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OCCUPATIONAL ALLERGIES (JA POOLE, SECTION EDITOR)

Occupational Rhinitis: Classification, Diagnosis, and Therapeutics

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Abstract

Purpose of Review Occupational rhinitis (OR), an inflammatory disease of the nose, refers to any nasal symptoms reported to be work-related. The purpose of this review is to provide a current overview of the classification, diagnosis, and treatment of OR.

Recent Findings Occupational rhinitis (OR) can further be classified into allergic or non-allergic depending on the causative agent(s) and pathogenesis. Presenting symptoms are similar to non-OR including nasal congestion, anterior and posterior rhinorrhea, sneezing, and nasal itching. Despite its high prevalence in a spectrum of workplaces, OR is under reported as it is often considered a nuisance rather than a potential precursor to occupational asthma (OA). The diagnosis of OR is obfuscated as it is difficult to determine if this condition was caused by environmental determinants in or outside the workplace. Furthermore, workers may have a pre-existing history of allergic or non-allergic rhinitis leading the clinician and worker to overlook inciting agents in the workplace. In this case, a diagnosis of OR is still possible depending on the exposures but must be differentiated from work-exacerbated rhinitis. Further complicating the diagnosis of OR is the lack of evidence-based research focused on this condition as it is often trivialized due to the perception that it has an insignificant impact on the worker's health. The reality is that OR can have a significant impact on the worker's quality of life and is associated with a number of comorbidities including occupational asthma, recurrent sinusitis, headaches, eustachian tube dysfunction, and sleep disorders similar to non-occupational rhinitis. However, one significant difference between these disorders is that workers diagnosed with OR are eligible for worker's compensation. Treatment of OR involves avoidance of the inciting agent(s) and medications similar to those used to treat non-OR conditions.

Summary This review summarizes recent progresses on the etiology, risk factors, diagnosis, and therapy of OR. In addition, suggested areas of further research with potential targets for modifications in the workplace environment as well as therapeutic interventions will be discussed.

Keywords Occupational rhinitis · Workplace rhinitis · IgE · Rhinitis · Inflammatory disease

Abbreviations

OR Occupational rhinitis
OA Occupational asthma

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Introduction

Occupational rhinitis (OR) refers to rhinitis that develops as a result of work place exposure to an inciting agent in a previous asymptomatic individual. The European Academy of Allergy and Clinical Immunology defines OR as an inflammatory disease of the nose, characterized by intermittent or persistent symptoms (nasal congestion, rhinorrhea, itching, etc) attributable to a particular work environment and not to stimuli encountered outside the workplace [1•, 2••].

There has been a growing recognition of OR as a public health concern because of its relatively high prevalence and societal burden. However, the incidence of OR in the general population remains largely unknown [3]. The clinical presentation of OR is heterogeneous as it varies depending on individual susceptibility, age, and the immunogenic property of the inciting allergens. If unrecognized and incorrectly treated,

similar to non-occupational rhinitis, OR can result in significant comorbidities and increased economic burden to the patient and the overall healthcare system.

OR Classification

Classification of OR is illustrated in Fig. 1 [4]. Occupational rhinitis is classified as being caused by inducers which can be high molecular weight (HMW, i.e., glycoproteins) proteins (MW > 1000 kd), or low molecular weight (LMW) chemicals (< 1000 kd) capable of eliciting a specific IgE (sIgE) response or after exposure to chemical irritants. In the former case, there is usually a latency period between the time of initial exposure and clinical symptoms during which time the worker becomes sensitized. In contrast, workers developing non-allergic irritant rhinitis develop symptoms immediately after a chemical exposure and require no latency period. This later condition is also referred to as reactive upper airways disease dysfunction (RUDS). Work exacerbation rhinitis is also triggered by chemical exposures but in this situation, the worker has a pre-existing history of chronic rhinitis. Exposure to a high concentration of irritating chemical gas may result in *corrosive OR*, which leads to nasal mucosa break down and subsequent ulceration. Corrosive OR can lead to permanent physiologic functional alteration of the nose [2, 5–8•].

Epidemiology

The epidemiology of OR is unclear as it often is not reported by the worker or workers may leave the workplace due to symptoms without pursuing workplace accommodations to reduce or prevent their symptoms. There have been several studies that reported the incidence of OR in laboratory animal workers (10–42%) and bakers (23–50%). It has been reported that the occupations at most risk for OR are laboratory handlers, veterinarians, bakers, furriers, livestock breeders, boat builders, farmers, and food processing workers [9••, 10••]. Table 1 summarizes the prevalence and exposures for a select number of occupations [4].

Risk Factors

Risk factors for OR are not well defined. Risk factors will vary between industries and individuals but often depend on the level of exposure [11]. Atopy or the genetic predisposition for allergen sensitization is the most common risk factor for HMW inducers. There is a strong association between atopy and the LMW-inducer trimellitic anhydride (TMA) as well [22]. Smoking as a risk factor has not been well characterized [12, 13, 23].

