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## Position paper

# Occupational rhinitis

The present document is the result of a consensus reached by a panel of experts from European and nonEuropean countries on Occupational Rhinitis (OR), a disease of emerging relevance, which has received little attention in comparison to occupational asthma. The document covers the main items of OR including epidemiology, diagnosis, management, socio-economic impact, preventive strategies and medicolegal issues. An operational definition and classification of OR tailored to that of occupational asthma, as well as a diagnostic algorithm based on steps allowing different levels of diagnostic evidence, are proposed. The needs for future research are pointed out. Key messages are issued for each item.

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### Key messages

Definition and classification

- Occupational rhinitis (OR) is an inflammatory disease of the nose, which is characterized by intermittent or persistent symptoms (i.e., nasal congestion, sneezing, rhinorrea, itching), and/or variable nasal airflow limitation and/or hypersecretion arising out of causes and conditions attributable to a particular work environment and not to stimuli encountered outside the workplace.
- Work-related rhinitis may be distinguished into: (i) OR that arises out of causes and conditions attributable to a particular work environment and (ii) work-exacerbated rhinitis that is pre-existing or concurrent rhinitis exacerbated by workplace exposures.

Epidemiology

- Surveys of workforces exposed to sensitizing agents indicate that OR is two to four times more common than OA, although the contribution of workplace exposures to the general burden of rhinitis remains unknown.

*Abbreviations*: HMW, high molecular weight; LMW, low molecular weight; NPT, nasal provocation test; OA, occupational asthma; OR, occupational rhinitis; WER, work-exacerbated rhinitis.

- The level of exposure is the most important determinant of IgE-mediated sensitization to occupational agents and OR.
- Atopy is a risk factor for the development of IgE-mediated sensitization to high molecular weight (HMW) agents, but the association with clinical OR caused by HMW agents is less well substantiated.

Relationships with occupational asthma

- A majority of patients diagnosed with OA also suffer from OR, which most often precedes the development of OA, especially when HMW agents are involved.
- Occupational rhinitis is associated with an increased risk of asthma, although the proportion of subjects with OR who will develop OA remains uncertain.

Investigation and diagnostic approach

- Questionnaires and the clinical history have a low specificity for diagnosing OR.
- Immunological tests (skin prick tests and specific IgE antibodies) are sensitive but not specific tools for diagnosing OR caused by most HMW agents and some low molecular weight agents (i.e., platinum salts, acid anhydrides, and reactive dyes).
- In the presence of work-related rhinitis symptoms, objective assessment using nasal provocation challenges in the laboratory or at the workplace should be strongly recommended.

Management

- Complete avoidance of exposure to the agent causing allergic OR should still be recommended as the safest and most effective therapeutic option.
- When complete elimination of causal exposure is expected to induce important adverse socio-economic consequences, reduction of exposure with relevant pharmacotherapy may be considered an alternative approach, especially in workers with a lower risk of developing asthma (e.g. workers without nonspecific bronchial hyper-responsiveness, with mild/recent disease or with a short expected duration of exposure); these workers should, however, benefit from close medical surveillance aimed at an early detection of OA.

Socio-economic impact

- The socio-economic impact of OR remains unknown, but is likely to be substantial in terms of work productivity as can be extrapolated from data available for allergic rhinitis in general.

Prevention

- Primary prevention strategies should focus on reducing exposure to potentially sensitizing agents.
- Identification and exclusion of susceptible workers is not efficient, particularly when the marker of susceptibility (e.g. atopy) is prevalent in the general population.
- Surveillance programs aimed at an early identification of OR should include periodic administration of questionnaires and immunological tests when available.
- Surveillance of workers should focus on the first 2–5 years after entering exposure.
- The possibility of OA should be carefully evaluated in all workers with OR.

Medico-legal aspects

- Workers with OR should theoretically be considered impaired on a permanent basis for the job that caused the condition as well as for jobs with similar exposures.
- Compensation of OR should aim at providing incentives to accommodate workers to unexposed jobs and offering vocational rehabilitation programs to minimize the adverse socio-economic consequences of the disease.

Occupational rhinitis (OR) is a disease of emerging relevance, which has received little attention in comparison to other forms of rhinitis (1). There is currently no consensus on the definition and classification of OR. In addition, diagnostic procedures and strategies for the management of subjects with OR remain poorly standardized. This is a particularly important point as an accurate and early recognition of OR in surveillance programs is not only important *per se,* but is also useful in the prevention and early diagnosis of OA.

The purpose of this document was to issue key messages and consensus recommendations based on existing scientific evidence and the expertise of a panel of physicians coming from different European and nonEuropean countries. This executive summary is based on a comprehensive and critical review of available information on the different aspects of OR including diagnostic procedures, management, societal burden, and preventive strategies. The whole document is available online at EAACI website (http://www.eaaci.net; accessed 26 April 2008).

## Definition and classification

The similarities and tight interactions between rhinitis and asthma (1) support the need for homogeneous definitions of OR and OA. The most widely accepted


 

definition of OA refers to the pathophysiological changes that occur in the lower airways, i.e. 'variable airflow limitation and/or bronchial hyperresponsiveness and/or inflammation' (2–4). A similar approach cannot easily be translated to OR because: (1) nasal airflow limitation is not always present in OR; and (2) the various methods used for assessing nasal patency, nonspecific hyperresponsiveness, and inflammation have not been thoroughly validated (5, 6), and (3) these procedures are still largely underused in clinical practice. Nevertheless, considering that inflammatory changes in the mucosa are common features of both rhinitis and asthma, the following consensus definition of OR is proposed:

Occupational rhinitis is an inflammatory disease of the nose, which is characterized by intermittent or persistent symptoms (i.e. nasal congestion, sneezing, rhinorrea, 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 concept of this broad definition is the *causal* relationship between work exposure and the development of the disease. In addition, this definition is based on demonstrable pathophysiological changes and it does not place restriction according to the underlying mechanism.

There is accumulating evidence that the workplace environment can induce or trigger a wide spectrum of rhinitis conditions involving immunological and nonimmunological mechanisms (7–10). These various conditions should be referred to as 'work-related rhinitis' and should be further distinguished according to the clinical features, etiopathogenic mechanisms and the strength of the evidence supporting the causal relationship.

According to the revised nomenclature for allergy recently recommended by the European Academy of Allergy and Clinical Immunology (11) and the classification of work-related asthma proposed by panels of experts (2–4) different types of 'work-related rhinitis' may be delineated as detailed below and summarized in Fig. 1. This review will, however, focus on immunologically mediated OR, as there are only scarce data on the other forms of work-related rhinitis.

