

REVIEW

Epidemiology of occupational rhinitis: prevalence, aetiology and determinants

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Introduction

Occupational asthma (OA) and occupational rhinitis (OR) are closely associated and share aetiological agents [1,2]. The prevalence of OR in subjects with OA is 76–92% [2,3]. Although the prevalence and determinants of OA have been widely studied, the epidemiology of OR has been investigated less, mainly because it is not considered such a serious disease. In the general population rhinitis is three times more prevalent than asthma [4,5] and tends to occur three times more frequently in occupational settings [6]. OR may be a marker of the likelihood of developing OA. In fact, when asthma and rhinitis are present concomitantly, symptoms of rhinitis often develop before those of asthma, as reported in occupational [2,7] and nonoccupational settings [4]. However we do not know why some patients with OR develop OA and some do not. A standard definition of OR for epidemiological studies is not available. Only very recently has the European Community provided a definition of 'Occupationally caused allergic rhinitis' [8] which unfortunately excludes some cases of OR caused by low molecular weight agents, because an allergic mechanism has not been identified. For the purpose of this review we considered as OR any rhinitic symptom reported as work-related, with the exclusion of malignant diseases. This manuscript reviews the prevalence and more common aetiological agents of OR and its relationship with OA. Exposure, atopy, and smoking are also reviewed as potential determinants of OR.

Methods for assessing prevalence

The data reviewed here come from cross-sectional studies conducted in various working populations. The prevalence of OR was assessed using several different questionnaires. Although a validated questionnaire for OA, which includes questions specifically designed to investigate rhinitis, was developed conjointly by the University of Cincinnati

Occupational Allergy Laboratory and the National Institute of Occupational Safety and Health (NIOSH) [9], it has never been used to assess OR.

As prevalence of OR depends on the methods used for diagnosis (questionnaire, objective evaluations) OR frequency may be overestimated (information bias) or underestimated (healthy worker effect), making analysis and comparison of results difficult [10].

Immunological assessment of OR, OA and nonoccupational rhinitis are similar. Sensitization to an occupational agent is not sufficient to diagnose OR, because it signifies only an immunological response to the specific occupational exposure. However, specific IgE-mediated mechanisms correlate with OA [11–15] and, less frequently, with OR [12,13,15]. Skin tests and serum IgE have been used extensively to assess sensitization to a specific agent (Table 1). Sensitivity and specificity have been evaluated with divergent results [16–19]. Other objective assessments for diagnosing OR have used several nonstandardized methodologies [20–25].

Objective methods for evaluating occupational rhinitis

Documentation of OR requires demonstration of response to the occupational agent, i.e. by reproduction of clinical disease on challenge with the specific substance [20,21,23,25].

Nasal challenges (NC) are obviously more conclusive when performed in a controlled, laboratory setting, with known and available substances, and specially equipped facilities. They are more difficult when dealing with an unknown agent, multiple agents, dangerous agents or when specific testing facilities are not available. In these instances, a workplace challenge is recommended. Care must be taken to ensure a normal work environment, with neither worker nor employer manipulating the environment unduly.

NC have obviously some disadvantages; first of all they are time-consuming and difficult to apply in large epidemiological studies. The methodology is not standardized

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Table 1. Prevalence of occupational rhinitis

