

Occupational rhinitis

Denyse Gauthrin^{a,b}, Martin Desrosiers^{c,d} and Roberto Castano^{b,e}

Purpose of review

This review updates existing knowledge on occupational rhinitis based on epidemiological and clinical research studies published from 2003 to 2005.

Recent findings

The review covers new developments on the pathophysiology, diagnosis, monitoring and management of occupational rhinitis. This article also provides updated information on the prevalence and incidence of both occupational rhinitis and work-related symptoms of rhinitis, as well as on causal agents and personal risk factors associated with this condition.

Summary

Occupational rhinitis is frequently under-diagnosed due to a lack of physician awareness. Diagnosis is suspected when symptoms occur in relation to work. Differentiating between immunological sensitization and irritation may be difficult. Given the high prevalence of rhinitis in the general population from all causes, objective tests confirming the occupational origin are essential. Measures of inflammatory parameters via nasal lavage and objective assessment of nasal congestion both offer practical means of monitoring responses. Growing experience with acoustic rhinometry and peak nasal inspiratory flow suggests that these methods will have an increasingly important role in monitoring and diagnosing in the future. Recent findings indicate that work-related rhinitis is to some extent preventable. Surveillance of sensitized workers may allow early detection of occupational rhinitis.

Keywords

allergic rhinitis, occupational asthma, occupational rhinitis, risk factors, specific nasal challenge

Abbreviations

DEE	diesel exhaust emissions
HMW	high-molecular-weight
LMW	low-molecular-weight
NGF	nerve growth factor
NIR	non-infectious rhinitis
PNIF	peak nasal inspiratory flow
SPT	skin-prick test
SRR	age-standardized rate ratio

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Introduction

Occupational rhinitis is a domain of increasing interest in occupational medicine [1]. This type of rhinitis is defined as that occurring secondary to exposure in the workplace to high-molecular-weight (HMW) agents, low-molecular-weight (LMW) agents and irritant substances through immunological or less well known non-immunological pathogenic mechanisms. This condition often coexists with occupational asthma. Occupational rhinitis has been reported as an early stage of respiratory impairment. If exposure to the offending agent persists, occupational rhinitis may develop into asthma [2].

This review updates existing knowledge on occupational rhinitis based on epidemiological and clinical research studies published between the years 2003 and 2005.

Prevalence

Varying estimates of the prevalence of occupational rhinitis have been reported. This variation is due in part to criteria used for diagnosis (e.g. symptoms reported with/without specific sensitization), geographical area and the type of occupation. A small number of studies now provide prevalence figures based on specific inhalation tests as shown in Table 1 [3–8,9^{*}]. In a study conducted among university employees exposed to laboratory animals, the prevalence was 42% for self-reported work-related symptoms of rhinitis, 15% for probable occupational rhinitis (rhinitis symptoms + skin-prick test [SPT] reactivity to laboratory animal), and 6% for occupational rhinitis confirmed by specific challenge test [3]. These results confirm the low specificity of symptom questionnaires for the diagnosis of occupational rhinitis.

Swine confinement units entail exposure to toxic gases, ammonia, endotoxins and dusts. A survey among veterinarians showed a prevalence of 38% for work-related rhinitis/conjunctivitis and 62% for allergic rhinitis [4].

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^aHôpital du Sacré-Cœur, Departments of Medicine and of Social and Preventive Medicine, University of Montreal, ^bDepartment of Epidemiology, Biostatistics and Occupational Health, McGill University, ^cHôtel-Dieu de Montreal, Department of Surgery, University of Montreal, ^dMcGill University Health Center, Departments of Otolaryngology and Allergy, McGill University and ^eCenter for Asthma in the Workplace, Hôpital du Sacré-Cœur, Montreal, Quebec, Canada

Correspondence to Denyse Gauthrin PhD, Associate Professor, Hôpital du Sacré-Cœur, 5400 Gouin Blvd West, Montreal, Qc, Canada, H4J 1C5
Tel: +514 338 2222, ext. 2568; fax: +514 338 3123;
e-mail: d.gauthrin@umontreal.ca

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Table 1 Prevalence studies of work-related symptoms of rhinitis and of occupational rhinitis