## Occupational rhinitis

*Allergic OR.* Work-related rhinitis symptoms are caused by immunologically mediated hypersensitivity reactions resulting from antibody- or cell-mediated mechanisms. This entity is characterized clinically by the development of nasal hypersensitivity to a specific occupational agent appearing after a latency period, which is necessary to acquire immunological sensitization to the causal agent. Once initiated, the symptoms recur on re-exposure to the sensitizing agent at concentrations not affecting other similarly exposed workers. In allergic OR, the causal role of occupational agents can be documented on an individual basis through nasal provocation test (NPT),

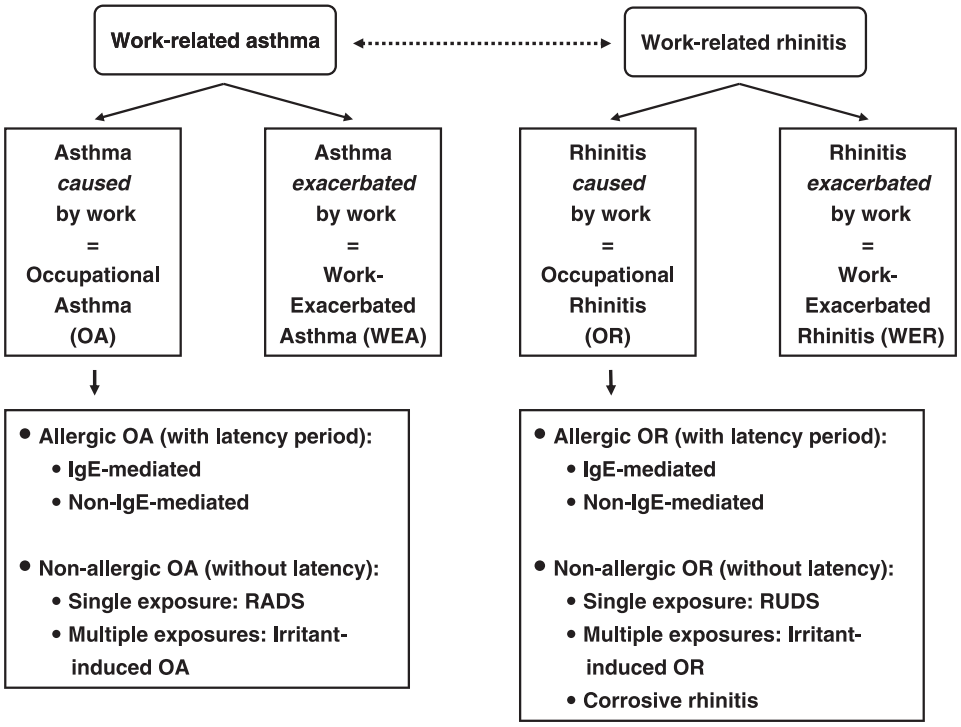


*Figure 1.* Parallel classification of occupational rhinitis and asthma. RADS, reactive airways dysfunction syndrome; RUDS, reactive upper airways dysfunction syndrome.

 

showing reduction in nasal patency, increased volume of nasal secretions, and/or nasal inflammation. Allergic OR encompasses both IgE-mediated OR and nonIgE-mediated OR.

1. IgE-mediated OR: can be caused by a wide variety of high molecular weight (HMW) agents (i.e. glycoproteins from vegetal and animal origin) and some low molecular weight agents (LMW) for which an IgE-mediated mechanism has been proven, such as platinum salts, reactive dyes, and acid anhydrides.
2. Non-IgE-mediated OR: can be induced by LMW agents (e.g. isocyanates, persulphate salts, woods) acting as haptens for which the allergic mechanism has not yet been fully characterized.

*Nonallergic OR*. This category encompasses different types of rhinitis caused by the work environment through irritant, nonimmunological mechanisms. It has been documented that single or multiple exposures to very high concentrations of irritant compounds can lead to transient or persistent symptoms of rhinitis (12–14). Such cases of acute-onset 'irritant-induced OR' usually occur without a latency period, although the absence of latency may be obscured when workers are repeatedly exposed to high levels of irritants at work. This entity is quite similar to the situation of the 'reactive airways dysfunction syndrome' (2, 4), so that the term 'reactive upper airways dysfunction syndrome' has been proposed (15). In these cases of irritant-induced OR, evidence supporting a causal relationship with the workplace can be drawn only from the temporal association between exposure to unusually high levels of irritants and the development of rhinitis.

The term 'irritant-induced OR' may also refer to symptoms of rhinitis reported by subjects repeatedly exposed at work to irritants (vapours, fumes, smokes, dusts) without identifiable exposure to high concentration of irritants. A variety of occupational exposures have been associated with rhinitis symptoms, nasal airflow obstruction, and/or nasal inflammation, usually with a predominant neutrophilic component (16, 17).

The term 'corrosive rhinitis' has been used to describe the most severe form of 'irritant-induced OR', which is characterized by permanent inflammation of the nasal mucosa (sometimes associated with ulcerations and perforation of the nasal septum) that may develop after exposure to high concentrations of irritating and soluble chemicals (8, 10, 18).

### Work-exacerbated rhinitis

Work-exacerbated rhinitis (WER) should be defined as pre-existing or concurrent (allergic or nonallergic) rhinitis that is worsened by workplace exposures (10, 19), while the disease has not been caused by the work environment. It is indeed highly likely that rhinitis symptoms can be triggered by a wide variety of conditions at work, including irritant agents (e.g., chemicals, dusts, fumes), physical factors (e.g., temperature changes), emotions, second-hand smoke, and strong smells (e.g., perfumes).

The clinical features of a WER are similar to those of OR, so that the possibility of a WER should be considered only after careful exclusion of a specific sensitization to a workplace agent through appropriate diagnostic procedures. The mechanisms involved in the development of WER have been scarcely explored. The nasal response to irritant stimuli seems to be affected by age, gender and the presence of allergic rhinitis (20, 21).

## Epidemiology

### Prevalence and incidence

The prevalence and incidence of OR in the general population have almost never been specifically investigated. Data from the Finnish Register of Occupational Diseases (1986–1991) suggest that occupations at increased risk include furriers, bakers, livestock breeders, food-processing workers, veterinarians, farmers, electronic/electrical products assemblers, and boat builders (22).

The results of cross-sectional studies conducted in various working populations exposed to a wide range of HMW and LMW agents, as recently reviewed (23), are reported in Table 1. Available data indicate that OR is usually 2–4 times more prevalent than OA (23, 24). Prevalence estimates of rhinitis and OR are largely affected by the criteria used for identifying the condition (24). The incidence of work-related nose symptoms has been investigated in a few prospective cohort studies that are summarized in Table 2 (25–30).

### Risk factors

Exposure and atopy have consistently emerged as the main potential determinants for the development of OR. A dose–response gradient between the level of exposure and IgE-mediated sensitization has been substantiated for various HMW agents (31–37). However, much of the evidence relates to immunological sensitization rather than to clinical OR (23). Atopy has been associated with an increased risk of specific sensitization to a variety of HMW agents (23, 24) and with clinical OR caused by these agents (Table 1) (28, 38, 39). Available studies have provided inconsistent results regarding the relationships between atopy and OR (23, 40). The relationships between smoking and occupational sensitization and OR remain controversial (41–43). There is some evidence from cohort studies (40, 44) that nonspecific bronchial hyper-responsiveness may be associated with an increased risk for the subsequent development of work-related nasal symptoms.