Agents	Occupation	Ref	Subjects <i>n</i>	Prevalence* %	Asthma: rhinitis ratio†	Specific skin test %‡	Specific serum IgE, %‡	Skin test with common allergens %
High molecular weight agents								
<i>Laboratory animal allergens</i>								
Laboratory animals (<i>rat, mouse, rabbit, guinea-pig</i>)	Laboratory workers	[7]	399	15/NS	1 : 1.9	ND	ND	ND
Laboratory animals	Laboratory workers	[46]	179	25/NS	1 : 2.1	16 +	ND	39 +
Laboratory animals	Laboratory workers	[11]	146	23/NS	1 : 2.2	15 +	ND	24 +
Mouse	Laboratory workers	[47]	121	24/NS	1 : 5.9	32 +	21 +	NS
Laboratory animals (<i>rat, mouse, rabbit, guinea-pig</i>)	Laboratory workers	[48]	69	21/NS	1 : 4.3	16 +	11 +	40 +
Laboratory animals (<i>rat, mouse, rabbit, guinea-pig, cat, hamster</i>)	Laboratory workers	[12]	101	30/NS	1 : 3.0	46 + §	46 + §	37 +
Rat	Laboratory workers	[13]	179	17/NS	1 : 1.7	12 +	10 +	40 +
Laboratory animals (<i>rat, mouse, rabbit, guinea-pig</i>)	Laboratory workers	[14]	138	33/NS	1 : 2.8	13 +	37 +	43 +
Laboratory animals (<i>rat, mouse, rabbit, guinea-pig, hamster, dog, cat, monkey</i>)	Laboratory workers	[49]	5641	19/NS	1 : 2.9	ND	ND	ND
Rat	Laboratory workers	[15]	238	13/NS	1 : 1.9	10 +	ND	40 +
Mouse	Laboratory workers	[50]	377	11/NS	1 : 2.8	10 +	6 +	24 + ¶
Rat	Laboratory workers	[50]	458	17/NS	1 : 2.7	18 +	11 +	25 + ¶
Rat	Laboratory workers	[51]	74	12/20	1 : 4.5	ND	7 +	ND
Rat	Laboratory workers	[51]	219	15/26	1 : 3.0	ND	13 +	ND
Rat	Laboratory workers	[51]	357	10/23	1 : 3.9	ND	8 +	ND
<i>Other animal-derived allergens</i>								
Pig	SCW	[52]	132	ND/8	NA	0 +	ND	ND
Pig	SCW	[53]	53	ND/47	NA	ND	ND	ND
Wool	Wool textile workers	[54]	2151	ND/18	NA	ND	ND	ND
Pig	SCW	[55]	1504	23/NS	1 : 2.6	ND	ND	ND
<i>Insects and mites</i>								
Locust	Laboratory workers	[56]	43	35/NS	1 : 1.3	43 +	NS	40 +
Storage mites	Farm workers	[57]	290	ND/30	1 : 2.0**	37 +	ND	27 +
Storage mites	Farm workers	[58]	440	ND/65	1 : 2.2**	ND	12 +	34 +
Fruit fly (<i>D. melanogaster</i>)	Laboratory workers	[20]	22	32/NS	1 : 1.7	36 +	36 +	ND
Locust	Laboratory workers	[17]	15	60/NS	1 : 1.8	67 +	53 +	67 +
Storage mites	Farm workers	[59]	101	15/58	1 : 0.7	30 +	18 +	39 +
Sheep blowfly (<i>Lucilia cuprina</i>)	Technicians	[60]	54	24/NS	1 : 2.2	ND	35 +	ND
Beneficial arthropods	Laboratory workers	[61]	13	46/NS	1 : 2.0	ND	62 +	15 +
Storage mites	Cattle farmers	[62]	149	16/19	1 : 2.7	18 +	ND	23 +
Spider mites (<i>T. urticae</i> , <i>P. citri</i>)	Horticulture and citric culture workers	[63]	150	2/30	††	36 +	36 +	NS
<i>Grain dust</i>								
Grain dust	Grain elevators	[64]	300	64/NS	1 : 1.5	18 +	ND	28 +
Grain dust	Grain elevators	[65]	610	ND/34	1 : 1.1**	9 +	ND	18 +
Grain dust	Grain elevators	[66]	248	37/NS	1 : 3.4	28 +	ND	13 +

Table 1. continued

Agents	Occupation	Ref	Subjects <i>n</i>	Prevalence* %	Asthma: rhinitis ratio†	Specific skin test %‡	Specific serum IgE, %‡	Skin test with common allergens %
Grain dust	Grain elevators	[67]	315	ND/28	1 : 2.2**	ND	ND	ND
Flour								
Flour, grain mites, flour beetle, moulds	Bakers	[68]	279	19/38	1 : 1.5	38 +	ND	40 +
Flour, α-amylase	Bakers	[69]	226	18/NS	1 : 2.8	14 +	ND	24 +
Flour, α-amylase, <i>L. destructor</i>	Bakers	[19]	264	29/NS	1 : 2.0	22 +	ND	34 +
Flour	Packers (confectionery industry)	[70]	53	ND/24	1 : 4.3	26 +	NS	NS
Flour	Bakers	[71]	393	21/NS	NS	ND	10 +	ND
Latex								
Latex	Glove manufacture	[72]	68	76/NS	1 : 1.3	11 +	ND	ND
Latex	Hospital workers	[73]	273	9/NS	1 : 5.0	5 +	ND	25 +
Latex	Hospital workers	[24]	268	9/ND	††	ND	ND	ND
Latex	Dental students/staff	[74]	203	12/NS	1 : 2.2	10 +	ND	17 +
Latex	Textile factory	[75]	10	20/40	1 : 2.0	20 +	20 +	40 +
Other plant allergens								
Tobacco leaf	Tobacco manufacturing	[76]	222	ND/9	1 : 1.7**	8	ND	24 +
Green coffee/castor beans	Dockers	[77]	218	13/23	1 : 2.3	ND	ND	33 +
Guar gum	Carpet manufacturing	[78]	162	36/NS	1 : 1.6	5 +	8 +	24 +
Cayenne peppers (<i>Capricum annum</i>)	Hot pepper workers	[79]	22	ND/59	1 : 2.6**	ND	ND	ND
Pollens and moulds	Lawn cutters	[80]	128	25/43	1 : 3.2	‡‡	ND	32 +
Green coffee/castor beans	Coffee workers	[81]	211	ND/35	1 : 1.6**	15–22 +	ND	22 +
Dried fruits and teas	Dried fruit/tea workers	[82]	54	ND/41	††	78 +	ND	ND
Saffron flower (<i>Crocus sativus</i>)	Saffron workers	[83]	50	16/NS	1 : 2.7	6 +	6 +	NS
Cocoa	Packers (confectionery)	[70]	40	ND/30	1 : 6.0**	60 +	NS	NS
Green coffee beans	Coffee workers	[84]	68	7/ND	1 : 2.0	13 +	ND	53 +
Biological enzymes								
Papain	Pharmaceutics	[85]	23	87/ND	1 : 1.7	ND	43 +	ND
α-amylase	Pharmaceutics	[21]	80	ND/59	1 : 2.0	31 +	52 +	17 +
Lactase	Pharmaceutics	[86]	210	16/NS	1 : 1.6	31 +	ND	ND
Protease, lipase, cellulase, carboxyhydrase	Detergent industry	[87]	1064	3/6	1 : 0.6	NS	36 +	10 +
Lactase	Pharmaceutics	[88]	94	7/NS	1 : 1.2	22 +	ND	35 +
Fish and seafood protein								
Prawn	Prawn workers	[89]	50	22/ND	NA	24 +	16 +	18 +
Crab	Snow-crab processors	[3]	303	18/ND	1 : 0.9	22 +	ND	11 +
Fish protein, endotoxin	Trout processors	[90]	8	37/NS	1 : 0.7	ND	0 +	ND
Fish-feed (<i>C. thummi thummi</i>)	Aquarists and fish-food factory workers	[91]	225	24/ND	1 : 1.5	40 +	34 +	ND
Clam protein	Clam-processors	[92]	57	7/ND	1 : 2.0	7 +	7 +	21 +
Shrimp protein	Shrimp-processors	[92]	57	5/ND	1 : 1.5	16 +	14 +	21 +

