

Occupational Allergic Diseases: High Disease Burden Yet Frequently Overlooked



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The recognition that occupational allergens are potential sources of work-related respiratory and skin diseases has been documented for centuries. As early as 440-370 BC, Hippocrates described respiratory symptoms in several workforces such as metal workers, tailors, horsemen, farmhands, and fishermen potentially exposed to workplace allergens. In 1713, in a landmark book on occupational diseases, Ramazzini reported specific breathing afflictions in grain handlers, later recognized as occupational asthma (OA) and hypersensitivity pneumonitis (HP).

In contrast to the pneumoconioses, in which exposure to large quantities of asbestos or silica dust cause respiratory diseases in many unprotected workers, recognition of occupational hypersensitivity resulting from exposure and sensitization to workplace substances may be more challenging. The prevalence of occupational allergic respiratory and skin disorders has substantially increased in Western countries during the industrialization era in the 20th century and now in many other parts of the developing world.¹ Many industrial processes use or produce proteinaceous substances that can act as complete allergens. We now recognize that some reactive chemicals encountered at work can act as haptenic ligands by combining with autologous proteins in the lung or skin to form complete allergens, inducing sensitization and eliciting allergic occupational diseases such as OA.^{2,3} A working knowledge of the hundreds of high-molecular-weight protein substances and low-molecular-weight chemicals that are potential causative agents of occupational allergic disorders is useful in their evaluation and management.

The impact of occupational allergic diseases on individual workers and society is large, affecting not only the health of patients but also threatening their ability to work at specific jobs and in certain work areas, often leading to absenteeism, loss of productivity, and ultimately job loss. Early recognition of these conditions is key for optimal management, but these diseases are

often overlooked. Perhaps partially because of lack of physician awareness, OA is severely underdiagnosed and underreported; the median time to its diagnosis is 4 years after onset of symptoms.⁴ Similarly, occupational contact dermatitis (OCD) is highly prevalent, yet many cases go unrecognized.² Thus, it is incumbent upon the allergist, dermatologist, pulmonologist, or occupational physician to aggressively evaluate workers presenting with work-related symptoms, facilitating early diagnosis and appropriate management.

The purpose of this theme issue is to heighten awareness and elevate the knowledge base among practitioners of allergy and related specialties on occupational respiratory and cutaneous allergic diseases affecting the upper and lower airways and the skin. This can be accomplished by reading these state-of-the-art updates in this issue related to OA, occupational rhinitis (OR), and OCD. Although less common than the aforementioned conditions, occupational HP is addressed, because it is extremely important to diagnose and manage this condition early; failure to do so can lead to severe respiratory impairment and even death due to chronic pulmonary fibrosis.⁵

In their review of diagnosis and management of OA, Vandenplas et al⁶ introduce definitions of OA, distinguishing cases of OA induced by irritant and sensitizing agents. OA is challenging, but reliance on history alone will often lead to an inaccurate diagnosis. This is important because failure to confirm OA can result in unmitigated exposure to an occupational sensitizer with progression of asthma, whereas an incorrect diagnosis of OA with subsequent removal from a job unnecessarily could have dire economic consequences for the worker. To avoid this conundrum, the authors propose a stepwise clinically useful algorithm for evaluating sensitizer-induced OA in the workplace. This objective approach combines data from various tools including spirometry, nonspecific bronchial hyper-responsiveness (eg, methacholine inhalation test), fractional exhaled nitric oxide, sputum eosinophil counts, serial assessments of peak expiratory flow rates both at work and away from work, and specific inhalation testing (if available). The authors provide a valuable resource by reviewing current evidence defining the test characteristics (eg, sensitivity and specificity) of each tool.

During the last 2 decades, asthma has been identified as a heterogeneous condition composed of several phenotypes. The recognition of these phenotypes has allowed proposing personalized treatments especially for allergic and eosinophilic asthma. Similarly, several phenotypes have been identified for OA that impact approaches to management. In this issue, Tarlo and Quirce⁷ propose different OA phenotypes according to the type of agent causing the disease. They also define the OA-chronic obstructive pulmonary disease overlap syndrome, a phenotype recently described among workers with OA and not fully reversible airway obstruction.