 

Table 1. Prevalence and etiological agents in occupational rhinitis*

| Agents | Occupation | Prevalence (%) |
|---|---|---|
| *High molecular weight agents* | | |
| Laboratory animals | Laboratory workers | 6–33 |
| Other animal-derived allergens | Swine confinement workers | 8–23 |
| Insects and mites | Laboratory workers, farm workers | 2–60 |
| Grain dust | Grain elevators | 28–64 |
| Flour | Bakers | 18–29 |
| Latex | Hospital workers, textile factory workers | 9–20 |
| Other plant allergens | Tobacco, carpet, hot pepper, tea, coffee, cocoa, dried fruit and saffron workers | 5–36 |
| Biological enzymes | Pharmaceutical and detergent industries workers | 3–87 |
| Fish and seafood proteins | Trout, prawn, shrimp, crab and clam workers; aquarists and fish-food factory workers | 5–24 |
| *Low molecular weight agents* | | |
| Diisocyanates | Painters, urethane mould workers | 36–42 |
| Anhydrides | Epoxy resin production, chemical workers, electric condenser workers | 10–48 |
| Wood dust | Carpentry and furniture making workers | 16–36 |
| Metals (platinum) | Platinum refinery workers | 43 |
| Drugs (psyllium, spiramycin, piperacillin) | Health care and pharmaceutical workers | 9–41 |
| Chemicals | Reactive dye, synthetic fiber, cotton, persulphate, hairdressing, pulp and paper, shoe manufacturing workers | 3–30 |

*Adapted from reference (23).

Table 2. Incidence of occupational asthma and rhinitis

| Reference/agent | Subjects (*n*) | Years/duration (years) of follow-up | Incidence of OA (×100 person years) | Incidence of OR (×100 person years) |
|---|---|---|---|---|
| Cullinan et al. 1999/laboratory animals (25) | 342 | 1990–1993/2.7 | 3.5 | 7.3 |
| Rodier et al. 2003/laboratory animals (26) | 387 | 1993–1995/3.7 | 2.7 | 12.1 |
| Draper et al. 2003/laboratory animals (30) | 17 300 | 1999–2000/1.0 | 0.2 | 0.3 |
| Cullinan et al. 2001/flour (27) | | 1990–1993/3.3 | 4.1 | 11.8 |
| Gautrin et al. 2002/flour (28) | | 1993–1997/1.4 | NA | 13.1 |
| Archambault et al. 2001/latex (29) | | 1993–1995/2.7 | 1.8 | 0.7 |

OA, occupational asthma; OR, occupational rhinitis; NA, not available.

## Relationships with occupational asthma

With regard to the association between rhinitis and asthma of occupational origin, Malo et al. have documented that rhinitis symptoms are common among subjects with OA, 92% patients with OA reporting symptoms of OR (45). The prevalence of rhinitis symptoms was not different for HMW and LMW agents, although the intensity of symptoms was more pronounced for HMW agents.

Symptoms of OR have been reported to develop before those of OA in 20–78% of affected subjects (19, 45–50). There is some suggestion that symptoms of OR were more often reported to precede OA in the case of HMW compared to LMW agents (45, 46). A longitudinal study of patients seeking compensation for OR from the Finnish Register of Occupational Diseases showed an increased risk of asthma (RR 4.8, 95%CI 4.3–5.4) among those with OR compared to subjects with other occupational diseases (51).

## Investigation and diagnostic approach

The investigation of OR includes both assessing the presence of rhinitis and demonstrating its work-relatedness. The diagnosis needs to be confirmed by means of objective methods, as misdiagnosis may have substantial social and financial consequences. The different steps involved in the diagnosis of OR are the clinical history, nasal examination, immunological tests (for allergic OR), and NPT.

In addition, the possibility of lower airways involvement should be carefully evaluated by means of questionnaire, spirometry, and measurement of nonspecific airway responsiveness (52, 53).

### Clinical and occupational history

Detailed medical and occupational history remains a key step in the investigation and diagnosis of OR. The main purpose of the medical history of OR is to establish the timing of nasal symptoms in relation with occupational exposure, as suggested for OA (54, 55). History taking should address the following features: duration of employment at current job before onset of symptoms (latency period); agents, tasks or processes associated with the onset or aggravation of symptoms; improvement away from work (weekends or prolonged holidays). The clinical history should also gather information on the

 

nature, severity, and impact of rhinitis symptoms. Nasal symptoms reported by workers suffering from OR are similar to those experienced by individuals from the general population with non-OR (i.e. rhinorrhea, sneezing, nasal blockage, and itchy nose). Conjunctival complaints often accompany these symptoms, especially in allergic IgE-mediated OR. (45). Although an essential step of the diagnostic approach, the clinical history is not specific enough to establish a diagnosis of allergic OR (19, 24–28).

### Nasal examination

The macroscopic appearance of the nasal mucosa can be assessed using anterior rhinoscopy and nasal endoscopy. These techniques, however, do not allow quantitative assessment of nasal changes. Their main value is to rule out other nasal pathologies that may mimic rhinitis or aggravate nasal obstruction (e.g. septal deviations, nasal polyps) in patients with rhinitis.

### Physiological assessment

*Nasal patency*. Objective methods that can be used for assessing nasal patency during the investigation of OR include rhinomanometry, acoustic rhinometry and peak nasal inspiratory flow (5, 56, 57). These techniques share a great inter-individual variability that limits their applicability in clinical practice. Thus, it is not possible to rely on comparisons with reported values of healthy subjects to make a diagnosis of rhinitis. Nevertheless, the above methods have well-defined reproducibility, whereby their use is justified for evaluating nasal response to NPTs.

*Nasal inflammation*. Nasal secretions can be collected and weighted for quantifying the secretory activity, especially after allergen challenges (58, 59). Inflammatory cells and mediators can be measured in nasal secretions (6). The use of nasal lavage in clinical practice is still limited because of lack of a standardized and validated method. This technique is useful in situations where subjects serve as their own controls as it occurs during NPT or exposure at the workplace. Inflammatory cells can also be assessed using nasal biopsies (6), whose applicability is limited by their invasive character, or using nasal scrapings or brush samples, which are simple and relatively painless procedures (60).

*Nonspecific nasal hyper-reactivity*. In contrast to bronchial hyper-reactivity in asthma, nasal hyper-reactivity is not so much documented in OR. Nasal challenge tests with histamine, methacholine (61–63) and cold dry air (64, 65) have been proposed as a method to quantify nonspecific upper airway hyper-reactivity. Histamine is by far the most commonly used stimulus and hyper-reactivity to histamine has been convincingly demonstrated to occur after allergen provocation (66, 67). Methacholine hyper-reactivity has also been reported to increase after allergen provocation (68) but not all studies reproduced these findings (69). Intranasal cold dry air has been shown to be superior to histamine challenge in measuring nasal hyper-reactivity in nonallergic noninfectious perennial rhinitis (64, 65).