Table 1. continued

Agents	Occupation	Ref	Subjects <i>n</i>	Prevalence* %	Asthma: rhinitis ratio†	Specific skin test %‡	Specific serum IgE, %‡	Skin test with common allergens %
Low molecular weight agents								
<i>Diisocyanates</i>								
Diphenyl-methane diisocyanate	Urethane mould workers	[9]	243	36/45	1 : 10.0	1 +	1 +	ND
Toluene diisocyanate	Painters	[93]	312	42/ND	1 : 6.6	ND	ND	ND
<i>Anhydrides</i>								
Trimellitic anhydride	Epoxy resin production	[94]	20	10/ND	1 : 0.7	ND	30 +	NS
Methyl tetrahydrophthalic anhydride	Epoxy resin production	[23]	43	60/NS	††	NS	23 +	9 +
Pyromellitic dianhydride	Chemical workers	[95]	92	48/ND	NS	NS	16 +	ND
Methyl tetrahydrophthalic anhydride	Electric condenser workers	[96]	147	43/50	††	ND	65 +	ND
<i>Wood dust</i>								
Mansonina (<i>Mansonina altissima</i>)	Carpentry (fixtures)	[97]	50	27/NS	1 : 30.0	ND	ND	ND
Mansonina (<i>Mansonina altissima</i>)	Carpentry (fixtures)	[98]	49	36/NS	††	ND	ND	ND
Western red cedar (<i>Thuja plicata</i>)	Furniture making	[99]	1320	ND/9	1 : 2.8	NS	NS	54 +
Several woods	Furniture making	[100]	268	16/NS	††	ND	ND	ND
<i>Metals</i>								
Platinum	Platinum refinery	[16]	107	ND/43	1 : 1.6**	14 +	24 +	33 +
<i>Drugs</i>								
Psyllium	Health care workers	[101]	743	9/NS	1 : 3.0	ND	ND	ND
Spiramycin	Pharmaceutics	[102]	51	41/NS	1 : 3.5	NA	ND	41 +
Psyllium	Hospital workers	[103]	193	32/NS	1 : 3.0	3 +	12 +	36 +
Psyllium	Psyllium production	[18]	92	29/NS	1 : 1.5	5 +	10 +	39 +
<i>Chemicals</i>								
Reactive dyes	Reactive dye product	[104]	309	20/NS	1 : 0.8	8 +	17 +	59 +
Carmines	Reactive dye product	[105]	10	30/NS	1 : 1.5	30 +	10 +	0 +
Polyamide, polyester and para-amide	Synthetic fibre production	[106]	668	15/18	1 : 2.0	ND	ND	ND
Cotton and synthetic fibres	Cotton and synthetic fibre mills	[107]	1452	11/NS	NS	ND	ND	NS
Persulphates	Persulphate product	[108]	32	3/NS	††	0 +	ND	25 +
Solvents and organic dusts	Shoe manufacturing	[109]	376	ND/46	NA	ND	ND	ND
Azo and reactive dyes	Textile dyeing	[110]	135	ND/38	NA	ND	ND	ND
Polyester	Synthetic fibre production	[111]	400	ND/26	NA	ND	ND	ND
Persulphates	Hairdressing	[25]	500	2/17	1 : 2.0	4 +	ND	NS
Chlorine	Pulp and paper production	[43]	211	ND/47	NS	ND	ND	ND
Unidentified (multiple irritant exposure)								
(?) Air conditioned building	Office workers	[112]	129	27/NS	1 : 9.0	NA	NA	ND
(?) Sulphur dioxide, formaldehyde, glutaraldehyde	Radiographers	[113]	2354	8/17	1 : 1.1	ND	ND	ND

*Prevalence of occupational rhinitis/prevalence of rhinitis (including occupational rhinitis). †Occupational asthma:occupational rhinitis ratio, unless otherwise stated. ‡In all exposed workers. §% positive skin tests or serum IgE to laboratory animals. ¶% positive skin tests to house dust mite. **Asthma:rhinitis ratio. ††No occupational asthma cases. ‡‡Specific skin test allergens were pollens and moulds. SCW, Swine confinement workers; NA, not applicable; ND, not done; NS, results not stated.