Authors, year, country	No. studied	Type of exposure	Occupation	Prevalence				Diagnostic means
				Rhinitis symptoms	Positive specific SPT	Rhinitis symptoms and specific SPT	Positive SNP	
Ruoppi <i>et al.</i> , 2004, Finland [3]	156	Laboratory animals	University animal workers	42% (65/156)	51% (24/47)	15% (24/156)	6% (10/156)	Questionnaire, specific SPT, nose exam, SNP
Susitaival <i>et al.</i> , 2003, California, USA [4]	1416	Mostly small animals	Veterinarians	38% (514/1353) (rhino-conjunctivitis) 69%	ND	NA	NA	Questionnaire
Andersen <i>et al.</i> , 2004, USA [5]	122	Swine (endotoxin, dust, ammonia)	Swine veterinarians		ND	NA	NA	Questionnaire
Ijadunola <i>et al.</i> , 2004, Nigeria [6]	91 and 111 controls	Wheat flour	Flour mill workers	56% vs 28% (in controls) ($P < 0.05$)	ND	NA	NA	Questionnaire
Chloros <i>et al.</i> , 2004, Greece [7]	1021 and 469 controls	Tobacco dust	Tobacco workers and hospital workers (controls)	27.3% vs 17.9% (in controls) ($P < 0.001$)	6/1021	6/1021	53 in 76 of 279 subjects reporting rhinitis	Questionnaire, rhinomanometry, SNP, SPT, specific IgE
Arbak <i>et al.</i> , 2004, Turkey [8]	64 and 62 controls	Fir and pine wood; paint and varnish; toluene; formaldehyde	Furniture-decorating apprentices and other students (controls)	34.4% vs 19.4% (in controls) ($P = 0.04$)	ND	NA	NA	Questionnaire
Kaukiainen <i>et al.</i> , 2005, Finland [9*]	1000 and 1000 controls	Paints, solvents, dusts	Construction painters and carpenters (controls)	45.4% vs 33.3% (in controls) ($P < 0.001$)	ND	NA	NA	Questionnaire

SPT, skin-prick test; OR, occupational rhinitis; SNP, specific nasal provocation test; ND, not done; NA, non-applicable; IgE, immunoglobulin E.

Results from surveys conducted among farmers, jointly in European countries ($n = 7188$) and California ($n = 1839$), revealed a lower prevalence of rhinitis in Europe (12.7%) than in California (23.9%) [10]. Other surveys have assessed the prevalence of self-reported rhinitis symptoms among furniture-decorating apprentices in Turkey [8] and construction painters in Finland [9*].

Incidence

A contribution to the appraisal of the risk of occupational rhinitis in various occupations and to the identification of causal agents was made by Hytonen *et al.* [2]. The study analysed 1244 incident cases of occupational rhinitis reported from 1986 to 1991 to the Finnish Register of Occupational Diseases. The diagnosis was based on patients' symptoms and signs, SPTs or radioallergosorbent tests and provocation tests. The relative risk of occupational rhinitis in different occupations was expressed as the age-standardized rate ratio (SRR), using the whole cohort of workers as the standard population. The greatest risk of occupational rhinitis was among furriers (SRR = 30.0), followed by bakers and livestock breeders (SRR = 22.0), food-processing workers, veterinarians, farmers, assemblers of electrical, electronic and telecommunication products, and boat builders were also at increased risk (SRR ranging from 7.3 to 13.0).

Other approaches to estimate the incidence of occupational rhinitis include register [11] and population-based studies [12], and prospective studies in specific workforces [12–14]. In the United Kingdom, the incidence of occupational rhinitis to laboratory allergens for 1999–2000 was estimated at 2.54/1000 person-years among individuals working with small animals [11].

A survey [15] conducted among 2044 subjects showed an increased risk of developing non-infectious rhinitis (NIR) in men reporting occupational exposure to wood dust, textile dust, fire fumes, quick-drying glues and paint hardeners and in women reporting exposure to paper dust and textile dust. Cleaners compared with the rest of the study population were at increased risk of developing NIR.

As depicted in Table 2 [16–19,20*], findings from Canadian prospective studies performed in apprentices exposed to HMW agents [13,16,19] agree with those obtained among recently employed workers in bakeries [18] or animal facilities in the United Kingdom [17].