Pathophysiology of OR

As mentioned, OR is a heterogeneous condition that can be further classified as allergic and non-allergic (or irritant) [7, 8•]. For allergic OR, the mechanism of action is the same as for allergic rhinitis outside the workplace. Allergic OR occurs in an individual who is exposed to a HMW protein and in some cases it can be a LMW chemical that results in sIgE-mediated sensitization. Upon re-exposure, the inciting agent is capable of cross-linking antigen binding sites on sIgE bound to mast cell high-affinity IgE receptors (FcER1) resulting in release of preformed and newly formed bioactive mediators like histamine and leukotrienes, respectively. In contrast, non-allergic OR is induced by LMW chemical exposures to which skin sIgE or serologic testing is negative. Specific mechanisms for

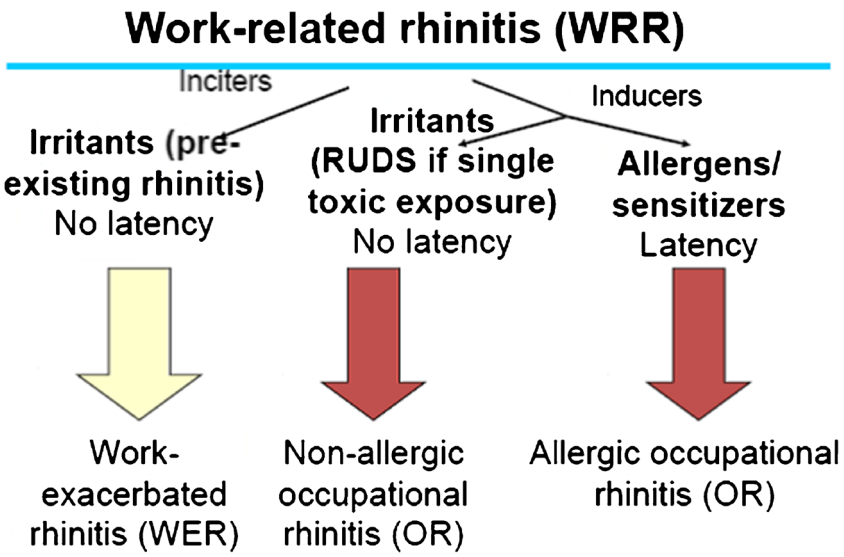

Fig. 1 Classification of work-related rhinitis

Table 1 Prevalence of OR in different industries

Industry/exposure	Prevalence (%)	References
Laboratory animal workers	10–42	[5]
Bakers	23–50	[4]
Latex exposed workers	0.12–20	[11, 12]
Foodstuffs (spices, vegetables, lupin) workers	5–54	[13–15]
Seafood (shrimp, crab, turbot) workers	5–50	[16, 17••]
Wood dusts (processing, carpentry)	10–78	[18–20]
Detergent enzymes (production hospital use)	2–19	[8•, 21]
Organic acid anhydrides (epoxy resin production)	10–28	[22, 23]
Diisocyanates (2-component paints, polyurethane workers)	1–54	[24, 25••]
Platinum workers	28–43	[26]
Nondomestic cleaners (janitors hotel housekeepers)	35	[27]
Hairdressers	8–27	[28, 29]
Swine confinement workers	8–23	[30]

non-allergic OR are not as well defined but may involve activation of transient response potential calcium ion channels leading to depolarization of nociceptor nerve fibers resulting in neuropeptide release (i.e., substance P and neurokinin A) and increased signaling of the parasympathetic nervous system. Thus, although allergic and non-allergic OR may have similar clinical presentations, their inciting agents and mechanisms of action are completely different.

Diagnosis of OR

In general, chronic non-occupational allergic and non-allergic rhinitis is a common disorder which can obfuscate a diagnosis of OR. However, establishing an accurate differential diagnosis which includes OR is the first step for establishing a correct diagnosis.

Risk factors such as occupational exposures, personal history of atopy, smoking, non-work environmental exposures, work absenteeism, or presenteeism should all be obtained by history [11, 14–16]. Occupational exposures associated with a high prevalence of OR are laboratory animals, flour and other food products, acid anhydrides, cleaning products, and strong irritants [10••]. Although remaining an important risk factor, smoking has not been found to be significantly associated with OR in many studies [12, 13]. However, a recent questionnaire-based study with a cohort of 8000 adults from Finland demonstrated a significant increase in occurrence of chronic rhinitis but not with allergic rhinitis [23]. Furthermore, active smoking and second-hand smoking combined with occupational exposure increased the risk of nasal symptoms [12].

Studies that focus on the quality of life for allergic OR patients are lacking. A cross-sectional study conducted by a group from Tunisia indicates that allergic OR impairs quality of life and work productivity. Although a majority of the surveyed patients were female, workers from the textile and clothing industries, both presenteeism and overall activity impairment were positively correlated with severe nasal obstruction and activity limitation score [17••]. The authors cautioned over interpretation of their findings due to variability in questionnaire administration to each worker, the age and gender of the patients, the type of industry and exposures, and pre-existing health conditions of the workers at the time they were surveyed [17••].