Table 2. Exposure-rhinitis and exposure-sensitization relationships owing to occupational agents

Agents	Occupation	Ref	Exposure evaluation	Exposure level	<i>n</i>	Prevalence of occupational rhinitis, %	Specific skin test %
Laboratory animal allergens							
Laboratory animal	Laboratory workers	[46]	Job description	Unexposed	29	0*	NS
				Users	127	25*	NS
				Handlers	52	33*	NS
Laboratory animal	Laboratory workers	[11]	Job description	Unexposed	26	23*	NS
				Users	101	34*	NS
				Handlers	19	42*	NS
Mouse	Laboratory workers	[47]	Job description	Unexposed	40	5*	NS
				Users	98	26*	NS
				Handlers	33	36*	NS
Rat	Laboratory workers	[13]	Job description	Unexposed	34	NS	0
				Users	125	NS	12
				Handlers	54	NS	13
Laboratory animal	Laboratory workers	[14]	Job description	Unexposed	16	56*	NS
				Users	80	40*	NS
				Handlers	42	45*	NS
Rat	Laboratory workers	[15]	Total dust (mg/m ³)	≤ 0.32	87	9	4
				0.33–0.34	79	13	12
				> 0.34	69	19	14
Rat	Laboratory workers	[15]	RUA† (µg/m ³)	< 1.0	73	15	3
				1.0–30.0	113	11	13
				> 30.0	49	17	13
Rat	Laboratory workers‡	[119]	RUA (ng eq/m ³ , median)	0.15	21	NS	14
				0.68	92	NS	17
				4.20	4	NS	25
Rat	Laboratory workers‡	[119]	H/wk§	0–2.5	49	NS	8
				> 2.5–9.0	30	NS	13
				> 9.0	38	NS	32
Rat	Laboratory workers‡	[119]	H/wk × RUA¶	0–1.0	40	NS	7
				> 1.0–6.0	43	NS	12
				> 6.0	34	NS	35
Laboratory animal	Laboratory workers	[118]	H/wk	0–2	25	8*	ND
				> 2–14	25	24*	ND
				15–37	25	28*	ND
				> 37	24	17*	ND
Rat	Laboratory workers‡	[51]	RUA (ng eq/m ³)	0	252	NS	4
				> 0–0.25	117	NS	11
				> 0.25–1.25	205	NS	14
				> 1.25	76	NS	16
Rat	Laboratory workers‡	[51]	H/wk	0	251	NS	4
				> 0–2	85	NS	13
				> 2–8	159	NS	12
				> 8	155	NS	15
Rat	Laboratory workers‡	[51]	H/wk × RUA	0	242	NS	4
				> 0–0.5	125	NS	12
				> 0.5–8	155	NS	12
				> 8	118	NS	16

Table 2. continued

Agents	Occupation	Ref	Exposure evaluation	Exposure level	<i>n</i>	Prevalence of occupational rhinitis, %	Specific skin test %
<i>Other animal-derived allergens</i>							
Wool	Wool textile workers	[54]	Total dust (mg/m ³)	0–1	1210	15	ND
				> 1–10	740	19	ND
				> 10–100	187	37	ND
				> 100	6	17	ND
<i>Flour</i>							
Flour, bakery, mites, moulds	Bakers	[68]	Total dust (mg/m ³ , geometric mean)	< 0.34	125	13	28
				> 1.72 PE	39	20	54
				> 1.72 CE	70	30	35
Flour, α-amylase	Bakers	[19]	Total dust (mg/m ³)	< 1	104	11	3
				1–5	90	15	9
				> 5	62	31	10
Flour, α-amylase	Bakers	[19]	Flour aeroallergens (μg/m ³)	< 101	90	11	2
				101–215.3	83	14	9
				≥ 227.6	83	27	10
α-amylase	Bakers	[71]	Flour aeroallergens (μg/m ³ , geometric mean)	0.1	151	15*	4
				0.7	120	23*	8
				3.8	178	29*	14
<i>Fish and seafood protein</i>							
Fish-feed (<i>Chironomus thummi thummi</i>)	Aquarists and fish-food factory workers	[91]	Amount of <i>C. thummi thummi</i> larvae used per month (mg)	< 5	71	19*	35**
				5–25	73	24*	57
				> 25–100	33	34*	62
				> 100	15	49*	38
<i>Anhydrides</i>							
Methyl tetrahydrophthalic anhydride (MTHPA)	Epoxy resin production	[120]	MTHPA exposure (mg/m ³ , mean)	0.010	23	ND	9
				0.014	46	ND	15
				0.085	54	ND	19
Tetrachlorophthalic anhydride	Epoxy resin production	[116]	Job description	Office	4	ND	0
				Coil assembly	32	ND	25††
				Utility/ maintenance	6	ND	67
				Evermould	7	ND	43
Tetrachlorophthalic anhydride	Epoxy resin production	[116]	Duration of employment (years)	< 0.33	5	ND	0
				0.33–1.33	15	ND	27
				> 1.33	15	ND	53
<i>Chemical</i>							
Reactive dyes	Dyehouse operatives	[122]	Exposure groups	Intermittent	42	NS	9
				Partial	101	NS	4
				Continuous	41	NS	22