It is interesting to note that in both the British and the Canadian cohort studies, work-related rhinoconjunctivitis symptoms appear to be of allergic origin in 32–40% of symptomatic subjects exposed to laboratory animals, while of allergic origin in only 10% of those exposed to flour. Symptoms of rhinitis at work in subjects without

Table 2 Prospective studies on the incidence of work-related symptoms of rhinitis and of occupational rhinitis

Authors, year, country	No. studied	Type of work (exposure)	Duration of follow-up (months)	Incidence		
				Rhinitis symptoms	Rhinitis symptoms and specific SPT	
Archambault <i>et al.</i> , 2001, Quebec, Canada [16]	122	Apprentice dental hygienists (latex)	32	7.3% (8/110)	1.8% (2/110)	
Cullinan <i>et al.</i> , 1999, UK [17]	342	Laboratory employees (rats)	32	7.3 per 100 py ($n = 84$)	7.9%* (27/342)	
Rodier <i>et al.</i> , 2003, Quebec, Canada [13]	417	Apprentice animal workers (lab animals)	44	24.0% (93/387)	9.6% (37/387)	
Cullinan <i>et al.</i> , 2001, UK [18]	300	Bakers (flour, alpha-amylase)	40	11.8 per 100 py ($n = 86$)	5%* (flour/alpha-amylase) (15/300); 3%* (flour) (9/300)	
Gautrin <i>et al.</i> , 2002, Quebec, Canada [19]	230	Apprentice pastry-makers (flour)	17	13.1 per 100 py ($n = 30$)	1.6% (3/186)	
Walusiak <i>et al.</i> , 2004, Poland [20*]	287	Apprentice bakers (flour)	1 – 12/12 – 24/1 – 24* [†]	6.5%/10.8%/16.5%* [‡]	4.5%/8.4%/12.5%§ (36/287)* [‡]	

*derived from [17]; **derived from [18]; †between 1 and 12 months/between 12 and 24 months/between 12 and 24 months/between 1 and 24 months; § confirmed by + specific nasal provocation test; py, person-years; SPT, skin-prick test.

positive specific SPT may be non-specific, non-work-related or related to non-allergic exposures in the workplace, as commented by Tarlo *et al.* [14]. Unlike in these studies, Walusiak *et al.* [20[•]] found only two out of 36 subjects with occupational rhinitis, confirmed by specific challenge, with no specific sensitization.

The incidence of symptoms of work-related rhinoconjunctivitis is greatest in the first 12–20 months of employment or apprenticeship [17,18,21] and increases with the duration of exposure over a 24-month period [20[•]]. The short latency period for the incidence of work-related rhinitis symptoms and disease indicates a need for surveillance in the first years of exposure [14]. To detect symptomatic sensitization, surveillance programs may have to be of longer duration. Smith reported a 7.3-year latency period for the acquisition of either work-related rhinitis or asthma symptoms and sensitization in bakers taking part in a 10-year surveillance program [22].

Risk factors

A history of atopic symptoms is common among workers with occupational rhinitis (57%, 27/47) [3]. Identified predictors for work-related nasal symptoms include positive SPT to work-specific allergens [19,23], to common allergens such as grass pollen [13] and atopy [20[•]], upper and lower airway symptoms to common allergens [23], non-specific nasal symptoms [19], and respiratory symptoms upon exposure to dust or strong odours [13].

An exposure–response relation between intensity of exposure to alpha-amylase, rat urinary aeroallergens and work-related eye/nose symptoms has been demonstrated in longitudinal studies [18,24[•],25].

Certain exposures may have a protective role in preventing the development of occupational rhinitis and occupational asthma. In a case–control study conducted in Poland among farmers, non-specialized farming was shown to have a protective role for occupational respiratory allergy (odds ratio = 0.23; 95% CI 0.11–0.47) [26[•]]. The results of this study support the hypothesis that endotoxin exposure, measured in farming environments [27], may protect against respiratory allergy.

Pathogenic mechanisms

Inflammation of the nasal passages can occur via specific sensitization, acute or chronic irritation of the nasal mucosa, or a combination of both. Mechanisms of sensitization to HMW compounds are classical IgE-mediated pathways, while sensitization to LMW compounds involves both IgE and other less well understood mechanisms.

In a review of irritant-induced changes, Shusterman [28] suggested that large particles, water-soluble gases and

vapours are likely to have their initial irritant effects in the mucous membranes of the upper airway and eyes. Shusterman *et al.* [29] address the mechanisms of irritant compared with allergen sensitivity. Chlorine inhalation produces nasal congestion in allergic rhinitics without mast cell degranulation. This study emphasizes that allergic rhinitics are more sensitive to occupational exposures to irritant agents, even at sub-toxic levels, as compared with non-rhinitic controls.