### Immunological tests

The demonstration of IgE-mediated sensitization to occupational agents can be achieved by means of skin prick test and/or assessment of serum allergen-specific IgE antibodies. However, the sensitivity and specificity of immunological tests in comparison with NPTs have been evaluated in only few studies (24, 49). Positive immunological test may occur in a substantial proportion of exposed asymptomatic individuals (40, 70–73). On the other hand, a negative test result makes the diagnosis of OR unlikely, provided that the appropriate allergens have been tested. The major limitation of immunological tests in the investigation of occupational allergy results from the lack of commercially available and standardized extracts for most occupational agents, especially LMW agents.

### Nasal provocation tests

These tests are still considered the gold standard for confirming the diagnosis of OR (57, 74–77). NPTs can be performed either in the laboratory under controlled conditions or at work under natural conditions. The methods that can be used to deliver occupational agents and to measure nasal response during NPTs have been critically reviewed (5, 6, 23, 57, 59, 74–79) and recommendations have been published by the European Academy of Allergy and Clinical Immunology (78) and the Committee on Objective Assessment of the Nasal Airways of the International Rhinologic Society (57). The major limitation of these tests results from the fact that various criteria have been used for defining a positive response, but there is lack of validated comparison between these criteria (58).

### Diagnostic algorithm

A consensus diagnostic algorithm has been elaborated (Fig. 2) by taking into account the following practical constraints: (i) the validity of the tests used for diagnosing OR remains largely uncertain and (ii) the level of reliability may vary according to the purpose of the diagnostic evaluation and its expected socio-economic impact.

The first step includes a thorough clinical and medical history, as well as nasal examination. The second step involves the evaluation of sensitization to suspected occupational agents through immunological tests for HMW agents and some LMW agents (i.e. platinum salts, reactive dyes, and acid anhydrides). A suggestive clinical history


 

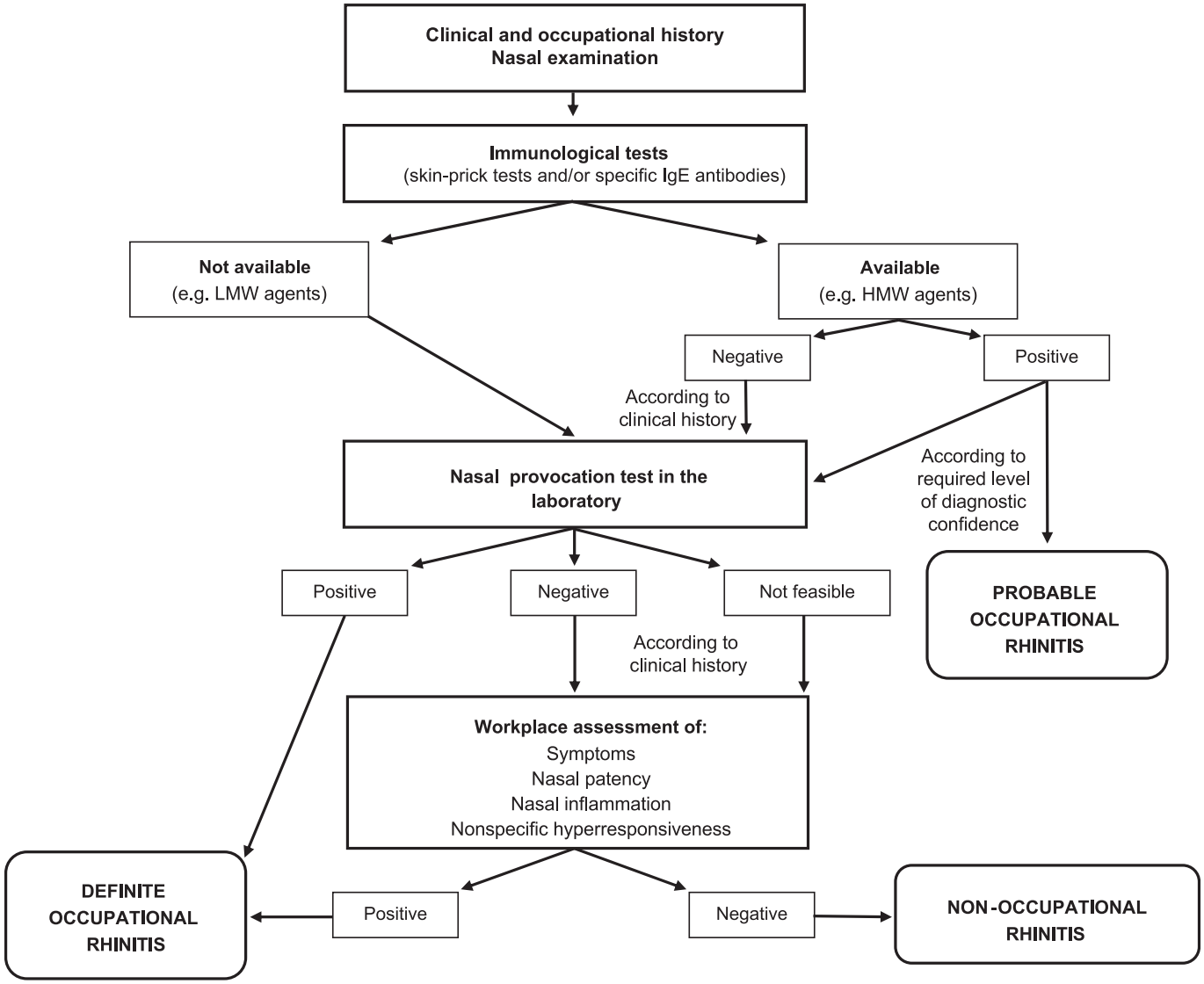


*Figure 2.* Diagnostic algorithm.

associated with a positive immunological tests for a well-standardized extract could be considered as probable OR.

The next step involves the objective evaluation of the causal relationship between rhinitis and the work environment through NPTs in the laboratory. If NPT is positive, a definite diagnosis of OR can be established. If NPT is negative, further evaluation of work-related changes in nasal parameters at the workplace is recommended, especially in the presence of a highly suggestive clinical history. Assessment at the workplace may be first considered when NPT in the laboratory is not feasible.

## Management

The management of OR has a two-sided objective: (i) minimizing nasal symptoms and their impact on the patients' well-being and (ii) preventing the development of OA. Therapeutic options include environmental interventions aimed at avoiding exposure to the causal agent and pharmacologic treatment (16). Because of the tight relationships between OR and OA, a closer collaboration between different specialists, ENT, pneumologists and physicians with expertise in occupational medicine and in environmental hygiene may be recommended.

### Environmental interventions

Treatment strategies should focus on avoidance of exposure to the agent causing allergic OR. However, complete avoidance of exposure often implies considerable professional changes for affected workers and is associated with substantial socio-economic consequences

 

(80, 81). Thus, reduction of exposure may be considered a reasonable alternative, provided that workers with OR undergo close medical surveillance.