*Work-related symptoms, $\geq$ 69% of which were rhinitis. †RUA = rat urinary aeroallergens. ‡Workers with under 4 years exposure. §H/wk = hours per week working with rats. ¶Median RUA were multiplied by H/wk. **Results of IgE antibodies to *C. thummi thummi*. Results of specific skin tests overlapped with serum IgE, but were not shown [66]. ††Results of serum IgE antibodies to tetrachlorophthalic anhydride. ND, not done; NS, results not stated. CE, current exp; PE, past experience.

and neither is the optimal method for evaluation (symptoms, rhinomanometry, acoustic rhinometry, mediators, etc.) [26] and criteria for positive response. Sometimes results of different methods do not concur [27,28].

While objective means for assessing nasal physiological responses are numerous, these have primarily been used for research purposes and have not yet been incorporated into clinical practice. Thus, a brief description of the different methods available is presented.

Measuring secretions

Secretions can be collected for evaluation of secretory activity in terms of weight by using measures such as weighing tissue papers or plastic wrap, or using filter paper or disk methods [29]. These techniques are useful when nasal responses are characterized by strong secretions, such as after high-dose allergen challenges. In the real-life, low-level exposure challenges used in OR, this is rarely the case and therefore their use is limited in studies of OR [25].

Secretions can also be rinsed off the nasal mucosa by the additional means of nasal lavage for collection. This method obviously does not allow quantification of secretion weight, but is useful where the quantity of secretions is not high. It is somewhat cumbersome for real-life situations.

Whatever the means of collection, the secretions can be analysed for measures of markers of inflammation, mediators and cells [23,24,30].

Assessing congestion

Many methods exist for objective evaluation of nasal congestion. Rhinomanometry measures resistance to flow by simultaneously measuring pressure and flow [31]. Anterior rhinomanometry uses a pressure transducer placed in the anterior nostril, with a mask adapted for measurement of flow. Critics suggest that the distortion of the anterior nares alters the flow measurement. For this reason, posterior rhinomanometry has been developed. The transducer is placed posteriorly, in the oro- or naso-pharynx. However, contact of the sensor with the base of tongue stimulates nausea in approximately 20% of patients, rendering the technique impossible [32]. Both of these techniques are difficult to use when nasal congestion is severe or in the presence of postoperative changes. Furthermore, the technique depends on patient collaboration, and the equipment is somewhat awkward to transport.

Head out body pletysmography, as developed by Cole [33], frees the head from external distortion by using plethysmography to measure the change in pressure, and measure nasal flow with a sensor that does not obstruct the nares. Although described as having good reproducibility, it requires a fixed installation and is expensive.

Acoustic rhinometry uses a piezoelectric spark to generate a three-dimensional image of the nasal passages [34]. This allows measurement of nasal volume and the cross sectional area. Advantages are ease of use, freedom from patient collaboration, and speed of data acquisition. These properties render it ideal for rapid, repeated measurements such as challenges and combined with its portability, make it ideal for assessment of nasal workplace disorders [35].

Nasal peak flow can be measured in forced nasal inhalation or exhalation. It has been used in workers exposed to methyltetrahydrophthalic anhydride to evaluate the response after specific nasal challenge [23] and in workers exposed to irritants to evaluate nasal obstruction during a working week [36]. However, in histamine nasal challenge nasal peak flow measurement was insensitive compared to rhinomanometry [37].

Other methods

Methacholine and histamine nasal provocation tests have been used to diagnose nonspecific nasal hyperreactivity. Plavec *et al.* [22] showed a significant increase in nonspecific nasal hyperreactivity during the working period compared to a period of 2 weeks without exposure.

Reversibility of baseline nasal congestion with a vasoconstrictor was used to assess presence of rhinitis in a study of Dutch tunnel workers [38]. While this is an interesting and novel method, it is not standardized and does not differentiate between pre-existing rhinitis and workplace-induced rhinitis.

Biopsy in the registering of the response to nasal challenges has been used in research work [39,40], but it is difficult to recommend such an invasive procedure as routine.

Prevalence and aetiological agents in occupational rhinitis

The aetiological agents of OR, like those of OA [41], can be classified as high or low molecular weight compounds. In almost all high molecular weight compounds (HMWC) an IgE-dependent mechanism has been demonstrated. Even though several low molecular weight compounds (LMWC) produce specific IgE antibodies by combining with a protein to form a hapten-protein conjugate [42], an IgE-dependent mechanism has been elicited only for a minority of LMWCs.

