

Occupational rhinitis: consensus on diagnosis and medicolegal implications

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Purpose of review

Work-related rhinitis is a common disease in many working groups, frequently associated with asthma. The purpose of this review is to summarize the specific literature published within the past 12 months, to discuss the diagnostic workup and to illustrate the medicolegal aspects pertaining to this disease.

Recent findings

Recently, there has been a growing scientific interest in work-related rhinitis, which includes both occupational rhinitis and work-exacerbated rhinitis. The epidemiological relevance and the relationships to asthma have been evaluated. New etiologic agents and populations at risk have been identified. A new definition and classification, and a diagnostic algorithm, have been proposed.

Summary

In consideration of the epidemiological relevance and of the medicolegal implications, occupational rhinitis should be considered in daily clinical practice by all physicians. In adults with late-onset rhinitis, occupational causes should be queried and patients in whom an occupational association is suspected should be referred for specific assessments.

Keywords

diagnosis, management, occupational rhinitis, work-related rhinitis

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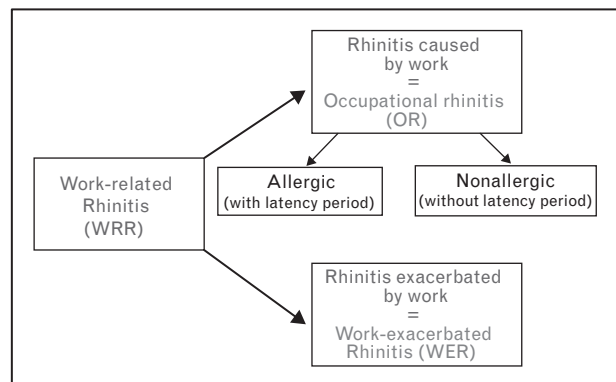
Introduction

Occupational rhinitis has gained increasing interest in recent years. Searching PubMed for the years 2009–2010 having as key words ‘occupational rhinitis’, ‘work-related rhinitis’ and ‘work-exacerbated rhinitis,’ we found 88 papers, including case reports, original articles, reviews, position papers and consensus documents of scientific societies. The Position Paper of the European Academy of Allergy and Clinical Immunology (EAACI) has covered most aspects of this entity, providing an operative definition, a new classification of all the forms of rhinitis related to work, and a diagnostic algorithm [1•]. Another EAACI official document [2•] issued key messages and suggestions on the use of noninvasive methods for assessment of nasal inflammation in the investigation and diagnosis of occupational airway diseases, including occupational rhinitis. Several comprehensive reviews [3•–7•] have highlighted the epidemiological, diagnostic, therapeutic and prognostic implications of this disease. Single case reports and epidemiological studies have described new etiologic agents and shed light on new emerging occupations at risk. Some original papers have dealt with mechanisms and specific diagnostic tools, and others have focused on

the relationships between occupational rhinitis and occupational asthma. The purpose of this review is to summarize the scientific evidence on occupational rhinitis that has been published within the years 2009–2010, to discuss the diagnostic strategies and to illustrate the medicolegal aspects pertaining to this relevant occupational disease.

Definition and classification

The EAACI Position Paper [1•] classifies occupational rhinitis among ‘work-related rhinitis’ (WRR), which also includes ‘work-exacerbated rhinitis’, that is, preexisting or concurrent (allergic or nonallergic) rhinitis that is worsened by workplace exposures. Occupational rhinitis 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’. The central concepts of this comprehensive definition are the description of occupational rhinitis as an inflammatory disease and the causal relationship between work exposure and

Figure 1 Classification of work-related rhinitis

Modified from [1**].

the development of the disease. Analogous to occupational asthma [8], occupational rhinitis may be allergic, consequent to exposure to a sensitizing agent acting through an immunological mechanism, and characterized by the presence of a latency period between exposure and symptom onset, and *nonallergic*, that is, mediated by irritant, non-immunological mechanisms, occurring after single or multiple exposures to high concentrations of irritant compounds, usually without a latency period [1**] (Fig. 1). Nonallergic occupational rhinitis resulting from a single exposure to a high concentration of irritants is also referred to as reactive upper airways dysfunction syndrome (RUDS). Allergic occupational rhinitis is the most frequently recognized, and most of the papers we will review deal with this form of rhinitis.

Epidemiology

WRR is a frequent disease. Occupational rhinitis due to high molecular weight (HMW) agents tends to be three times more prevalent than occupational asthma [9]. Moreover, recent papers have shown that the prevalence of WRR due to multiple agents is very high, ranging from 31 to 61% [1**]. In 2009–2010, several epidemiological studies or surveys investigating rhinitis in various work exposures were published.