Occupational as well as environmental exposures can be a cause of perennial allergic rhinitis [30[•]]. New research that may contribute to the understanding of the role of neurogenic mechanisms in the pathogenesis of this type of rhinitis was conducted. Fischer *et al.* [30[•]] assessed the neuropeptide profile of nerves of the nasal mucosa in biopsies taken from rhinitics and controls. This study demonstrated an increase of vasoactive intestinal peptide-containing nerve fibres among the group of rhinitics, suggesting a modulatory role of the upper airway innervation in perennial allergic rhinitis.

Nerve growth factor (NGF) is a neurotrophin that plays a role in airway inflammation. Using an animal model to investigate the source of NGF in the nasal mucosa, Wilfong and Dey [31[•]] demonstrated an increase of NGF in nasal lavage fluids after provocation with toluene diisocyanate. Most interestingly, the findings suggested nasal epithelium as being a primary source of NGF.

Causal agents

Reports of occupational rhinitis confirmed by specific nasal provocation are increasing. In Spain, Miralles *et al.* [32] described two cases of occupational rhinitis induced by artichoke and Armentia *et al.* [33] reported a case of occupational rhinitis due to leek. In Finland, a case of rhinoconjunctivitis due to deer ked (elk fly) was reported in a subject working in the forest [34]. Munoz *et al.* [35] described a series of eight patients with confirmed occupational asthma to persulfate salts accompanied by occupational rhinitis in six subjects. SPT to persulfates were positive in five of them. This suggested that an IgE-dependent mechanism may be implicated in the pathogenesis of occupational rhinitis due to this agent.

Industrial enzyme production and utilization constitute a hazard for respiratory sensitization. Baur [36[•]] reviews the characteristics and significance of occupational and environmental exposures to airborne enzymes.

Exposure to metal salts like platinum can also cause respiratory allergy. In a study conducted by Cristaudo *et al.* [37[•]], the prevalence of rhinitis and asthma symptoms with specific sensitization among workers in a catalyst industry was 12% (18/153) and 6.5% (10/153),

respectively. As commented by Malo [38[•]], these figures resemble those reported in studies on probable occupational rhinitis and occupational asthma due to LMW agents.

Sensitization to mites in workers with work-related rhinitis symptoms is reported in Finnish laboratory workers (storage mites) [39] and in Swedish greenhouse workers (predatory mites) [40].

The deleterious effect of exposure to irritant gases on risk of occupational rhinitis was documented in a longitudinal study [41[•]] conducted in workers exposed to ozone gases in pulp mills. The risk of NIR by self-reported ozone gassing exposures was higher in bleachery workers exposed to ozone in comparison with those non-exposed (Hazard ratio (HR) = 3.4, 95% CI 1.3–8.7).

Diagnosis and monitoring

As symptoms of occupational rhinitis resemble those of rhinitis from other causes, a high index of suspicion on the part of the clinician is required. Generally, symptoms are those of irritation, with nasal or ocular pruritus, sneezing, nasal obstruction or watery rhinorrhea predominating.

As even in high-risk groups, the frequency of rhinitis symptoms may lead to an over-estimate of the true incidence of occupational rhinitis, confirmation of a causal link between the suspected workplace agent and symptoms by objective means is essential.

While SPTs are frequently used to assess sensitization, this may not be indicative of clinical disease. In addition, many substances are not available as extracts suitable for SPTs. Thus, specific nasal challenge in a controlled setting continues to be the gold standard means for diagnosing occupational rhinitis.

Specific nasal challenge can be performed in a laboratory setting or at the workplace. While the response may be assessed using symptoms alone, objective means of documenting nasal responses during the challenge are being increasingly used and are focused mainly on measures of inflammation assessed in nasal lavage [42^{••}], and measures of nasal congestion through means such as rhinomanometry, acoustic rhinometry and peak nasal inspiratory flow [43^{••}].

