy to food-derived allergens. AIMS Allergy and Immunology. 1(1):21–30. https://doi.org/10.3934/Allergy.2017.1.21.
14. Quirce S, Vandenplas O, Campo P, et al. Occupational hypersensitivity pneumonitis: an EAACI position paper. Allergy. 2016;71: 765–79.
15. Brant A. Baker's asthma. Curr Opin Allergy Clin Immunol. 2007;7(2):152–5.
16. Quirce S, Diaz-Perales A. Diagnosis and management of grain-induced asthma. Allergy Asthma Immunol Res. 2013;5:348–56.
17. Cianferoni A. Wheat allergy: diagnosis and management. J Asthma Allergy. 2016;9:13–25. Review
18. Walters GI, Kirkham A, McGrath EE, et al. Twenty years of SHIE LD: decreasing incidence of occupational asthma in the West Midlands, UK? Occup Environ Med. 2015;72(4):304–10.
19. • Moscato G, Maestrelli P, Bonifazi F, et al. OCCUPATION study (OCCUPationl asthma: a naTIONal based study): a survey on occupational asthma awareness among Italian allergists. Eur Ann Allergy Clin Immunol. 2014;46(1):26–9. **A national study demonstrating the scarce awareness of Italian allergists on occupational asthma**
20. Mbatchou Ngahane BH, Nde F, Ngomo E, et al. Sensitization to workplace respiratory allergens among bakery workers in Douala, Cameroon: a cross-sectional study. Allergy Asthma Clin Immunol. 2015;11(1):13.
21. Brant A, Berriman J, Sharp C, et al. The changing distribution of occupational asthma: a survey of supermarket bakery workers. Eur Respir J. 2005;25:303–8.
22. •• Raulf M. Allergen component analysis as a tool in the diagnosis of occupational allergy. Curr Opin Allergy Clin Immunol. 2016;16(2): 93–100. **An in-depth comprehensive review of the component-resolved diagnosis in occupational allergy**
23. Simonis B, Hölzel C, Stark U. Glucoamylase: a current allergen in the baking industry. Allergo J Int. 2014;23(8):269–73.

24. Lipińska-Ojrzanowska A, Wiszniewska M, Pas-Wyroślak A, et al. Sensitization to xylanolytic enzymes: an underestimated health hazard among bakers. Occup Med (Lond). 2016;66(5):415–8.
25.• Jones M, Welch J, Turvey J, et al. Prevalence of sensitization to 'improver' enzymes in UK supermarket bakers. Allergy. 2016;71(7):997–1000. **An original paper showing that specific sensitization in symptomatic bakers should be identified only considering a wide range of workplace antigens**
26. Jeebhay MF, Cartier A. Seafood workers and respiratory disease: an update. Curr Opin Allergy Clin Immunol. 2010;10:104–13.
27. Lopata AL, Jeebhay MF. Airborne seafood allergens as a cause of occupational allergy and asthma. Curr Allergy Asthma Rep. 2013;13(3):288–97.
28.• Lucas D, Lodde B, Jepsen JR, et al. Occupational asthma in maritime environments: an update. Int Marit Health. 2016;67(3):144–52. A**n update review paper of the current knowledge on occupational asthma in a maritime context, providing recommendations regarding medical surveillance of workers at risk**
29. Boulet LP, Laberge F. Occupational asthma to fish. Occup Environ Med. 2014;71(11):804.
30.• Jones M. Laboratory animal allergy in the modern era. Curr Allergy Asthma Rep. 2015;15(12):73. https://doi.org/10.1007/s11882-015-0575-4. **An in-depth review paper discussing the complexity of mechanisms involved in laboratory animal allergy**
31.• Tafuro F, Ridolo E, Goldoni M, et al. Work-related allergies to storage mites in Parma (Italy) ham workers. BMJ Open. 2015;5(5):e007502. **This interesting paper provides strong evidence that storage mites play a role in the onset of allergic respiratory disorders in ham production workers**
32.• Mazurek JM, White GE, Rodman C, et al. Farm work-related asthma among US primary farm operators. J Agromedicine. 2015;20(1):3142. **This study documents the prevalence of current asthma and farm work-related asthma among US primary farm operators**
33. Perotin JM, Barbe C, Nguyen KL, et al. Work-related respiratory symptoms in Champagne vineyard workers. Eur Ann Allergy Clin Immunol. 2015;47(5):140–4.
34. Quinot C, Dumas O, Henneberger PK, et al. Development of a job-task exposure matrix to assess occupational exposure to disinfectants among US nurses. Occup Environ Med. 2017;74(2):130137.
35. Siracusa A, De Blay F, Folletti I, et al. Asthma and exposure to cleaning products—a European Academy of Allergy and Clinical Immunology task force consensus statement. Allergy 2013;68(12):1532–1545. Review.
