

Inhalation challenge test in the diagnosis of occupational rhinitis

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ABSTRACT

Background: Evaluations of rhinitis reactions in inhalation challenges (ICs) are sparse compared with research on nasal challenges. This study evaluates the outcome of IC tests in assessing occupational rhinitis (OR). It presents the largest rhinologic IC data in the literature, analyzing the exposure method of various agents causing OR and their relation to asthma.

Methods: Challenge tests performed on 829 individuals with suspected cases of OR were reviewed. Results from both exposures with occupational agents ($n = 1229$) and placebo ($n = 838$) were evaluated.

Results: A total of 10% of the occupational ICs ($n = 123$) were positive, suggesting OR, and 13% ($n = 161$) showed asthmatic reaction in the same challenge. In control challenges 2% showed rhinitis and 6% showed asthma symptoms. The most common agents tested were molds (160 tests), flours, and animal fodders (115 tests) and formaldehyde (122 tests). Obeche wood dust and latex produced positive nasal reactions the most frequently, followed by acid anhydrides.

Conclusion: Although IC is a resource-intensive methodology, the evaluation of nasal symptoms and signs together with bronchial reactions saves time and expense compared with the organization of multiple individual challenges. We encourage the simultaneous evaluation of both nasal and bronchial reactions in IC tests.

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Key words: Allergy, asthma, chamber challenge, chemical, exposure, flour, inhalation challenge, nose, occupational rhinitis, work

The literature concerning rhinitis reactions in inhalation challenges (ICs) is sparse; yet occupational rhinitis (OR) increases the risk of occupational asthma more than three-fold.¹ Airway mucosa forms a continuum from the nose to the lower bronchi—rhinitis and asthma are closely associated diseases and the prevalence of OR in subjects with occupational asthma is 76–100%.^{2,3} Evaluation of rhinitis is an important part of airway evaluation in patients with any airways symptoms. The purpose of this study was to evaluate the outcome of an occupational IC test in assessing OR in patients with a suspicion of both upper and lower airway occupational symptoms. We present the largest rhinologic IC data in the literature and discuss the strengths and weaknesses of the challenge method.

Because in Finland insurance compensations for occupational diseases cover the examinations, medications, reduced salary, and possible retraining due to occupational diseases, occupational diseases are thoroughly examined. In compensated OR cases, IC tests are performed to confirm causality between the allergen or occupational agent and the disease.

The ICs for southern Finland (with a population of ~1.3 million) and all challenges to chemicals for the whole country (population ~5.2 million) are performed in the Finnish Institute of Occupational Health (FIOH). The purpose of this study was to summarize the results of IC tests performed in the

7-year period of 1997–2003 in the FIOH and to analyze the results of various suspected agents causing both upper and lower airways symptoms of both OR and asthma.

MATERIALS AND METHODS

Altogether, 3895 otolaryngology consultations were performed at the FIOH in 1997–2003 because of suspected upper airway disease. In cases where the suspected allergen was either chemical or the patient had both upper and lower airway symptoms related to work, the patients, 21% (829) in all, were examined by an IC test. Patients with lower airway or laryngeal problems only were excluded from this study. Symptoms of rhinitis without lower airway symptoms were studied by local nasal challenge.⁴ However, as an exception to this, patients with suspicion of chemical-induced rhinitis were challenged in the exposure chamber and were included in this study. With these terms, 2067 consecutive ICs were included in this study. The age of the patients varied between 18 and 65 years with a mean age of 44 years.

Symptoms suggesting occupational allergic rhinitis were nasal obstruction, rhinorrhea, sneezing, itching of the nose, and/or postnasal drainage. The inclusion criteria for performing the IC were the following: (1) exposure to a known occupational allergen or chemical or mold damage was found in the workplace, (2) the symptoms referred to work-related allergic rhinitis, (3) there were no other obvious reasons for the rhinitis, (4) both upper and lower airway occupational symptoms were suspected or the chemical had an irritating nature, and (5) there were no contraindications for the IC test.

With most patients, sensitization to the most common environmental allergens and suspected occupational aeroallergens was tested by a skin-prick test (SPT) in our clinic. SPT results from our database files were included in this study. If

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SPTs had been conducted recently, they were not repeated. SPTs were performed according to published guidelines.⁵ The SPTs were performed based on the information obtained on the allergen exposure. A person was diagnosed with atopy if he/she had a positive SPT to one or more of the environmental allergens: birch, alder, meadow fescue, timothy, mugwort, dandelion, horse, dog, cat, cow, house-dust mites *Dermatophagoides farinae* or *D. pteronyssinus*, or the mold *Cladosporium herbarum*. SPTs were performed by commercial allergens when available (ALK, Copenhagen, Denmark). Flours (10% w/v), wood dusts, spices, and fresh plants were tested with in-house-prepared crude mixtures with phosphate-buffered saline. Enzymes and chemical SPTs were tested in coca-glycerol vehicle. The maximum concentrations used were with ethanolamines and chloramine-T 1%; amines and aziridine formaldehyde and glutaraldehyde 1%; methacrylates and persulphates 2% enzymes, 100 µg/mL; human serum album conjugates of acid anhydrides and isocyanates 1% w/v.