Cross-sectional studies

A Tunisian study on 600 apprentices in a textile and clothing training center showed that WRR was 8.5% and was associated with atopy [10]. In a study on 2245 commercial pesticide applicators, the use of the herbicide pendimethalin or the insecticide organophosphate phorate was associated with at least three episodes of current rhinitis in the past year [11]. Although this study confirmed the results of Chatzi *et al.* [12] on grape farmers exposed to multiple pesticides, it has several limitations: no relationship of nasal symptoms to pesticide exposure was recorded

and no clear exposure–response relationship was found. A Swedish study showed that 1048 workers exposed to metalworking fluids had a higher prevalence of chronic rhinitis compared with controls [13]. A Dutch study on 109 workers exposed to liquid detergent enzymes showed that sensitization to at least one enzyme was 14.2% [14]. Moreover, there was one case of occupational asthma and two of probable occupational rhinitis. Workers with the highest exposure reported more work-related rhinitic symptoms. In 69 workers at a beverage processing plant exposed to hydrogen peroxide, Mastrangelo *et al.* [15] showed more severe nose, throat and eye symptoms compared with controls. A Korean study showed that 74 workers exposed to laboratory animal allergens (LAAs) and 33 office workers with no direct contact with laboratory animals had more sensitization to LAAs than 30 nonexposed controls, suggesting that indirect exposure may also cause specific sensitization [16].

Longitudinal studies

In an 8-year follow-up the incidence of sensitization to bell pepper pollen, WRR and asthma symptoms was 9, 19 and 8%, respectively [17*]. Atopy and smoking were risk factors for developing WRR and asthma symptoms among workers in bell pepper horticulture.

Surveys

A survey carried out in South Korea on more than 18 000 patients reported an increased prevalence of chronic rhinosinusitis in plant and machinery operators and assemblers, elementary occupations, crafts and related trade workers and the unemployed [18]. The French survey RNV3P reported that from 2001 to 2007 referrals for work-related asthma and rhinitis showed a decreasing trend in exposure to organic dusts and chemical products other than cleaning products and cosmetics [19].

‘New’ agents causing occupational rhinitis

Since 2008 several case reports of occupational rhinitis caused by sensitizers, both high and low molecular weight (LMW) agents, seldom if ever described previously, have been published (Table 1) [20–31]. In the majority of cases occupational rhinitis was associated with occupational asthma and atopy [20,22–30]. The diagnosis was based on work-related rhinitis symptoms, specific skin prick test (SPT) and inhalation challenges. Recently, de la Hoz *et al.* [32*] published an interesting review on occupational rhinosinusitis and upper airway disease in firefighters and other workers exposed to dust, smoke, and combustion products after the terrorist attacks on the World Trade Center (WTC) on 11 September 2001. In a large proportion of workers there was persistent rhinosinusitis and upper airway disease, which characteristically appeared rather insidiously over an exposure of weeks to months at the WTC site. Although WTC-related upper

Table 1 'New' agents causing occupational rhinitis: case reports (2008–2010)