Assessment of inflammatory parameters appears to be potentially a more useful technique in the context of nasal challenge rather than as a means of differentiating affected from non-affected individuals at baseline state. Using nasal lavage, Palczynski *et al.* [44] assessed mast cell tryptase, eosinophilic cationic protein (ECP) and markers of vascular permeability in six subjects with chloramine T-induced asthma and rhinitis, and in 13

controls at 30 min, 4 hours and 24 hours after challenge. They found increases in all three markers in only the affected group. Using the same challenge model, they obtained similar findings in a population of laboratory animal workers [45]. In this study, the intensity of the inflammatory reaction correlated with an increase in expiratory nasal resistance.

In a study [46] of former Swedish bakers with rhinitis, the markers of airway inflammation using nasal lavage were no different from controls, despite onset of symptoms at work and positive SPTs to flour or alpha-amylase. These results probably reflect a lack of sensitivity of the measurement technique used or a lack of published identifiable threshold values rather than the absence of inflammatory response in the pathogenesis of the disorder.

Objective measures of nasal congestion are increasingly reported as research tools and in clinical settings. Peak nasal inspiratory flow (PNIF) was used in the assessment of sensitization to HBTU (2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate) and TBTU (2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate) – two chemical products widely used in peptide synthesis and coupling – in a worker with suspected occupational asthma and occupational rhinitis [47]. In both cases, PNIF decreased by more than 60% and severe sneezing and rhinorrhea were induced, while nasal challenge with the same concentration of substance was negative in 10 non-atopic subjects. The assessment of changes in nasal airflow during nasal challenge tests using PNIF showed decreases of 81 and 85%, respectively, in two case studies of workers with sensitization to artichoke [31[•]].

Acoustic rhinometry offers a reproducible, subject-independent means of assessing nasal congestion. In Denmark, acoustic rhinometry was used to assess nasal congestion in 159 woodworkers exposed to different concentrations of wood dust and 19 controls [48]. Significant increases in nasal congestion were recorded after 4 and 7 hours of work amongst those more exposed. This study highlights that despite good reproducibility of measures, the wide range of normal values for acoustic rhinometry makes its use best for within individual comparisons.

The techniques of nasal lavage and acoustic rhinometry can also be performed simultaneously. Monitoring of nasal parameters over the workweek with both techniques was performed in a group of 31 Norwegian waste-control workers exposed to bio-aerosols [49]. Comparing measurements before and after exposure showed an increase in the percentage of neutrophils in nasal lavage. This increase correlated positively with increases in ECP and myeloperoxidase (MPO), and showed a close to significant correlation with nasal swelling.

The applicability of nasal lavage and acoustic rhinometry in the clinical setting is also depicted in a case report of a patient with suspected occupational rhinitis to xerographic toner [50].

Serial nasal cytology was used as a means of assessing changes in the nasal mucosa associated with chronic workplace exposure to diesel exhaust emissions (DEE) in a population of exposed ($n = 136$) and non-exposed ($n = 58$) non-smoking Swiss custom workers [51]. Significant goblet cell hyperplasia and a significant increase in lymphocytes were noted in exposed workers as compared with non-exposed workers. These changes were interpreted as manifestations of chronic irritation of the nasal mucosa with an inflammatory response. Of note is the fact that DEE levels were between 1/3 and 1/6 of the maximal permitted value, suggesting this technique is sensitive even when DEE concentrations are below the permitted levels. Nevertheless, considering that DEE is a mixture of mucous membrane-irritating gases (e.g. formaldehyde, sulfur dioxide, acrolein), further research is needed to assess the role of DEE constituents on the nasal mucosa.

Research on the measurement of exhaled nitric oxide as a marker of upper and lower airways inflammation is on the rise. A study [52*] was conducted in latex-sensitized and non-sensitized healthcare workers complaining of rhinitis and dyspnoea at work and who were investigated by specific inhalation challenges. The study showed significant differences in the increase of nitric oxide levels compared with those at baseline between sensitized and non-sensitized subjects, 22 hours after challenge to latex. In contrast, baseline measurements did not differentiate the two groups.

Management and prevention

Symptomatic control of rhinitis may be accomplished using conventional pharmacotherapy with antihistamines, or intranasal topical corticosteroids.

Immunotherapy has been suggested as a means of control for natural rubber latex allergy but for occupational rhinitis, results have been disappointing [53]. Clinical improvement was mostly in cutaneous symptoms, with no difference in clinical scores for rhinitis or asthma. On specific inhalation testing, a reduced response was noted in the asthma but not in the rhinitis group.