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Most workers with OA also suffer from OR, which often precedes OA. In this theme issue, Vandenplas et al⁸ provide a comprehensive review of the risk factors, pathophysiology, and objective diagnostic testing including specific nasal provocation as well as management approaches for OR. Allergen immunotherapy (AIT) and new biologic treatments have been proven effective in treating nonoccupational allergic rhinoconjunctivitis and IgE-dependent asthma. Although removal from exposure is the treatment of choice for allergic occupational diseases, it is not always possible in clinical practice. Selected patients with OA and/or OR could benefit from AIT or omalizumab. In their review, Smith and Sastre⁹ examine the current evidence for treatment with biologics and AIT (both subcutaneous and sublingual modalities) with various occupational allergens, including wheat flour, furry animals, natural rubber latex, and Hymenoptera venom. Although many studies are observational and underpowered, there is some evidence to support beneficial short- and long-term efficacy of AIT in certain worker populations. Treatment with subcutaneous AIT is largely limited by the availability of commercial therapeutic allergen extracts. It is noteworthy that many outdoor workers and cleaning workers may also derive on-the-job benefits from either subcutaneous or sublingual AIT with commercial therapeutic aeroallergens (eg, standardized pollen and house-dust mite products) with proven efficacy in atopic subjects.^{10,11}

Although occupational HP is not nearly as prevalent as OA, early recognition during the acute stages of the disorder is key to prevent chronic HP, which can be potentially life-threatening. Ojanguren et al¹² present a thorough literature review of occupational HP examining the relevant roles of radiographic imaging, serologic assays, bronchoscopy, and lung biopsy in diagnosis. The authors critically assess interventions and their impact on clinical outcomes.

In contrast, occupational dermatitis is not a life-threatening condition but has a large impact on the quality of life of many workers and is more prevalent than occupational lung disorders. In their review, Milam et al¹³ cite the large annual economic burden (\$1.5 billion) due to its very high prevalence (10%-17.6%) as well as its considerable direct (use of health care resources) and indirect (absenteeism and loss of productivity) costs. The key challenge in evaluating workers with contact dermatitis is understanding the multiple potential occupational sources of contact irritants and allergens. The authors provide a valuable review of relevant irritants and allergens common to specific jobs and occupations.

The legalization of cannabis in several countries or states has created a new industry involving a workforce assigned to cultivating and processing plant products. Nayak et al¹⁴ discuss allergic diseases that could emerge in workers involved in the production of cannabis. To date, the authors note that 4 cannabis allergen components have been identified and characterized (eg, nonspecific lipid transfer protein). Cannabis work may pose potential hazards for future development of sensitization in exposed workers and elicitation of diverse manifestations including allergic contact urticaria, ACD, OA, and occupational anaphylaxis. The actual incidence or prevalence of occupational allergy in cohorts of cannabis-exposed workers is yet to be defined.

The number and sources of allergens causing occupational diseases is constantly growing. Changes in manufacturing

processes or changes in laws can lead to the emergence of new work-related allergic disorders. Together, the articles in this issue shed light on the prevalence of occupational allergic diseases and provide rational evidence-based approaches for establishing accurate diagnoses and management. Not all allergists, pulmonologists, and dermatologists have made the effort to develop broad expertise in evaluating and diagnosing occupational disorders. The articles in this thematic issue are intended to motivate and enhance the knowledge base of practicing specialists who may be on the front lines and asked to initially evaluate a patient with work-related respiratory and/or cutaneous symptoms. All such evaluations must include a thorough investigation of the nature of the job and work area and specific details of exposures to specific natural allergens or chemicals encountered while at work. This may require seeking complete information from a patient's employer about specific substances encountered at work, often in the form of material safety data sheets. If available history and exposure is consistent with OA, OR, and/or OCD, the consultant can objectively confirm the diagnosis using approaches described in these articles or refer to a colleague who is able to do so. Either option is essential to recognize a new case early so that appropriate interventions are implemented on behalf of the affected worker in a timely fashion to mitigate further harmful exposure to causative agents. This can reduce impairment and possibly prevent chronic disability.¹⁵

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