Available data indicate that rhinitis could be an early marker of OA. However, having few quantitative estimates (51, 82, 83) of the long-term risk of asthma among patients with OR, it may be reasonable to recommend complete avoidance from exposure in the following settings:

1. The worker has nonspecific bronchial hyper-responsiveness as these subjects have a higher risk of developing asthma (84).
2. The adverse socio-economic consequences can be minimized by relocating the worker to unexposed jobs within the same company or by appropriate job retraining.

### Pharmacotherapy and immunotherapy

Pharmacotherapy of OR is similar to that of non-occupational allergic rhinitis and should be instituted according to evidence-based guidelines (1). In allergic OR, medications should not be considered a suitable alternative to elimination or reduction in workplace exposure to the sensitizing agent.

Several studies have reported some improvement in respiratory symptoms during immunotherapy with purified rodent proteins, wheat flour extracts, and natural rubber latex. However, allergen immunotherapy is currently limited by the nonavailability of standardized extracts for most occupational allergens and should be used with caution and close supervision until more data are available (85).

## Socio-economic impact

The impact of OR on work productivity has been rarely studied (19, 86). In a 2-year study in Norwegian bakeries, some workers left their jobs because of work-related rhinitis, conjunctivitis and/or skin problems, but none because of asthma (19).

There is little information on the psycho-social impact of OR, although it has been increasingly recognized that allergic diseases may impair patients' quality of life (87). The negative impact of OR on daily life has been investigated in only one study conducted among greenhouse workers (88).

## Prevention

As OR is acknowledged as a risk factor for the development of OA, the prevention of work-related rhinitis may also provide an excellent opportunity to prevent the development of OA.

### Primary prevention

Epidemiological data indicate that the level of exposure to sensitizing agents is the most important determinant of IgE-mediated sensitization and OR and, by implication, reducing or eliminating workplace exposure to sensitizing agents should be the most effective approach to minimize the incidence of the disease.

*Controlling exposure at the workplace*. Examples of effective prevention resulting from reduction of exposure have been documented in enzyme detergent production (89), platinum refining workers (90), laboratory workers (91), and healthcare workers using latex gloves (92). Reducing exposure to safe levels remains, however, quite difficult in field practice, because the threshold level (or dose) of an agent that can elicit sensitization and respiratory reactions remains largely uncertain.

*Identification of susceptible workers*. The positive predictive values of available susceptibility markers are too low for screening out potentially susceptible individuals (93, 94). This is particularly true in the case of atopy, which is a highly prevalent trait in the general population. Excluding atopic individuals from jobs entailing exposure to HMW allergens would reduce dramatically the number of potential new employees and would be unduly discriminatory. There is a role for a better education on the risk of sensitization of those individuals attending vocational schools (93).

### Secondary prevention

The short latency period for the development of OR (25, 82) outlines the need for surveillance of individuals at risk in the very first years of exposure (95). Accordingly, surveillance programs should be implemented during vocational training.

Medical surveillance programs should include the following components (93, 96, 97): (i) preplacement and periodic administration of a questionnaire aimed at detecting work-related symptoms; (ii) detection of sensitization to occupational agents by means of skin prick tests or serum specific IgE antibodies when these tests are available and standardized; (iii) early referral of symptomatic and/or sensitized workers for specialized medical assessment, including NPT in the laboratory and/or at the workplace (24); and (iv) investigation of possible asthma in all workers with confirmed OR.

## Medico-legal aspects

### Assessment of impairment/disability

Considering that persistence of exposure to an agent causing allergic OR will lead to worsening of the disease and is associated with a risk of asthma, patients with


 

ascertained OR should, theoretically, be considered impaired on a permanent basis for the job that caused the condition as well as for jobs with similar exposures. Evaluating the level of functional impairment caused by OR is hampered by the absence of reference values for physiological tests. The severity of rhinitis should be assessed according to the grading schemes recommended in official documents (1, 98–100).

### Compensation

Policies governing compensation of OR vary widely from one country to another (Table 3). These differences are caused by a number of factors, including administrative regulations and different ways of defining OR, determining causality, and evaluating the level of disability. The criteria used for determining eligibility for compensation are not uniform. Depending on countries' regulations, compensation may cover different aspects: physiological impairment, work disability, loss of income, healthcare costs and professional retraining. However, available data for OA indicate that financial compensation does not adequately offset the socio-economic consequences of the disease (81). There is now growing consensus that compensation systems should be directed at accommodating workers to unexposed jobs within the same company and to offer structured rehabilitation programs when required (94).

## Unmet needs and research areas

### Definition and classification

- Characterization of the clinical features and pathophysiological mechanisms of 'nonallergic OR' and 'WER'.

### Epidemiology

- Quantification of the contribution of OR to the general burden of rhinitis in the general population.
- Development and validation of an international questionnaire to identify OR in epidemiological surveys and clinical practice.
- Further characterization of the role of atopy and smoking in the development of OR.
- Elucidation of the interaction between upper and lower airway responses to sensitizing and irritant agents in the workplace.

### Diagnosis

- Standardization of occupational allergen extracts for skin prick tests and for assessment of serum specific IgE.
- Standardization and validation of techniques used for measuring nonspecific nasal hyper-reactivity, nasal airflow, and nasal inflammation.
- Development and standardization of NPT, including standardization of end points, evaluation of the role of nasal NO measurement, and identification of the most useful biological markers of nasal response.

### Management

- Specific assessment of the impact of OR in terms of QoL and economic burden to evaluate the cost-effectiveness of therapeutic and preventive interventions.
- Prospective assessment of the efficacy and safety of immunotherapy with occupational agents in controlling rhinitis symptoms and preventing the development of OA.

Table 3. Compensation for occupational rhinitis in different countries

| | Belgium | Denmark | France | Ireland | Italy | the Netherlands | Portugal | Spain | Finland | Poland | United Kingdom | Germany | Austria | Luxembourg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| List of agents | | + | + | | | | | + | | | + | + | | |
| List of occupational diseases | | | | +* | | | | + | | + | | | | |
| Open system | + | + | | | + | + | + | | + | + | | | | |
| Determinants of the degree of disability | † | | ‡ | | | ‡ | | | + | | + | | | |
| Needs of medication | | + | | + | + | | + | | + | | + | | | + |
| Symptoms at work | + | + | + | + | + | | + | | + | | + | | | + |
| Worker's possibilities to avoid further exposure | | + | | | | | | | | | | | | |
| Degree of disability | NA | 5–10% | <10% | NA | ≤ 3% | NA | 10–20% | NA | 10% | ≤ 15% | NA | NA | NA | NA |

*Rhinitis is not mentioned, but can be recognized under 'inflammation or ulceration of the mucous membrane of the respiratory passages or mouth produced by dust or liquid or vapor'.

†Also nasal dyspermeability, nasal septal perforation, problems of smell, nasal bleeding and various other symptoms.

‡All these parameters may be taken into account depending on the individual case; none are obligatory.

NA, not available.

 

Prevention

- Identification of parameters influencing the prognosis of OR.
- Assessment of the effects of environmental interventions on the clinical and physiological indices of rhinitis, such as the level of nonspecific nasal hyper-responsiveness, and nasal inflammation.
- Assessment of the impact of environmental interventions on the development of OA in subjects with OR.