OR may also be the effect of upper airway exposure to irritants [43,44]. Chronic rhinitis after an acute exposure to an irritant has been defined as the reactive upper airways dysfunction syndrome (RUDS), a form of OR without a latency period [40,43]. A nonimmunological mechanism

Table 3. Atopy and smoking in occupational rhinitis and specific sensitization

Agents	Ref	Prevalence of		Prevalence of	
		Occupational rhinitis %* atopic/nonatopic	Specific sensitization % atopic/nonatopic	Occupational rhinitis %* smokers/nonsmokers	Specific sensitization % smokers/nonsmokers
<i>Laboratory animal allergens</i>					
Laboratory animal	[11]	23/23	NS	NO	NO
Mouse	[47]	29/3	25/4	ND	ND
Laboratory animal	[48]	29/10	ND	ND	ND
Rat	[13]	8/8	NS	ND	ND
Laboratory animal	[14]	NO	23/5	NS	NS
Rat	[15]	14/14	22/1	16/13	13/7
Rat	[50]	NS	30/14	NS	15/19
Mouse	[50]	NS	17/9	NS	7/12
Rat	[51]	12/7	18/4	NS	NS
<i>Insects</i>					
Locust	[56]	NS	65/28	NS	NS
<i>Grain dust</i>					
Grain dust	[64]	NO	56/8	NS	NS
Grain dust	[65]	36/33	NS	37/28	NS
Grain dust	[66]	NS	NS	37/48	NS
<i>Flour</i>					
Flour	[71]	NO	16/8	NO	NO
<i>Latex</i>					
Latex	[73]	NS	10/3	NS	3/5
Latex	[123]	NS	11/3	NS	NS
Latex	[74]	NS	18/3	NS	NS
<i>Other plant allergens</i>					
Green coffee and castor beans	[77]	NS	11/10	NS	11/6
Pollens and molds	[80]	35/17	NA	NO	NO
Green coffee and castor beans	[81]	ND	56/13	ND	34/14
Green coffee beans	[84]	NS	22/3	NS	12/8
<i>Biological enzymes</i>					
Protease, lipase, cellulase, carboxyhydrase	[87]	NO	NO	NS	10/3
Lactase	[88]	9/10	42/16	NS	NS
<i>Fish and seafood protein</i>					
Crab	[3]	NS	66/17	NS	NS
Shrimp	[92]	NS	38/3	NS	NS
<i>Anhydrides</i>					
Methyl tetrahydrophthalic anhydride	[96]	48/33	NS	44/42	NS
<i>Metals</i>					
Platinum salts	[121]	ND	17/13	ND	27/3
<i>Drugs</i>					
Psyllium, senna	[124]	NS	25/12	NS	21/16
<i>Chemicals</i>					
Reactive dyes	[104]	NS	16/19	NS	28/2

*Subjects with occupational asthma were excluded. NO, no association; NA, not applicable (specific skin test allergens were pollens and moulds); ND, not done; NS, results not stated.

has been hypothesized, but the pathogenesis, evolution, prognosis and the relationship between RUDS and OR need to be studied further [40,45]. A recent study on 211 workers exposed to chlorine showed persistent nasal symptoms after an acute inhalation accident may be associated with lower respiratory tract abnormalities [43].

High molecular weight compounds (Table 1)

Laboratory animal allergens [7,11–15,46–51]

Between 1980 and 1999, 12 reports studied animal allergy in 8696 laboratory workers, 5641 of whom were evaluated in one Japanese study [49]. Prevalence of OR ranged from 10% [51] to 33% [14] and was 2–4 times higher than OA. The prevalence of specific IgE antibodies to animal proteins ranged from 6% to 46%. In workers exposed to rats [13,50] and mice [47,50] skin tests with urine allergens were positive more often than specific serum IgE antibodies.

Other animal-derived allergens [52–55]

Few reports have studied the prevalence of rhinitis in workers exposed to other animal-derived proteins. Although two studies showed a high prevalence of rhinitis [53] and OR [55] in swine confinement workers, Brouwer *et al.* [52] reported rhinitis symptoms in only 8%. The prevalence of rhinitis in wool textile workers and the general population overlapped [54].

Insects and mites [17,20,56–63]

Different types of insects can give rise to OA and OR which is twice as prevalent, being high in laboratory workers exposed to locusts [17,56], fruit flies [20], sheep blowflies [60], beneficial arthropods [61], and spider mites [63]. OR in farm workers and cattle farmers may be caused by storage-mite exposure [57–59,62]. The prevalence of occupational sensitization in workers exposed to insects was high, particularly in laboratory workers. Sensitivity of both skin tests and specific serum IgE to locust extracts in relation to symptoms was found to be 100%, whereas specificity was 88% for skin tests and 73% for serum IgE [17].

Grain dust [64–67]

Four reports published between 1977 and 1985 showed a high prevalence of nasal symptoms in grain elevator workers exposed to grain dust. OR tended to be more prevalent than OA. The prevalence of sensitization among grain elevator workers ranged from 9% to 28% [64–66].

Flour [19,68–71]

Flour proteins are the main cause of baker's asthma, but baker's rhinitis, which is 1.5–3.4 times more prevalent, has been less studied. Four reports [19,68,69,71] showed an 18–29% prevalence of work-related nasal symptoms. Positive skin test responses to flour and other noncereal allergens were associated with exposure intensity, but not with work-related symptoms [19]. The prevalence of specific sensitization in bakers and packers was reported between 10% and 38%.