36. Wiszniewska M, Walusiak-Skorupa J. Occupational allergy: respiratory hazards in healthcare workers. Curr Opin Allergy Clin Immunol. 2014;14(2):113–8.
37. Mazurek JM, Weissman DN. Occupational respiratory allergic diseases in healthcare workers. Curr Allergy Asthma Rep. 2016;16(11):77. Review.
38. Casey ML, Hawley B, Edwards N, et al. Health problems and disinfectant product exposure among staff at a large multispecialty hospital. Am J Infect Control. 2017;1;45(10):1133–1138.
39.• Folletti I, Siracusa A, Paolocci G. Update on asthma and cleaning agents. Curr Opin Allergy Clin Immunol. 2017;17(2):90–5. **A updated review paper on cleaning-related asthma**
40. Lipinska Ojrzanowska AA, Wiszniewska M, WalusiakSkorupa JM. Work-related asthma among professional cleaning women. Arch Environ Occup Health. 2017;72(1):5360.
41. Rosenman KD, MillerickMay M, Reilly MJ, et al. Swimming facilities and work-related asthma. J Asthma. 2015;52(1):528.
42. Bureau G, Lévesque B, Dubé M, et al. Indoor swimming pool environments and self-reported irritative and respiratory symptoms among lifeguards. Int J Environ Health Res. 2017;25:1–17.
43. Cruz MJ, Muñoz X. Work-related asthma: the dawn of knowledge? Arch Bronconeumol. 2017;53(4):180–1.
44. Vila-Rigat R, Panadès Valls R, Hernández Huet E, et al. Prevalence of work-related asthma and its impact in primary health care. Arch Bronconeumol. 2015;51:449–55.
45. Muñoz X, Cruz MJ, Bustamante V, et al. Work-related asthma: diagnosis and prognosis of immunological occupational asthma and work-exacerbated asthma. J Investig Allergol Clin Immunol. 2014;24(6):396–405. Review.
46.• Moscato G, Pala G, Folletti I, et al. Occupational rhinitis affects occupational asthma severity. J Occup Health. 2016;58(3):310–3. **An original paper demonstrating a significant association between occupational rhinitis and asthma severity**
47.• Sander I, Rihs HP, Doekes G, 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. **An original paper showing adavantages and limitations of molecular diagnosis in baker's allergy**
48.• Vandenplas O, Froidure A, Meurer U, et al. The role of allergen components for the diagnosis of latex-induced occupational asthma. Allergy. 2016;71:840–9. **An updated paper showing the clinical utility of molecular diagnosis in occupational asthma caused by latex**
49. Tonini S, Perfetti L, Pignatti P, et al. Occupational asthma induced by exposure to lima bean (Phaseolus lunatus). Ann Allergy Asthma Immunol. 2012;108(1):66–7.
50. Pignatti P, Yacoub MR, Testoni C, et al. Evaluation of basophil activation test in suspected food hypersensitivity. Cytometry B Clin Cytom. 2015;92(4):279–285.
51.•• Vandenplas O, Suojalehto H, Aasen TB, et al. ERS task force on specific inhalation challenges with occupational agents specific inhalation challenge in the diagnosis of occupational asthma: consensus statement. Eur Respir J. 2014;43:1573–87. **Seminal consensus paper describing the indications and methodological aspects of specific inhalation challenge with occupational agents**
52.• de Olim C, Bégin D, Boulet LP, et al. Investigation of occupational asthma: do clinicians fail to identify relevant occupational exposures? Can Respir J. 2015;22(6):341–347. Epub 2015 Sep 30. **This interesting paper shows that there may be a gap between hygienists and clinicians in identifying the causal agent of OA, which may result in misdiagnosis.**
53. Quirce S, Lemière C, de Blay F, et al. Non-invasive methods for assessment of airway inflammation in occupational settings. Allergy. 2010;65:445–58.
54.• Racine G, Castano R, Cartier A, et al. Diagnostic accuracy of inflammatory markers for diagnosing occupational asthma. J Allergy Clin Immunol Pract. 2017;5(5):1371–1377. **An elegant paper showing that sputum cell count analysis and a methacholine challenge before and after exposure to the offending agent may represent an effective alternative in diagnosing OA when SICs are unavailable**
55. Pala G, Pignatti P, Moscato G. Occupational non-asthmatic eosinophilic bronchitis: current concepts. Med Lav. 2012;103(1):17–25.
56.• Jolly AT, Klees JE, Pacheco KA, et al. Work-related asthma. J Occup Environ Med. 2015;57(10):e1219. **This in-depth review summarizes evidence-based diagnostic and treatment guidelines for work-related asthma (WRA)**
57.• Vandenplas O, Suojalehto H, Cullinan P. Diagnosing occupational asthma. Clin Exp Allergy. 2017;47(1):618. Review. **A useful and practical paper providing a technical dossier of the diagnostic value of the available methods for diagnosing occupational asthma**.