Compensation

- Definition of consensus criteria for grading impairment/disability resulting from OR.

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## References

1. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 2008;**63**(Suppl. 86):8–160.
2. Chan-Yeung M. Assessment of asthma in the workplace. ACCP consensus statement. American College of Chest Physicians. Chest 1995;**108**:1084–1117.
3. Vandenplas O, Malo JL. Definitions and types of work-related asthma: a nosological approach. Eur Respir J 2003; **21**:706–712.
4. Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI. Definition and classification of asthma in the workplace. In: Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, editors. Asthma in the workplace, 3rd Edn. New York, NY: Marcel Dekker Inc., 2006:1–8.
5. Nathan RA, Eccles R, Howarth PH, Steinsvag SK, Togias A. Objective monitoring of nasal patency and nasal physiology in rhinitis. J Allergy Clin Immunol 2005;**115**:S442–S459.
6. Howarth PH, Persson CG, Meltzer EO, Jacobson MR, Durham SR, Silkoff PE. Objective monitoring of nasal airway inflammation in rhinitis. J Allergy Clin Immunol 2005;**115**:S414–S441.
7. Shusterman D. Review of the upper airway, including olfaction, as mediator of symptoms. Environ Health Perspect 2002;**110**(Suppl. 4): 649–653.
8. Slavin RG. Occupational rhinitis. Ann Allergy Asthma Immunol 2003;**90**: 2–6.
9. Castano R, Theriault G, Gautrin D. The definition of rhinitis and occupational rhinitis needs to be revisited. Acta Otolaryngol 2006;**126**:1118–1119.
10. Castano R, Theriault G. Defining and classifying occupational rhinitis. J Laryngol Otol 2006;**120**:812–817.
11. Johansson SG, Hourihane JO, Bousquet J, Bruijnzeel-Koomen C, Dreborg S, Haahtela T et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy 2001;**56**:813–824.
12. Meggs WJ, Elsheik T, Metzger WJ, Albernaz M, Bloch RM. Nasal pathology and ultrastructure in patients with chronic airway inflammation (RADS and RUDS) following an irritant exposure. J Toxicol Clin Toxicol 1996;**34**:383–396.
13. Leroyer C, Malo JL, Girard D, Dufour JG, Gautrin D. Chronic rhinitis in workers at risk of reactive airways dysfunction syndrome due to exposure to chlorine. Occup Environ Med 1999; **56**:334–338.
14. Hoffman CD, Henneberger PK, Olin AC, Mehta A, Toren K. Exposure to ozone gases in pulp mills and the onset of rhinitis. Scand J Work Environ Health 2004;**30**:445–449.
15. Meggs WJ. RADS and RUDS – the toxic induction of asthma and rhinitis. J Toxicol Clin Toxicol 1994;**32**:487–501.
16. Hellgren J, Karlsson G, Toren K. The dilemma of occupational rhinitis: management options. Am J Respir Med 2003;**2**:333–341.
17. Christiani DC, Malo JL, Siracusa A. Upper airways involvement. In: Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, editors. Asthma in the workplace. New York, NY: Taylor & Francis, 2006:785–796.
18. Castano R, Theriault G, Gautrin D. Categorizing nasal septal perforations of occupational origin as cases of corrosive rhinitis. Am J Ind Med 2007; **50**:150–153.
19. Storaas T, Steinsvag SK, Florvaag E, Irgens A, Aasen TB. Occupational rhinitis: diagnostic criteria, relation to lower airway symptoms and IgE sensitization in bakery workers. Acta Otolaryngol 2005;**125**:1211–1217.
20. Shusterman DJ, Murphy MA, Balmes JR. Subjects with seasonal allergic rhinitis and nonrhinitic subjects react differentially to nasal provocation with chlorine gas. J Allergy Clin Immunol 1998;**101**:732–740.
21. Shusterman D, Murphy MA, Balmes J. Differences in nasal irritant sensitivity by age, gender, and allergic rhinitis status. Int Arch Occup Environ Health 2003;**76**:577–583.
22. Hytonen M, Kanerva L, Malmberg H, Martikainen R, Mutanen P, Toikkanen J. The risk of occupational rhinitis. Int Arch Occup Environ Health 1997;**69**: 487–490.
23. Siracusa A, Desrosiers M, Marabini A. Epidemiology of occupational rhinitis: prevalence, aetiology and determinants. Clin Exp Allergy 2000;**30**:1519–1534.
24. Ruoppi P, Koistinen T, Susitaival P, Honkanen J, Soininen H. Frequency of allergic rhinitis to laboratory animals in university employees as confirmed by chamber challenges. Allergy 2004;**59**:295–301.
25. Cullinan P, Cook A, Gordon S, Nieuwenhuijsen MJ, Tee RD, Venables KM et al. Allergen exposure, atopy and smoking as determinants of allergy to rats in a cohort of laboratory employees. Eur Respir J 1999;**13**:1139–1143.
26. Rodier F, Gautrin D, Ghezzo H, Malo JL. Incidence of occupational rhinoconjunctivitis and risk factors in animal-health apprentices. J Allergy Clin Immunol 2003;**112**:1105–1111.
27. Cullinan P, Cook A, Nieuwenhuijsen MJ, Sandiford C, Tee RD, Venables KM et al. Allergen and dust exposure as determinants of work-related symptoms and sensitization in a cohort of flour-exposed workers; a case-control analysis. Ann Occup Hyg 2001;**45**:97–103.


 