Latex [24,72–75]

In the last decade latex gloves have come into widespread use in health care and hospital workers in order to prevent the spread of human immunodeficiency virus. The prevalence of OR was 9% in two reports and 12% in another [24,73,74]. In a surgical glove manufacturing plant the prevalence of work-related nasal symptoms was very high [72] and in a textile factory two out of 10 workers exposed to latex threads had OR [75]. In workers exposed to latex, specific skin tests were positive in 5% to 20%.

Other plant allergens [70,76–84]

Work-related nasal symptoms have been described in workers exposed to tobacco leaf, green coffee and castor beans, guar gum etc, with prevalences ranging from 5% to 36%. The prevalence of positive skin tests to occupational allergens varied from low [76,78,83,84] to very high [70,82].

Biological enzymes [21,85–88]

Biological enzymes are used in the detergent, pharmaceutical and food industries. Since 1969 several investigators have observed symptoms of asthma and rhinoconjunctivitis in detergent manufacturing workers exposed to proteolytic enzymes. OR ranged from 3% in these workers [87] to 7–16% in those with exposure to lactase [86,88], and to 87% in workers exposed to papain [85]. Specific sensitization to biological enzymes ranged from 22% to 52%.

Fish and seafood protein [3,89–92]

OA, OR, and occupational urticaria have been reported in fish and seafood-processing workers. In one British study and in two Canadian reports the prevalence of OR ranged from 5% to 22% [3,89,92]. Work-related nasal symptoms were reported by three of eight production workers from a small trout-processing factory [90] and by 24% of 225 aquarists and fish-food factory workers [91]. In crustacea

processors specific sensitization was found in 7% – 24% [3,89,92].

Low molecular weight compounds (Table 1)

Diisocyanates [9,93]

Diisocyanates are the most common cause of OA [41]. Two studies in exposed workers reported prevalences of work-related nasal symptoms of 36% and 42%, respectively, but specific IgE antibodies were found in only 1%, suggesting a non-IgE-dependent mechanism.

Anhydrides [23,94–96]

In workers exposed to trimellitic anhydride the prevalence of OR was 10% [94], whereas exposure to methyl tetrahydrophthalic anhydride or pyromellitic dianhydride was associated with a 48–60% prevalence [23,94–96]. Specific serum IgE antibodies have been found in 5% to 16% of workers.

Wood dust [97–100]

In the '60s exposure to mansonia (*Mansonia altissima*) caused a high prevalence of work-related nasal symptoms [97,98]. Consequently mansonia has been used much less in carpentry and furniture making in the last 20 years. In workers exposed to western red cedar and other wood dusts, the prevalence of rhinitis was not higher than in the general population [99,100].

Metals [16]

In workers exposed to platinum salts the prevalence of rhinitis was high. Platinum salts serum IgE had a good sensitivity in detecting rhinitis and asthma in exposed workers.

Drugs [18,101–103]

In pharmaceutical company workers OR owing to spiramycin was approximately 40% [102]. According to three reports on workers exposed to psyllium the prevalence of OR was 9%, 29% and 32%, respectively [18,101,103]. Psyllium specific serum IgE are more sensitive but less specific than specific skin tests in detecting OR [18].

Chemicals [25,43,104–111]

Two studies on workers exposed to reactive dyes reported the prevalence of work-related nasal symptoms at 20% and 30%, with specific IgE antibodies in 8% and 30%,

respectively [104,105]. Exposure to cotton and synthetic fibres was associated with a relatively high prevalence of OR [106,107]. Exposure to persulphate in production or hairdressing was associated with a low risk of OR and persulphate salt sensitization [43,108].

Unidentified agents [112,113]

In workers in air-conditioned offices a 27% prevalence of OR has been observed [112]. The causal agent has not so far been identified. In radiographers the prevalence of OR was 8% [113]. In these occupations work-related symptoms could be associated with low-level exposure to several irritants.

Relationship between onset of occupational asthma and occupational rhinitis

OR is usually 2–3 times more frequent than OA (Table 1). However, only a few studies have evaluated the relationship between the onset of OA and OR in subjects who have both nasal and pulmonary symptoms. In laboratory animal allergy OR occurred before OA in 45% of subjects and at the same time in 55%, but never afterwards [7]. The interval between onset of nasal and respiratory symptoms was 4.6 months, which was confirmed by later reports [12,46,114]. Cullinan *et al.* [115] observed the median length of employment before developing work-related chest symptoms was 18 months compared to 12 months for nose symptoms.

Malo *et al.* [2] showed nasal symptoms appeared before the onset of OA in 58% of exposed workers when HMWC were involved, but only in 25% when LMWC were concerned. Once again, the time lapse between OR and OA covered months (mean 22 months).

Main determinants of occupational rhinitis and occupational sensitization

Exposure, atopy, and smoking appear to emerge as the main potential determinants of OR in epidemiological studies.

Exposure (Table 2)

Exposure may be quantified by its length (duration) or its level (intensity). Duration, usually expressed as years of employment, has seldom been utilized in exposure-response studies [91,116]. Intensity has been measured as total dust or level of aeroallergens in the work environment, or estimated by job description, exposure groups or hours per week of specific exposure. Several papers have studied the relationship between occupational exposure and OR or

occupational sensitization, reviewed by Baur *et al.* [117] and by Bush *et al.* [6].