58. Vandenplas O, Dressel H, Nowak D, ERS Task Force on the Management of Work-related Asthma, et al. What is the optimal management option for occupational asthma? Eur Respir Rev. 2012;21:97–104.
59. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2016. Available from: www.ginasthma.org.

60. Tarlo SM, Balmes J, Balkissoon R, et al. Diagnosis and management of work-related asthma: American College of Chest Physicians Consensus Statement. Chest. 2008;134:1S–41S.
61.•• Moscato G, Pala G, Sastre J. Specific immunotherapy and biological treatments for occupational allergy. Curr Opin Allergy Clin Immunol. 2014;14(6):576–81. **An up-to-date review paper on allergen immunotherapy and biological treatments applied to occupational allergy**
62. Goddard AG, Azar AE. Work-related asthma secondary to IgE-mediated reactions to rodents successfully treated with immunotherapy. Ann Allergy Asthma Immunol. 2016;117(5):556558.
63. Olivieri M, Biscardo CA, Turri S, et al. Omalizumab in persistent severe bakers' asthma. Allergy. 2008;63:790–1.
64. Pérez Pimiento A, Bueso Fernández A, García Loria J, et al. Effect of omalizumab treatment in a baker with occupational asthma. J Investig Allergol Clin Immunol. 2008;18:490–1.
65.• Ollé-Monge M, Cruz MJ, Gomez-Ollés S, et al. Effect of anti-IgE in occupational asthma caused by exposure to low molecular weight agents. Allergy. 2017; https://doi.org/10.1111/all.13190. **A very elegant study performed in a mouse model of OA showed that anti-IgE mAb omalizumab has positive effects in OA induced by LMW agents such as persulfate salts**
66. Lipszyc JC, Gotzev S, Scarborough J, et al. Evaluation of the efficacy of a web-based work-related asthma educational tool. J Asthma. 2016;53(10):10715.
67. Mazurek JM, White GE, Moorman JE, et al. Patient physician communication about work-related asthma: what we do and do not know. Ann Allergy Asthma Immunol. 2015;114(2):97102.
68. Moscato G, Dykewicz MS, Desrosiers M, et al. Chapter 24. Occupational rhinitis. In: Asthma in the workplace, 4rd Ed. Edited by J-L Malo, M Chan-Yeung, DI Bernstein. CRC Press-Taylor & Francis, New York, 2013, pp. 344–356. eBook ISBN: 978-1-84184-925-6. DOI: https://doi.org/10.1201/b15116-26. - 20.
69.• Hox V, Steelant B, Fokkens W, et al. Occupational upper airway disease: how work affects the nose. Allergy. 2014;69(3):282–291. Review. **A comprehensive review giving insights on the relationships between nose and occupational exposure.**
70. Mazurek JM, Henneberger PK. Lifetime allergic rhinitis prevalence among US primary farm operators: findings from the 2011 Farm and Ranch Safety survey. Int Arch Occup Environ Health. 2017;90(6):507–15.
71. Hoffmeyer F, van Kampen V, Taeger D, et al. Prevalence of and relationship between rhinoconjunctivitis and lower airway diseases in compost workers with current or former exposure to organic dust. Ann Agric Environ Med. 2014;21(4):70511.
72. Schantora AL, Casjens S, Deckert A, van Kampen V, Neumann HD, Brüning T, et al. Prevalence of work-related rhino-conjunctivitis and respiratory symptoms among domestic waste collectors. Adv Exp Med Biol. 2015;834:53–61.
73. Raulf M, van Kampen V, Neumann HD, et al. Airway and blood inflammatory markers in waste collectors. Adv Exp Med Biol. 2017; https://doi.org/10.1007/5584_2017_25.
74. Schelkle M, Braun J, Jörres R, et al. Respiratory allergies among veterinarians: two cross-sectional surveys from 2006 to 2012. Int Arch Occup Environ Health. 2017; https://doi.org/10.1007/s00420-017-1226-y.
75. Stopponi R, Tacconi C, Folletti I, et al. Upper airway and eye involvement in polyurethane shoe sole production workers. G Ital Med Lav Ergon. 2016;38(2):89–95.
76. Moscato G, Galdi E. Asthma and hairdressers. Curr Opin Allergy Clin Immunol. 2006;6:91–5.
77. Foss-Skiftesvik MH, Winther L, Johnsen CR, et al. High occurrence of rhinitis symptoms in hairdressing apprentices. Int Forum Allergy Rhinol. 2017;7(1):43–9. https://doi.org/10.1002/alr.21834.
78. Brozek JL, Bousquet J, Baena-Cagnani CE, Global Allergy and Asthma European Network, Grading of Recommendations Assessment, Development and Evaluation Working Group, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol. 2010;126(3):466–76.