References	Patients (n)	Occupation	Agent	Age (years)	Diagnosis	Duration of exp. before occupational rhinitis	Other WRS	Prevention	Other observations
Casper <i>et al.</i> [20]	1	Cheese processing plant	Fungal and animal-derived enzymes	34	WRS; SSPT	1 year	Ocular erythema, urticaria	Respiratory protection → improvement of WRS	Atopic patient; immediate WRS
Graff <i>et al.</i> [21]	1	Metalworking factory	Tolyltriazole, corrosion inhibitor in metalworking fluids	30	WRS; SIC	4 years	Headache	NS	Symptoms of occupational rhinitis started 8 h after exposure and persisted for 24 h; negative SPT
Hilger <i>et al.</i> [22]	1	Pork processing industry	Pig-gut soaking water	39	WRS; SSPT; specific IgE	NS	Asthma, urticaria	Job relocation in the same company → free of symptoms	Atopic patient; immediate WRS; 1 year later → asthma after ingestion of cooked pork meat; 3 years later → asthma, rhinoconjunctivitis and dysphonia 30 min after ingestion of chicken meat
Kim <i>et al.</i> [23]	1	Grain industry	Rice powder	31	WRS; SSPT; SIC	1 year	Conjunctivitis	Job relocation	Atopic patient; immediate WRS
Linares <i>et al.</i> [24]	1	Farm	Crickets	28	WRS; SSPT; specific IgE; SIC	1 year	Asthma	Removal from exposure → free of symptoms	Atopic patient; immediate WRS
Loureiro <i>et al.</i> [25]	1	Pharmaceutical company	Fungal lipase	46	WRS; specific IgE; PPT to fungal lipase; SIC; INPFR monitoring	20 years	Asthma	NS	Atopic patient; symptoms of occupational rhinitis started 3 h after exposure and improved after work
Merget <i>et al.</i> [26]	1	Electroplating plant	Rhodium salts	27	WRS; SSPT	3 years	Asthma	Job relocation in the same company and respiratory protection → slight improvement of WRS	Atopic patient; immediate WRS
Pala <i>et al.</i> [27]	1	Pharmaceutical company	Sodium alendronate	40	WRS; SIC	10 years	/	Removal from exposure → free of symptoms	Atopic patient
Pala <i>et al.</i> [28]	1	Pharmaceutical company	7-TACA	44	WRS; SIC	8 months	Asthma	NS	Atopic patient; immediate WRS
Pala <i>et al.</i> [29]	1	Parquet floor worker	Cabreuva wood dust	53	WRS; SSPT; SIC	4 years	Asthma	NS	Atopic patient; symptoms of occupational rhinitis started 6–7 h after exposure and worsened during the night; negative SSPT
Pirson <i>et al.</i> [30]	1	Factory producing inulin from chicory	Dust of dry chicory roots	32	WRS; SIC; specific IgE by immunoblotting	A few months	Asthma; conjunctivitis		Atopic patient; oral allergy syndrome to raw fruits and vegetables; crossreactivity between chicory proteins and birch pollen
Shin <i>et al.</i> [31]	1	University hospital nurse	Porcine pancreatic extract	31	WRS; SSPT; specific IgE	4 years	Asthma	NS	Occupational asthma developed 2 years after occupational rhinitis onset

7-TACA, 7-amino-3-thiomethyl-3-cephalosporanic acid (cephalosporins intermediate product); INPFR, inspiratory nasal peak flow rate; NS, not stated; PPT, positive patch tests; SIC, specific inhalation challenge; SSPT, specific skin prick test; WRS, work-related symptoms.

airway disease is considered an irritant-induced disease, atopy was associated with upper airway disease prevalence and severity.

Relationship to occupational asthma

Occupational rhinitis is often associated with occupational asthma, especially when HMW agents are involved [1^{••}]. A recent review of 15 prevalence studies on laboratory animal workers has shown that almost all cases of occupational asthma were associated with occupational rhinitis [33]. Interestingly enough, work-related nasal symptoms are highly prevalent also among patients with work-exacerbated asthma [34[•]]. Symptoms of occupational rhinitis have been reported to develop before those of occupational asthma in 20–78% of affected patients [1^{••}]. Work-related nasal symptoms tend to develop 5–6 months before the onset of respiratory symptoms [9]. Consequently, occupational rhinitis may be considered a marker of the likelihood of developing occupational asthma. Recently, Hannu *et al.* [35] showed that occupational laryngitis may also develop before occupational asthma. Castano *et al.* [36[•]] prospectively assessed bronchial and nasal reactions simultaneously during specific inhalation challenges with various occupational agents and demonstrated a concomitant clinically significant reaction of the upper and lower airways after challenge in 76% of confirmed cases of occupational asthma. This provided strong evidence that the ‘united airway disease’ (UAD) concept [37] does apply to occupational causation, although, as commented by Seed *et al.* [38], this might not be consistent across the diverse range of respiratory sensitizers. A further support for the UAD concept in the occupational setting comes from a paper by Moscato *et al.* [39[•]]. These authors compared the clinical and inflammatory features of 12 patients with occupational asthma only and 14 patients with occupational asthma associated with occupational rhinitis, both caused by ammonium persulfate. The clinical and inflammatory features were not different in the two groups, but the finding of nasal inflammation in patients without clinical manifestation of rhinitis could be considered the expression of the UAD concept in persulfate respiratory allergy.