Studies on workers exposed to laboratory animals showed an exposure-OR relationship [11,15,46,47,118]. Conversely, workers with indirect exposure had more symptoms of laboratory animal allergy (LAA) and had been employed longer than animal users and handlers [14], suggesting that workers with LAA symptoms were relocated to jobs with less animal contact. In these reports exposure was assessed by job description [11,14,46,47], hours per week of specific exposure [118], or total dust or aeroallergens in the work environment [15]. Other studies showed only an exposure-sensitization relationship, but not an exposure-OR relationship [13,51,119]. Sensitization was associated with user and handler jobs [13], level of exposure, expressed as total dust [15], rat urinary aeroallergens (RUA) [15,51,119], and number of hours working with rats per week [51,119].

In a study on 2153 workers in 15 wool textile mills Love *et al.* [54] showed the relative risk of rhinitis doubled for a dust concentration of 30 mg/m³ and tripled for concentrations of 50–60 mg/m³. The prevalence of rhinitis correlated with employment duration.

In bakers exposure-OR and exposure-sensitization are related [19,68,71]. Musk *et al.* [68] demonstrated that OR and positive skin test responses to bakery allergens were linked to the level of total dust in the bakery and to past and current exposure. Cullinan *et al.* [19] showed OR and sensitization correlated with levels of total dust and flour aeroallergens. A relation between aeroallergen exposure and OR or specific sensitization was confirmed by Houba *et al.* [71].

In aquarists and fish-food factory workers sensitization to *Chironomus thummi thummi* and OR were associated with exposure, expressed as the amount of *C. thummi thummi* larvae used per month [91].

In workers exposed to LMWC, exposure and OR were not associated, but an exposure-sensitization relationship was shown in epoxy resin workers exposed to anhydrides [116,120], in platinum refinery workers [121], and dye-house operatives exposed to reactive dyes [122]. In this last study 45% employees exposed in the past to dyes but currently working in jobs without dye exposure had a specific sensitization, suggesting sensitization to dyes may have been one reason for their relocation.

Atopy (Table 3)

In this review any subject showing skin test reactivity to common aeroallergens was considered atopic. The relationship between atopy and OR due to HMWC is controversial, being reported in only two studies on laboratory workers [47,48]. Several other studies in laboratory workers linked atopy and OA [11,13–15,46] or specific sensitization

[12,14,15,47,50,51,56], but not atopy and OR. The association between atopy and specific sensitization to HMWC has also been observed in grain elevator [64], fish and seafood workers [3,92], bakers [19,69,71], workers exposed to latex [73,74,123], coffee [81,84], lactase [88], and pharmaceuticals [124]. Only a few studies have failed to show this association [17,69,87].

In workers exposed to LMWC the atopy-OR or atopy-specific sensitization relationships have seldom been evaluated and results are inconsistent [96,103,104,121,124].

Smoking (Table 3)

The relationships between smoking and occupational sensitization, OR and OA are controversial and sometimes contradictory [125]. The relationship between smoking and OR was studied in laboratory [11,15,46] and grain elevator workers [65,66], bakers [19], electric condenser [96] and psyllium production workers [18] and no relationship was found in any.

An association between smoking and occupational sensitization was observed in bakers [69], coffee [81], detergent [87], platinum refinery [121], and reactive dye production workers [104], but not in laboratory workers [11,50], bakers [19,71], or workers exposed to latex [73] or psyllium [18,103,124].

Conclusions

This manuscript reviewed prevalence and determinants of OR in cross-sectional studies conducted in different occupations. OR, a very frequent disease caused by several occupations, tends to be three times more prevalent than OA and has important socio-economic consequences. The high frequency, the large number of potential occupational hazards, and the possible role of OR as a marker of the likelihood of developing OA make regular assessment of prevalence of OR necessary.

In order to make international comparisons possible, a consensus on a standard definition of OR and on diagnostic methodology is urgently required. It is essential to develop and validate an international questionnaire that can be administered to workers in different occupations. The questionnaire could be supplemented by objective evaluations to diagnose rhinitis and/or OR. In fact, workers' awareness of occupational exposure to pollutants may increase self-reporting of symptoms (information bias) and the risk of overestimation. Therefore it is important to identify any objective assessment that could be of help in the diagnosis of OR, and evaluate its feasibility and acceptability. Given the advantages of acoustic rhinometry in assessing the prevalence of OR, it might be a valid approach, and could even be used in pre- and post-shift

measurements. The criteria for positive responses to objective evaluations also need to be standardized.

This review showed that exposure, which can be reliably estimated by means of job description or mean week exposure, may be the single most important determinant of occupational sensitization and OR. Atopy is a controversial risk factor for OR and a major risk factor for occupational sensitization when HMWC are involved. The role of smoking in OR and occupational sensitization is not clear and needs to be studied without prejudice. The link between smoking and OR due to occupational agents has yet to be explained in full.

The relation between potential risk factors and incidence of OR can be defined in longitudinal studies, which can also evaluate the efficacy of disease prevention. Moreover, prospective studies should be able to avoid the so-called 'healthy worker effect' (selection bias).

In conclusion, OR is a frequent disease with an intriguing relationship with OA, which deserves more attention and studies.

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