In the absence of a definite therapy for occupational rhinitis, avoidance of the offending substance is probably the best course to prevent progression of the disease. Stepwise escalation of avoidance measures with substitution of less hazardous materials, enclosure or ventilation of the work area, reduced exposure time, or use of protective gear constitute the mainstays of management [54].

The impact of occupational rhinitis on the development of asthma was studied in Finnish workers seeking compensation for occupational rhinitis. The relative risk of developing asthma was 4.8 (95% CI 4.3–5.4) in patients with occupational rhinitis as compared with patients receiving compensation for any other occupational disease. The risk was highest in the year following the diagnosis of occupational rhinitis [55].

Conclusion

Occupational rhinitis is a condition that is frequently under-diagnosed secondary to a lack of physician awareness. Differentiating between true sensitization and irritation may be difficult.

Given the high frequency of rhinitis from all causes in the general population, objective tests confirming the occupational origin are essential. Measures of inflammatory parameters via nasal lavage and objective assessment of nasal congestion both offer potentially practical means of monitoring responses during a specific nasal provocation test that continue to be the gold standard for the diagnosis of occupational rhinitis. Growing experience with acoustic rhinometry and PNIF suggests that they will play an increasing role in monitoring and diagnosis in the future. Finally, continued sensitization of physicians assessing workers for occupational disorders, including occupational asthma, will lead to early recognition of occupational rhinitis.

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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 (p. 128).

- 1 Slavin RG. Occupational rhinitis. *Ann Allergy Asthma Immunol* 2003; 90 (Suppl 2):2–6.
- 2 Hytonen M, Kanerva L, Malmberg H, *et al.* The risk of occupational rhinitis. *Int Arch Occup Environ Health* 1997; 69:487–490.
- 3 Ruoppi P, Koistinen T, Susitaival P, *et al.* Frequency of allergic rhinitis to laboratory animals in university employees as confirmed by chamber challenges. *Allergy* 2004; 59:295–301.
- 4 Susitaival P, Kirk JH, Schenker MB. Atopic symptoms among California veterinarians. *Am J Ind Med* 2003; 44:166–171.
- 5 Andersen CI, Von Essen SG, Smith LM, *et al.* Respiratory symptoms and airway obstruction in swine veterinarians: a persistent problem. *Am J Ind Med* 2004; 46:386–392.
- 6 Ijadunola KT, Erhabor GE, Onayade AA, *et al.* Prevalence of respiratory symptoms among wheat flour mill workers in Ibadan, Nigeria. *Am J Ind Med* 2004; 45:251–259.
- 7 Chloros D, Sichelidis L, Kyriazis G, *et al.* Respiratory effects in workers processing dried tobacco leaves. *Allergol Immunopathol (Madr)* 2004; 32:344–351.
- 8 Arbak P, Bilgin C, Balbay O, *et al.* Respiratory symptoms and peak expiratory flow rates among furniture-decoration students. *Ann Agric Environ Med* 2004; 11:13–17.