Mechanisms

Although mechanistic studies aiming specifically to elucidate pathogenic aspects and the genetic basis of occupational rhinitis are scarce, it is believed that occupational rhinitis and occupational asthma share pathogenic mechanisms [6[•]]. Inflammatory changes of the mucosa are the common feature of both occupational rhinitis and occupational asthma [2^{••}]. In allergic occupational rhinitis and occupational asthma inflammation is sustained by an immunological mechanism which can be IgE or non-IgE-mediated. IgE-mediated occupational rhinitis is

caused by a variety of HMW agents (i.e., glycoproteins from vegetal and animal origin) and some LMW agents, such as platinum salts, reactive dyes, and acid anhydrides. Non-IgE-mediated occupational rhinitis can be induced by LMW chemicals (e.g., isocyanates, persulfate salts, woods) acting as haptens for which the allergic mechanism has not yet been fully characterized [1^{••}]. There is some agreement that chemical respiratory allergy is commonly associated with a selective T helper 2 (Th2) cell immune response, and it is now well established that Th2-type immune responses support and sustain IgE antibody responses [40^{••}]. Where there remains real controversy is to what extent IgE antibody is associated with, and required for, chemical respiratory allergy, since not uncommonly symptomatic patients with diagnosed occupational asthma, or occupational rhinitis, lack detectable IgE antibody. Irritant-induced occupational rhinitis is pathologically characterized by focal desquamation of nasal epithelium and associated with glandular hypertrophy, lymphocytic infiltrates, and sensory nerve fiber proliferation [5[•]]. Nonallergic neural mechanisms may play a significant role in the pathogenesis of occupational rhinitis via induction of neurogenic inflammation [41]. Neurotrophins such as the nerve growth factor and tachykinins play a major role in the initiation of neurogenic inflammation, which may be clinically associated with nasal obstruction in the upper airway [42]. Tachykinins also have important immunomodulatory effects influencing inflammatory cells, and it could be important to define their role according to the specific type of occupational rhinitis [6[•]].

The effects of persulfates on the nasal mucosa and on immune cells in hairdressers with persulfate-induced rhinitis versus patients with rhinitis not previously exposed to bleaching powder were examined by Diab *et al.* [43]. They did not find any IgE reactivity in hairdressers with persulfate-induced rhinitis and suggested that the reaction may be driven by a Th1 cell activation. Likewise, in a group of 26 patients with occupational asthma only or occupational asthma associated with occupational rhinitis due to persulfate, Moscato *et al.* [39[•]] reported negative SPTs to persulfate in all patients, not supporting an IgE-mediated mechanism.

Investigation and diagnostic approach

The investigation of occupational rhinitis includes both assessing the presence of rhinitis and demonstrating its work-relatedness. In addition, due to the tight relationships between upper and lower airways, the possibility of lower airways involvement should be carefully evaluated by means of questionnaire, spirometry and measurement of nonspecific airway responsiveness [1^{••}].

A detailed medical and occupational history is the first step in the investigation of occupational rhinitis. In every

adult whose rhinitis begins or worsens while working, work-related rhinitis should be considered [1^{••}]. The main purpose of the clinical history is to establish the association between a specific occupational exposure and rhinitis symptoms. Information on duration of employment at current job before onset of symptoms (latency period), on agents, tasks or processes associated with the onset or aggravation of nose symptoms, and on improvement of symptoms away from work (weekends or holidays) should be collected. Type and severity of nasal symptoms should be investigated. Because of the frequent association with conjunctival and asthmatic symptoms, eye and respiratory symptoms should be queried. The clinical history has a low specificity to establish a diagnosis of occupational rhinitis, which must be confirmed by objective tests [1^{••}]. Direct nasal examinations using anterior rhinoscopy and nasal endoscopy allow other nasal pathologies that may mimic rhinitis, or contribute to aggravate nasal obstruction, to be ruled out. Rhinomanometry, acoustic rhinometry and peak nasal inspiratory flow (PNIF) can be used for assessing nasal patency; nevertheless, the great inter-individual variability limits their applicability in clinical practice, whereas the well defined reproducibility justifies their use for evaluating nasal response to nasal provocation tests (NPTs), during which patients act as their own control [1^{••}]. For immunologic assessment of IgE-mediated sensitization to occupational agents SPT in most cases is preferred to the measurement of serum sIgE because it is sensitive, rapid and inexpensive. The major limitation of immunological tests in the investigation of occupational rhinitis results from the lack of commercially available and standardized extracts for most occupational agents, especially LMW agents. Similarly to the clinical history, immunological tests have a high sensitivity but a low specificity in diagnosing occupational rhinitis [7[•]].