28. Gautrin D, Ghezzo H, Infante-Rivard C, Malo JL. Incidence and host determinants of work-related rhinoconjunctivitis in apprentice pastry-makers. Allergy 2002;**57**:913–918.
29. Archambault S, Malo JL, Infante-Rivard C, Ghezzo H, Gautrin D. Incidence of sensitization, symptoms, and probable occupational rhinoconjunctivitis and asthma in apprentices starting exposure to latex. J Allergy Clin Immunol 2001;**107**:921–923.
30. Draper A, Newman Taylor A, Cullinan P. Estimating the incidence of occupational asthma and rhinitis from laboratory animal allergens in the UK, 1999–2000. Occup Environ Med 2003;**60**:604–605.
31. Heederik D, Venables KM, Malmberg P, Hollander A, Karlsson AS, Renstrom A et al. Exposure-response relationships for work-related sensitization in workers exposed to rat urinary allergens: results from a pooled study. J Allergy Clin Immunol 1999;**103**:678–684.
32. Hollander A, Heederik D, Doekes G. Respiratory allergy to rats: exposure-response relationships in laboratory animal workers. Am J Respir Crit Care Med 1997;**155**:562–567.
33. Musk AW, Venables KM, Crook B, Nunn AJ, Hawkins R, Crook GD et al. Respiratory symptoms, lung function, and sensitisation to flour in a British bakery. Br J Ind Med 1989;**46**:636–642.
34. Houba R, Heederik D, Doekes G. Wheat sensitization and work-related symptoms in the baking industry are preventable. An epidemiologic study. Am J Respir Crit Care Med 1998; **158**:1499–1503.
35. Liebers V, Hoernstein M, Baur X. Humoral immune response to the insect allergen Chi t I in aquarists and fish-food factory workers. Allergy 1993;**48**:236–239.
36. Houba R, Heederik DJ, Doekes G, van Run PE. Exposure-sensitization relationship for alpha-amylase allergens in the baking industry. Am J Respir Crit Care Med 1996;**154**:130–136.
37. Cullinan P, Harris JM, Newman Taylor AJ, Hole AM, Jones M, Barnes F et al. An outbreak of asthma in a modern detergent factory. Lancet 2000; **356**:1899–1900.
38. Schumacher MJ, Tait BD, Holmes MC. Allergy to murine antigens in a biological research institute. J Allergy Clin Immunol 1981;**68**:310–318.
39. Beeson MF, Dewdney JM, Edwards RG, Lee D, Orr RG. Prevalence and diagnosis of laboratory animal allergy. Clin Allergy 1983;**13**:433–442.
40. de Meer G, Postma DS, Heederik D. Bronchial responsiveness to adenosine-5′-monophosphate and methacholine as predictors for nasal symptoms due to newly introduced allergens. A follow-up study among laboratory animal workers and bakery apprentices. Clin Exp Allergy 2003;**33**:789–794.
41. Siracusa A, Marabini A. Smoking and asthma in the workplace. Am J Respir Crit Care Med 1997;**155**:1168.
42. Nielsen GD, Olsen O, Larsen ST, Lovik M, Poulsen LK, Glue C et al. IgE-mediated sensitisation, rhinitis and asthma from occupational exposures. Smoking as a model for airborne adjuvants?. Toxicology 2005;**216**:87–105.
43. Siracusa A, Marabini A, Folletti I, Moscato G. Smoking and occupational asthma. Clin Exp Allergy 2006;**36**:577–584.
44. Gautrin D, Ghezzo H, Infante-Rivard C, Malo JL. Host determinants for the development of allergy in apprentices exposed to laboratory animals. Eur Respir J 2002;**19**:96–103.
45. Malo JL, Lemière C, Desjardins A, Cartier A. Prevalence and intensity of rhinoconjunctivitis in subjects with occupational asthma. Eur Respir J 1997;**10**:1513–1515.
46. Cortona G, Pisati G, Dellabianca A, Moscato G. Respiratory occupational allergies: the experience of the Hospital Operative Unit of Occupational Medicine in Lombardy from 1990 to 1998. G Ital Med Lav Ergon 2001; **23**:64–70.
47. Grammer LC, Ditto AM, Tripathi A, Harris KE. Prevalence and onset of rhinitis and conjunctivitis in subjects with occupational asthma caused by trimellitic anhydride (TMA). J Occup Environ Med 2002;**44**:1179–1181.
48. Munoz X, Cruz MJ, Orriols R, Bravo C, Espuga M, Morell F. Occupational asthma due to persulfate salts: diagnosis and follow-up. Chest 2003;**123**:2124–2129.
49. Walusiak J, Hanke W, Gorski P, Palczynski C. Respiratory allergy in apprentice bakers: do occupational allergies follow the allergic march? Allergy 2004;**59**:442–450.
50. Moscato G, Pignatti P, Yacoub MR, Romano C, Spezia S, Perfetti L. Occupational asthma and occupational rhinitis in hairdressers. Chest 2005;**128**:3590–3598.
51. Karjalainen A, Martikainen R, Klaukka T, Saarinen K, Uitti J. Risk of asthma among Finnish patients with occupational rhinitis. Chest 2003;**123**:283–288.
52. Bousquet J, Annesi-Maesano I, Carat F, Leger D, Rugina M, Pribil C et al. Characteristics of intermittent and persistent allergic rhinitis: DREAMS study group. Clin Exp Allergy 2005;**35**:728–732.
53. Demoly P, Bozonnat MC, Dacosta P, Daures JP. The diagnosis of asthma using a self-questionnaire in those suffering from allergic rhinitis: a pharmaco-epidemiological survey in everyday practice in France. Allergy 2006;**61**:699–704.
54. Bernstein DI, Korbee L, Stauder T, Bernstein JA, Scinto J, Herd ZL et al. The low prevalence of occupational asthma and antibody-dependent sensitization to diphenylmethane diisocyanate in a plant engineered for minimal exposure to diisocyanates. J Allergy Clin Immunol 1993;**92**:387–396.
55. Vandenplas O, Ghezzo H, Munoz X, Moscato G, Perfetti L, Lemière C et al. What are the questionnaire items most useful in identifying subjects with occupational asthma? Eur Respir J 2005; **26**:1056–1063.
56. Malm L. Measurement of nasal patency. Allergy 1997;**52**:19–23.
57. Malm L, Gerth van Wijk R, Bachert C. Guidelines for nasal provocations with aspects on nasal patency, airflow, and airflow resistance. International Committee on Objective Assessment of the Nasal Airways, International Rhinologic Society. Rhinology 2000;**38**:1–6.
58. Pirila T, Nuutinen J. Acoustic rhinometry, rhinomanometry and the amount of nasal secretion in the clinical monitoring of the nasal provocation test. Clin Exp Allergy 1998;**28**:468–477.
59. Airaksinen L, Tuomi T, Vanhanen M, Voutilainen R, Toskala E. Use of nasal provocation test in the diagnostics of occupational rhinitis. Rhinology 2007; **45**:40–46.
60. Scadding G, Lund V, editors. Investigative rhinology. London: Taylor and Francis, 2004.
61. Gerth van Wijk R, Dieges PH. Nasal reactivity to histamine and methacholine: two different forms of upper airway responsiveness. Rhinology 1994;**32**:119–122.
62. Plavec D, Somogyi-Zalud E, Godnic-Cvar J. Modified method of nonspecific nasal provocation with histamine for routine use. Ann Allergy 1994;**72**:321–328.
63. Marquez F, Sastre J, Hernandez G, Cenjor C, Sanchez-Hernandez JM, Sanchez J et al. Nasal hyperreactivity to methacholine measured by acoustic rhinometry in asymptomatic allergic and perennial nonallergic rhinitis. Am J Rhinol 2000;**14**:251–256.