Despite the high prevalence of OR, it remains underdiagnosed due to a lack of association with direct environmental factors. Diagnosis requires demonstrating specific IgE-mediated sensitization and nasal provocation to confirm that the exposure is causing clinical symptoms. Most studies trying to establish a diagnosis of OR lack proper internal controls, such as aged- and gender-matched workers without symptoms in the same workplace and also employ worders in a different occupation [18, 19].

There are many examples in the literature of confirmed OR secondary to HMW and LMW agents using methods similar to what has been proposed for the diagnosis of occupational asthma [1•, 2••, 3, 4]. In cases where a HMW agent is suspected, either skin testing or serologic testing, if available, should be performed to determine if an IgE-mediated mechanism of action is responsible. For LMW agents, skin or serologic testing is more problematic, as is nasal provocation, as inciting agents are mostly chemical irritants or noxious odorants. However, there are some examples of LMW agents such as TMA and platinum salts [20, 22] that can elicit sIgE-mediated responses, where provocation is possible in a controlled setting performed by experienced personnel. All patients with suspected OR should be excluded for

asthma before nasal provocation is performed to avoid inducing an asthma exacerbation [21, 24]. Guidelines currently exist that address the different approaches for preparing and applying intranasally the suspected OR agent and various methodologies used to confirm objective nasal provocation responses including anterior rhinomanometry, peak inspiratory nasal flow rates, and acoustic rhinometry as well as methods for assessing changes in nasal inflammation, blood flow, temperature, and pH [1•, 3]. There are also several validated patient-reported outcome scales that measure symptom scores before and after nasal provocation [3].

Therapeutic Options

Avoidance of the inciting agent is the primary treatment approach for preventing symptoms of OR. If possible, the worker may be able to be relocated to another workspace to avoid exposure. However, often depending on the industry and the worker's job skills this may prove challenging. If relocation is not possible, workers often quit their job resulting in the "healthy worker effect." This phenomenon refers to a skewing toward a healthy population which impacts epidemiologic studies trying to accumulate data on the prevalence of specific work-related diseases including OR. Workers' compensation or disability is difficult to obtain for OR as this condition is considered more of a nuisance than a potentially life-threatening illness like asthma. Furthermore, OR is often not well characterized enough to establish medical probability that is required to obtain these benefits. Effective avoidance was reported to result in resolution of symptoms in some studies. Two reports found that workers showed significant improvement in symptoms and quality of life when they changed jobs or retired [25••, 26]. Reduction of exposure may be considered an alternative option. Reduction of work place exposure can be achieved through use of protective equipment, ventilation system modifications to reduce airborne exposures, exposure time reduction to the inciting agent in the workplace, and if possible, replacement of the causative agent with an alternative non-sensitizing/irritating agent that does not compromise the work process [27, 28].

Medical management of OR involves the same therapies used to treat non-OR. For milder symptoms, oral second-generation H1-antihistamines and leukotriene-modifying agents can be prescribed if the causative agent is due to an underlying IgE-mediated sensitization. If the underlying cause is due to a non-allergic trigger, then these medications will not be very effective as a different mechanism of action is involved [4]. For moderate to severe symptoms, an intranasal corticosteroid (INCS) alone or an intranasal antihistamine (INAH) alone may suffice for either allergic or non-allergic OR conditions. For more severe symptoms, the combination of these two nose sprays works synergistically to better control nasal congestion, anterior and/or posterior drainage [29, 30, 31••, 32, 33]. In some circumstances such as laboratory animal handlers or veterinarians, allergen immunotherapy may be feasible. However, medical treatment should not supersede avoidance of the inciting agent as OR is often a precursor for the development of occupational asthma.

Conclusions, Challenges, and Future Directions

Occupational rhinitis causes distress, discomfort, and work inefficiency. A definite diagnosis is an essential step in the management of this condition as a decision for exposure avoidance is based on occupational causality of rhinitis. A well-developed occupational surveillance plan in the workplace if implemented would ensure early identification and successful management of OR [1•] as eliminating or minimizing exposure to the causative agent remains to be the primary treatment. However, although complete elimination of causal exposure is the best solution it is not always the most economically efficient option for the worker or employer.

Occupational rhinitis represents a heterogeneous condition that can be induced by a wide spectrum of sensitizing and/or irritant agents. Unfortunately, it remains largely unstudied. It is important to recognize OR as it is often a prodrome for development of OA. Research into the incidence and prevalence of OR in different workplaces secondary to different causative agents is needed. Employers need to be educated about being proactive at identifying OR as this can lead to significant cost savings by preventing lost worker productivity and worker's compensation claims. Occupational surveillance programs, which have been very successful at preventing sensitization and subsequent OA for several inciting agents such as detergent enzymes and TMA, should be designed to capture signs and symptoms of OR early on as this would enhance our understanding of the progression of workplace related respiratory diseases.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

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

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