NPTs are still considered the gold standard for confirming the diagnosis of occupational rhinitis [1^{••}]. A French study compared changes in nasal airway resistance (NAR), measured by posterior rhinomanometry during NPTs associated with pre and posttest clinical scores, with a prior probability, based on the patient's history determined by occupational physicians, in 41 hairdressers and 33 bakers referred for suspected occupational rhinitis [44]. The results of the study indicated that NPTs constitute a safe procedure of nasal reactivity with good levels of sensitivity and specificity in both hairdressers and bakers when nasal resistance and clinical scores are taken into account. The major limitation of NPTs results from the lack of standardized procedures [7[•]]. Various indices have been used to assess the nasal response, including symptom scores, quantification of nasal patency through rhinomanometry or acoustic rhinometry, and evaluation of nasal inflammation, but comparisons between these parameters are scarce. Sampling nasal

secretions has gained increasing interest, since it is a noninvasive method for monitoring nasal inflammation induced by occupational agents [2^{••}]. Pignatti *et al.* [45[•]] has described and validated a simple, reproducible and easy-to-perform method for assessing nasal blown secretions during NPTs. These authors identified a cut-off value of 4% and/or 1×10^4 eosinophils/ml for a significant postchallenge eosinophil increase, useful for defining a positive NPT response in addition to symptom score. Nevertheless, Castano *et al.* [36[•]] demonstrated that a significant decrease in nasal patency (assessed by acoustic rhinometry) may occur in individuals who failed to show an increase in eosinophils in nasal lavage during NPT, suggesting that different pathophysiologic mechanisms may be involved in the development of nasal responses to occupational agents. Therefore, both indices are complementary for assessing nasal responses during NPTs. The same authors [46] have also investigated the type and kinetics of late-phase nasal inflammatory response after NPT with HMW-occupational allergens in 10 patients tested positive for occupational rhinitis. A predominant postchallenge nasal eosinophilic inflammatory response was found, whereas no significant changes in nasal levels of neutrophils, myeloperoxidase and interleukin-8 were observed. A step by step consensus diagnostic algorithm has been elaborated by the above quoted EAACI Task Force [1^{••}]. The first step includes a thorough clinical and occupational history, as well as nasal examination. The second step involves the evaluation of sensitization to suspected occupational agents when standardized and validated tests are available. A suggestive clinical history associated with a positive immunologic test for an occupational agent could be considered as probable occupational rhinitis. The next step involves the objective evaluation of the causal relationship between rhinitis and the work environment through NPT with the suspected agent(s) in the laboratory. If NPT is positive, a definite diagnosis of occupational rhinitis can be established. If NPT is negative, further evaluation of work-related changes in nasal parameters at the workplace is recommended.

Medicolegal implications

The management of occupational rhinitis includes environmental interventions and appropriate therapy [1^{••}]. Environmental interventions are the first-line approach in managing occupational rhinitis [5[•]]. One Finnish paper has evaluated health-related quality of life (HRQoL) among patients with occupational rhinitis, with an average of 10 years after diagnosis [47[•]]. Continuous occupational exposure decreased QoL years after the diagnosis, and the authors concluded that, to restore the well being of patients with occupational rhinitis, medication only is not sufficient; reduction or cessation of exposure is necessary. In occupational asthma there is

evidence that, although it is beneficial from a clinical point of view, cessation of exposure may create work, financial and socioeconomic difficulties since it is more often obtained through a change of job or unemployment [48]. The long-term outcomes and the socio-economic impact of occupational rhinitis are scarcely known; however, complete avoidance of exposure is recommended in workers with increased nonspecific bronchial hyperresponsiveness, who are at increased risk of developing asthma, or in patients who may be relocated in the same company. In other patients reduction of exposure may be considered a reasonable alternative, provided that workers are submitted to close medical surveillance [1**]. Every patient with defined occupational rhinitis should be referred to compensation boards and the case notified to national or regional authorities [1**]. Policies governing compensation of occupational rhinitis vary widely from one country to another, and the physician who has made the diagnosis should be aware of national regulations and support the patient during the process.

Conclusion

Occupational rhinitis is a common disease in many working groups, frequently associated with asthma. Since occupational rhinitis is acknowledged as a risk factor for the development of occupational asthma, the prevention and early identification of work-related rhinitis may also provide an excellent opportunity to prevent the development of occupational asthma. An important role may be played by ear, nose and throat specialists and family physicians, who should consider and query occupational causes in adults with late-onset rhinitis and refer patients in whom an occupational association is suspected for further assessment [49]. Every patient with a defined diagnosis of occupational rhinitis should receive adequate compensation, according to national regulations.

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

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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