 

64. Braat JP, Mulder PG, Fokkens WJ, van Wijk RG, Rijntjes E. Intranasal cold dry air is superior to histamine challenge in determining the presence and degree of nasal hyperreactivity in nonallergic noninfectious perennial rhinitis. Am J Respir Crit Care Med 1998;**157**:1748–1755.
65. Togias A, Krishnamurthy A, Proud D, Kagey-Sobotka A, Lichtenstein LM, Naclerio RM. Antigen AG augments the upper airway reaction to cold dry air. Am Rev Respir Dis 1991;**143** (part 2 of 2):A37.
66. Walden SM, Proud D, Lichtenstein LM, Kagey-Sobotka A, Naclerio RM. Antigen-provoked increase in histamine reactivity. Observations on mechanisms. Am Rev Respir Dis 1991;**144**:642–648.
67. Baroody FM, Cruz AA, Lichtenstein LM, Kagey-Sobotka A, Proud D, Naclerio RM. Intranasal beclomethasone inhibits antigen-induced nasal hyperresponsiveness to histamine. J Allergy Clin Immunol 1992;**90**:373–376.
68. Klementsson H, Andersson M, Pipkorn U. Allergen-induced increase in nonspecific nasal reactivity is blocked by antihistamines without a clear-cut relationship to eosinophil influx. J Allergy Clin Immunol 1990;**86**:466–472.
69. Sanico AM, Philip G, Lai GK, Togias A. Hyperosmolar saline induces reflex nasal secretions, evincing neural hyperresponsiveness in allergic rhinitis. J Appl Physiol 1999;**86**:1202–1210.
70. Renstrom A, Malmberg P, Larsson K, Sundblad BM, Larsson PH. Prospective study of laboratory-animal allergy: factors predisposing to sensitization and development of allergic symptoms. Allergy 1994;**49**:548–552.
71. Cullinan P, Lowson D, Nieuwenhuijsen MJ, Sandiford C, Tee RD, Venables KM et al. Work related symptoms, sensitisation, and estimated exposure in workers not previously exposed to flour. Occup Environ Med 1994;**51**: 579–583.
72. Cristaudo A, Sera F, Severino V, De Rocco M, Di Lella E, Picardo M. Occupational hypersensitivity to metal salts, including platinum, in the secondary industry. Allergy 2005;**60**:159–164.
73. Krakowiak A, Krawczyk P, Szulc B, Wiszniewska M, Kowalczyk M, Walusiak J et al. Prevalence and host determinants of occupational bronchial asthma in animal shelter workers. Int Arch Occup Environ Health 2007;**80**:423–432.
74. Hytonen M, Sala E. Nasal provocation test in the diagnostics of occupational allergic rhinitis. Rhinology 1996;**34**:86–90.
75. Litvyakova LI, Baraniuk JN. Nasal provocation testing: a review. Ann Allergy Asthma Immunol 2001;**86**:355–364; quiz 364–5, 386.
76. Rajakulasingam K. Nasal provocation testing. In: Adkinson NF Jr, Yunginger JW, Busse WW, Bochner BS, Holgate ST, Simons FER, editors. Middleton's allergy principles & practice. Philadelphia, PA: Mosby, 2003:644–655.
77. Gosepath J, Amedee RG, Mann WJ. Nasal provocation testing as an international standard for evaluation of allergic and nonallergic rhinitis. Laryngoscope 2005;**115**:512–516.
78. Melillo G, Bonini S, Cocco G, Davies RJ, de Monchy JG, Frolund L et al. EAACI provocation tests with allergens. Report prepared by the European Academy of Allergology and Clinical Immunology Subcommittee on provocation tests with allergens. Allergy 1997;**52**:1–35.
79. Bachert C. Nasal provocation test: critical evaluation. In: Ring J, Behrendt HD, editors. New trends in allergy IV. Berlin: Springer-Verlag, 1997:277.
80. Moscato G, Dellabianca A, Perfetti L, Brame B, Galdi E, Niniano R et al. Occupational asthma: a longitudinal study on the clinical and socioeconomic outcome after diagnosis. Chest 1999;**115**:249–256.
81. Vandenplas O, Toren K, Blanc PD. Health and socioeconomic impact of work-related asthma. Eur Respir J 2003;**22**:689–697.
82. Gautrin D, Ghezzo H, Infante-Rivard C, Malo JL. Natural history of sensitization, symptoms and occupational diseases in apprentices exposed to laboratory animals. Eur Respir J 2001; **17**:904–908.
83. Elliott L, Heederik D, Marshall S, Peden D, Loomis D. Progression of self-reported symptoms in laboratory animal allergy. J Allergy Clin Immunol 2005; **116**:127–132.
84. Braman SS, Barrows AA, DeCotiis BA, Settipane GA, Corrao WM. Airway hyperresponsiveness in allergic rhinitis. A risk factor for asthma. Chest 1987; **91**:671–674.
85. Sastre J, Quirce S. Immunotherapy: an option in the management of occupational asthma? Curr Opin Allergy Clin Immunol 2006;**6**:96–100.
86. Brisman J, Jarvholm B. Bakery work, atopy and the incidence of self-reported hay fever and rhinitis. Eur Respir J 1999;**13**:502–507.
87. Gerth van Wijk R. Allergy: a global problem. Quality of life. Allergy 2002;**57**:1097–1110.
88. Groenewoud GC, de Groot H, van Wijk RG. Impact of occupational and inhalant allergy on rhinitis-specific quality of life in employees of bell pepper greenhouses in the Netherlands. Ann Allergy Asthma Immunol 2006; **96**:92–97.
89. Sarlo K. Control of occupational asthma and allergy in the detergent industry. Ann Allergy Asthma Immunol 2003; **90**:32–34.
90. Hugues EG. Medical surveillance of platinum refinery workers. J Soc Occup Med 1980;**30**:27–30.
91. Gordon S, Preece R. Prevention of laboratory animal allergy. Occup Med (Lond) 2003;**53**:371–377.
92. LaMontagne AD, Radi S, Elder DS, Abramson MJ, Sim M. Primary prevention of latex related sensitisation and occupational asthma: a systematic review. Occup Environ Med 2006;**63**:359–364.
93. Cullinan P, Tarlo S, Nemery B. The prevention of occupational asthma. Eur Respir J 2003;**22**:853–860.
94. Nicholson PJ, Cullinan P, Taylor AJ, Burge PS, Boyle C. Evidence based guidelines for the prevention, identification, and management of occupational asthma. Occup Environ Med 2005;**62**:290–299.
95. Tarlo SM, Liss GM. Practical implications of studies in occupational rhinoconjunctivitis. J Allergy Clin Immunol 2003;**112**:1047–1049.
96. Nicholson PJ, Newman Taylor AJ, Oliver P, Cathcart M. Current best practice for the health surveillance of enzyme workers in the soap and detergent industry. Occup Med (Lond) 2001;**51**:81–92.
97. Gannon PF, Berg AS, Gayosso R, Henderson B, Sax SE, Willems HM. Occupational asthma prevention and management in industry – an example of a global programme. Occup Med (Lond) 2005;**55**:600–605.
98. Fokkens W, Lund V, Bachert C, Clement P, Helllings P, Holmstrom M et al. EAACI position paper on rhinosinuitis and nasal polyps executive summary. Allergy 2005;**60**:583–601.
99. Spector SL, Nicklas RA, Chapman JA, Bernstein IL, Berger WE, Blessing-Moore J et al. Symptom severity assessment of allergic rhinitis: part 1. Ann Allergy Asthma Immunol 2003;**91**:105–114.
100. Fokkens W, Lund V, Mullol J. European position paper on rhinosinusitis and nasal polyps 2007. Rhinology 2007;**45** (Suppl. 20):1–139.


 