- 9 Kaukiainen A, Riala R, Martikainen R, *et al.* Respiratory symptoms and diseases among construction painters. *Int Arch Occup Environ Health* 2005; 78:452–458.
This well conducted large epidemiological survey demonstrated a higher risk for upper airways respiratory symptoms in construction painters.
- 10 Monso E, Schenker M, Radon K, *et al.* Region-related risk factors for respiratory symptoms in European and Californian farmers. *Eur Respir J* 2003; 21:323–331.
- 11 Draper A, Newman TA, 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.
- 12 Hellgren J, Lillienberg L, Jarlstedt J, *et al.* Population-based study of non-infectious rhinitis in relation to occupational exposure, age, sex, and smoking. *Am J Ind Med* 2002; 42:23–38.
- 13 Rodier F, Gautrin D, Ghezzi H, *et al.* Incidence of occupational rhinoconjunctivitis and risk factors in animal-health apprentices. *J Allergy Clin Immunol* 2003; 112:1105–1111.
- 14 Tarlo SM, Liss GM. Practical implications of studies in occupational rhinoconjunctivitis. *J Allergy Clin Immunol* 2003; 112:1047–1049.
- 15 Sibbald B, Rink E. Epidemiology of seasonal and perennial rhinitis: clinical presentation and medical history. *Thorax* 1991; 46:895–901.
- 16 Archambault S, Malo JL, Infante-Rivard C, *et al.* Incidence of sensitization, symptoms, and probable occupational rhinoconjunctivitis and asthma in apprentices starting exposure to latex. *J Allergy Clin Immunol* 2001; 107:921–923.
- 17 Cullinan P, Cook A, Gordon S, *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.
- 18 Cullinan P, Cook A, Nieuwenhuijsen MJ, *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.
- 19 Gautrin D, Ghezzi H, Infante-Rivard C, Malo JL. Incidence and host determinants of work-related rhinoconjunctivitis in apprentice pastry-makers. *Allergy* 2002; 57:913–918.
- 20 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.
This study presents interesting results from a prospective study on the incidence of respiratory allergy in apprentice bakers who were submitted to exhaustive investigations including allergen-specific inhalation challenges with objective measures of the nasal response.
- 21 Gautrin D, Ghezzi 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.
- 22 Smith T. Latent period for symptomatic sensitization in bakeries. *Occup Med (Lond)* 2005; 55:93–95.
- 23 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.
- 24 Brisman J, Nieuwenhuijsen MJ, Venables KM, *et al.* Exposure-response relations for work related respiratory symptoms and sensitisation in a cohort exposed to alpha-amylase. *Occup Environ Med* 2004; 61:551–553.
This article shows trends for exposure-response relationships between alpha-amylase and nose symptoms in bakers; sensitization to alpha-amylase was more common than sensitization to flour.
- 25 Nieuwenhuijsen MJ, Putcha V, Gordon S, *et al.* Exposure-response relations among laboratory animal workers exposed to rats. *Occup Environ Med* 2003; 60:104–108.
- 26 Walusiak J, Krawczyk-Adamus P, Hanke W, *et al.* Small nonspecialized farming as a protective factor against immediate-type occupational respiratory allergy? *Allergy* 2004; 59:1294–1300.
This study contributes with evidence on the protective role of some exposures on the development of respiratory allergy.
- 27 Ernst P, Cormier Y. Relative scarcity of asthma and atopy among rural adolescents raised on a farm. *Am J Respir Crit Care Med* 2000; 161:1563–1566.
- 28 Shusterman D. Toxicology of nasal irritants. *Curr Allergy Asthma Rep* 2003; 3:258–265.
- 29 Shusterman D, Balmes J, Avila PC, *et al.* Chlorine inhalation produces nasal congestion in allergic rhinitics without mast cell degranulation. *Eur Respir J* 2003; 21:652–657.
- 30 Fischer A, Wussow A, Cryer A, *et al.* Neuronal plasticity in persistent perennial allergic rhinitis. *J Occup Environ Med* 2005; 47:20–25.
An interesting study assessing changes in nasal mucosa nerve profiles in the pathogenesis of upper airway inflammation.
- 31 Wilfong ER, Dey RD. The release of nerve growth factor from the nasal mucosa following toluene diisocyanate. *J Toxicol Environ Health A* 2005; 68:1337–1348.
This study adds new knowledge on the involvement of nerve growth factor in nasal airway inflammation.
- 32 Miralles JC, Garcia-Sells J, Bartolome B, Negro JM. Occupational rhinitis and bronchial asthma due to artichoke (*Cynara scolymus*). *Ann Allergy Asthma Immunol* 2003; 91:92–95.
- 33 Armentia A, Lombardero M, Fernandez S, *et al.* Occupational rhinitis to leek (*Allium porrum*). *Allergy* 2005; 60:132–133.