General contraindications for the challenge tests were the following: the minimum interim period after respiratory infection was 6 weeks; before the challenges, nasal sprays were sustained for 5 days; tiotropium was sustained for 7 days; antihistamines were sustained for 3–7 days depending of the preparation; leukotriene antagonists, cough mixtures, and teophylline were sustained for 3 days; and oral corticosteroids were sustained for 2 days. Sympathomimetics were forbidden for 12–24 hours before the challenges and eye drops for allergies were forbidden during the days of challenge tests. Inhaled corticosteroids were not recommended for 2 days before the challenges, but if necessary they could be taken in one dose in the evening. The peak expiratory flow (PEF) and forced expiratory volume in 1 second (FEV₁) were recorded with a microspirometer (Fuchs Medical, Clement Clarke SN, U.K.). Fluctuations in FEV₁ on the control day before exposures were supposed to be <10%, or the best possible with medication. No reversible obstruction was allowed in spirometry. Auscultation revealed no asthmatic findings. FEV₁ had to be ≥60% of reference value before the IC was possible. PEF and FEV₁ were measured 15 minutes before the challenge test, after the challenge in 15-minute intervals for 1 hour, in 1-hour intervals up to 8 hours, and in 3-hour intervals until the following morning. Falls of ≥15% led to new measurements every 10–30 minutes. Challenge to a control substance was done in the 1st day to identify nonspecific bronchial and nasal reactions.

In the IC, the test agents were delivered out in a 6-m³ exposure chamber. Commercial allergens were inhaled through a dosimeter Spira facial mask (Laerdal Medical, Stavanger, Norway) covering both the nose and the mouth. Patients were instructed to breathe nasally and orally on alternate breaths. The challenges were conducted at daily intervals. The challenges were interrupted if the PEF fell by 15% or other major respiratory symptoms appeared. The concentrations of the challenge agents were adjusted to mimic the exposure situation in the workplace and to remain well below the Finnish occupational exposure limits, if existing, to avoid irritant reactions. Challenge agents were used either as such, mixed in lactose powder, or diluted if serious reactions were suspected based on medical history or SPT reactions.

Organic agents causing rhinitis and the maximum amounts

used are presented in a Table 1. Finnish occupational exposure levels are provided to show the generally tolerated level of the challenge agents and chemicals. The allergens used in the IC tests were commercial, if available. Three storage mite species (ALK) were tested in the challenges (*Lepidoglyphus destructor*, *Tyrophagus putrescentiae*, and *Acarus siro*). Three mold challenge agents were available (*Aspergillus fumigatus*, *Cladosporium cladosporioides*, and *Acremonium kilience*; ALK). Cow epithelia allergen was used (*Allergopharma*). Flours, wood dusts, fresh plants and flowers, baker's yeast (*Saccharomyces cerevisiae*), animal-derived agents, food ingredients, cosmetic, and laboratory agents were obtained from the patient's workplaces.

Inorganic agents that induced rhinitis as well as their maximum amounts and challenge methods used are presented in the Table 2. Chemicals and substances containing the suspected chemical to which the patients were exposed were obtained from patient's workplaces. Formaldehyde was tested with evaporation from commercial reagents (until 1999 liquid formalin, from 1999 onward paraformaldehyde extra pure powder from Merck, Darmstadt, Germany), but in some cases also with materials from the workplace. In the challenges, the agents from the workplaces often were mixtures of chemicals. In this evaluation the most likely agent behind the rhinitis reaction was marked as the causative factor.

Different placebo test agents were used depending on the occupational agent. Diluents were used with commercial allergens and metals. Lactose was the control agent to dusty agents and partly to wood dusts; the second control agent with wood dust was another wood dust. Coca solution (sodium chloride 0.5%, phenol 0.4%, and sodium hydrogen carbonate 0.3% diluted to aqua) was the control with gaseous, aerosol exposures and isocyanates; mint oil with smelling exposures; salad with vegetables and plants. Vinyl was control for latex; noncolored textiles with dyed textiles; black iron without nickel and chromium was used as a placebo for welding with stainless steel with nickel and chromium. One-component paint containing no allergens was used as a control for liquid epoxy paints and hardeners. For foodstuffs and cosmetics, materials resembling the allergenic agent, without the allergen, were used. Some ICs were performed with occupational agents first, and as the challenge appeared to be negative, no control agents were needed.