- 34 Laukkanen A, Ruoppi P, Makinen-Kiljunen S. Deer ked-induced occupational allergic rhinoconjunctivitis. *Ann Allergy Asthma Immunol* 2005; 94:604–608.
- 35 Munoz X, Cruz MJ, Orriols R, *et al.* Occupational asthma due to persulfate salts: diagnosis and follow-up. *Chest* 2003; 123:2124–2129.
- 36 Baur X. Enzymes as occupational and environmental respiratory sensitizers. *Int Arch Occup Environ Health* 2005; 78:279–286.
This review highlights the importance and implications of exposure to enzymes as a cause of occupational respiratory allergy.
- 37 Cristaudo A, Sera F, Severino V, *et al.* Occupational hypersensitivity to metal salts, including platinum, in the secondary industry. *Allergy* 2005; 60:159–164.
This study characterizes and provides evidence on the prevalence of sensitization in workers with rhinitis secondary to platinum salts.
- 38 Malo JL. Occupational rhinitis and asthma due to metal salts. *Allergy* 2005; 60:138–139.
This editorial discusses practical implications for prevention and surveillance of sensitization to metal salts at work.
- 39 Ruoppi P, Koistinen T, Pennanen S. Sensitisation to mites in laboratory animal workers with rhinitis. *Occup Environ Med* 2005; 62:612–615.
- 40 Kronqvist M, Johansson E, Kolmodin-Hedman B, *et al.* IgE-sensitization to predatory mites and respiratory symptoms in Swedish greenhouse workers. *Allergy* 2005; 60:521–526.
- 41 Hoffman CD, Henneberger PK, Olin AC, *et al.* Exposure to ozone gases in pulp mills and the onset of rhinitis. *Scand J Work Environ Health* 2004; 30:445–449.
This study provided evidence on the higher risk of rhinitis that is observed after peak occupational exposure to ozone.
- 42 Howarth PH, Persson CG, Meltzer EO, *et al.* Objective monitoring of nasal airway inflammation in rhinitis. *J Allergy Clin Immunol* 2005; 115 (3 Pt 2): S414–S441.
An essential and detailed review on the different approaches to objectively assess and monitor nasal airway inflammation.
- 43 Nathan RA, Eccles R, Howarth PH, *et al.* Objective monitoring of nasal patency and nasal physiology in rhinitis. *J Allergy Clin Immunol* 2005; 115 (3 Pt 2):S442–S459.
This is an excellent and complete review on the use of objective means to assess nasal patency for the investigation of rhinitis.
- 44 Palczynski C, Walusiak J, Krakowiak A, *et al.* Nasal lavage fluid examination in diagnostics of occupational allergy to chloramine. *Int J Occup Med Environ Health* 2003; 16:231–240.
- 45 Krakowiak A, Ruta U, Gorski P, *et al.* Nasal lavage fluid examination and rhinomanometry in the diagnostics of occupational airway allergy to laboratory animals. *Int J Occup Med Environ Health* 2003; 16:125–132.
- 46 Brisman J, Lillienberg L, Belin L, *et al.* Sensitisation to occupational allergens in bakers' asthma and rhinitis: a case-referent study. *Int Arch Occup Environ Health* 2003; 76:167–170.
- 47 Miralles JC, Negro JM, Alonso JM, *et al.* Occupational rhinitis and bronchial asthma due to TBTU and HBTU sensitization. *J Investig Allergol Clin Immunol* 2003; 13:133–134.
- 48 Schlunssen V, Schaumburg I, Andersen NT, *et al.* Nasal patency is related to dust exposure in woodworkers. *Occup Environ Med* 2002; 59:23–29.
- 49 Heldal KK, Halstensen AS, Thorn J, *et al.* Upper airway inflammation in waste handlers exposed to bioaerosols. *Occup Environ Med* 2003; 60:444–450.
- 50 Wittczak T, Walusiak J, Ruta U, Palczynski C. Occupational asthma and allergic rhinitis due to xerographic toner. *Allergy* 2003; 58:957.
- 51 Gluck U, Schutz R, Gebbers JO. Cytopathology of the nasal mucosa in chronic exposure to diesel engine emission: a five-year survey of Swiss customs officers. *Environ Health Perspect* 2003; 111:925–929.

- 52 Baur X, Barbinova L. Latex allergen exposure increases exhaled nitric oxide in symptomatic healthcare workers. *Eur Respir J* 2005; 25:309–316.
 - The results of this study suggest a potential role of exhaled nitric oxide as a marker of allergic airway inflammation.
- 53 Sastre J, Fernandez-Nieto M, Rico P, *et al.* Specific immunotherapy with a standardized latex extract in allergic workers: a double-blind, placebo-controlled study. *J Allergy Clin Immunol* 2003; 111:985–994.
- 54 Hellgren J, Karlsson G, Toren K. The dilemma of occupational rhinitis: management options. *Am J Respir Med* 2003; 2:333–341.
- 55 Karjalainen A, Martikainen R, Klaukka T, *et al.* Risk of asthma among Finnish patients with occupational rhinitis. *Chest* 2003; 123:283–288.