The degree of both rhinorrhea and nasal blockage was evaluated in the morning before the IC test and ~20 minutes after the end of the challenge. Rhinorrhea and nasal blockage were scored from 0 (dry or thin mucosa) to 3 points (dripping of mucus or mucosal swelling obstructing nasal cavity), similar to nasal challenges.^{4,6} In addition, the symptoms and signs of rhinitis and asthma during the challenge test were recorded. The rhinitis follow-up was regarded as positive if there was a status change of ≥4 score points from both nostrils. Acoustic rhinometry measurement was performed before and after the challenge in all cases, but it was considered mainly as supportive to the diagnosis.⁶ Nasal late reaction was measured only in isolated cases, with no clear reference values.

A PEF or FEV₁ drop of ≥20% was diagnostic. PEF or FEV₁ decreases of 15–20% with simultaneous expiratory wheezing or dyspnea during the hour after the occupational exposure also was considered a positive asthmatic reaction. The diurnal

Table 1 Exposure method used with organic agents causing rhinitis

Allergen or Exposure Agent	Exposure/Challenge Test Method	Concentration or the Amount of Allergen Used	Measured Air Concentrations Range (mg/m ³)*	Duration of Challenge (min)	Finnish Occupational Exposure Limit for 15 min and 8 hr (mg/m ³)
Commercial allergens (storage mites, animal epithelia, and molds)	Inhalation with dosimeter (Spira) and face mask; (1), 10 and 20 inhalations with 15-min intervals	According to the manufacturers instructions 1 mL 1:1000–1:1 w/v (150 mL, 0.6 s)	—	15–45	ND
Commercial allergens control agents: diluents	1 mL, atomizing with dosimeter	1:100 w/v 10 inhalations	—	15	ND
Flours, grains, and their control dust (lactose powder)	Blowing with 2-bar compressed air to a cup of dust every minute	60 mL, as such	Lactose 20	30	Total dust 10 and 5#
Wood dusts	Blowing with 2-bar compressed air to a cup of dust every minute or work mimicry	9–75 g, as such	—	30	Total dust 10 and 5#
Flowers and foodstuffs	Handling, binding, cutting, and cleaning	300–3000 g, mimicking work	—	30–45	ND
Enzymes	0.03–4% mixed with lactose, continuous concentration	Dusting, 1, 10, and 20 inhalations	Total dust 0.001–1300	15–45	ND
Pectin	10% mixed with lactose	Continuous concentration, 1, 5, and 5 inhalations	Total dust 1	25	ND
Spices	Dusting	60 g, as such	—	30	ND
Furs and cloths	Handling, dusting, and tearing	3–5 furs	—	30	ND
Latex (gloves) and control gloves	Handling	5–10 pairs of gloves	—	30	ND
Bacteria cultivation media	Mixing with water	60 g	—	15	ND

*Air concentration was measured if a suitable measurement method was available.

#Limit for flours and wood dusts will be changed to 2 mg/m³ in 2007. In new facilities wood-dust exposure limit will change to 1 mg/m³.

ND = not declared.

Table 2 Exposure method used with inorganic agents causing rhinitis

Allergen or Exposure Agent	Exposure/Challenge Test Method	Concentration or the Amount of Allergen Used	Measured air Concentrations Range (mg/m ³)*	Duration of Challenge (min)	Finnish Occupational Exposure Limit for 15 min and 8 hr (mg/m ³)
Acid anhydrides: PA MHHPA MTHPA	Mixing, heating to 40–100° C	20–50 mL	PA: 0.002–0.287; MHHPA: <0.0045–2.2; MTHPA: <0.018–4.3	30	PA: 0.2; MHHPA or MTHPA: 0.17 (8 hr)
Welding of stainless steel, welding of (unalloyed) iron as the control	Welding	2.5–12 covered electrodes	Total particles 5–20#	30–45	Total dust 10 and 5
Colophony	Soldering	Soldering wire heating, max. 390° C	Resin acid 1.15	30–60	ND
Disinfectants	Handling	80–250 mL	—	30	ND
Isocyanates: MDI and TDI	2 mL sprayed with an artist's fixative nozzle and compressed air to a cloth/near breathing zone	MDI: 10–520 mL, 3 and 6 mg/mL HDI: 1 and 5 mg/mL at separate days	MDI: <0.0020–0.014	30	Isocyanates: 0.035 (15 min)
Isocyanates: HDI in hardeners	Mixing	Three portions, 50–60 g of powder	HDI: <0.002–0.044	30	Isocyanates: 0.035 (15 min)
Persulphates (in hair bleach products)	Mixing, warming to 40° C	One to two portions of perm agent, 60–150 mL	—	30	ND
Thioglycolates (in perm wave solutions)	Mixing of 2–3 hair dye portions	60–110 mL	—	30	ND
Paraphenylenediamine (in hair dyes)	Evaporation and brushing	40 drops–100 mL	—	30	18 and 7
Methacrylate (<i>e.g.</i> , dental methacrylates or glues)	Squirting of hair spray or glue	14 sprays every 15 min	—	30	Ethyl acrylate: 21; methyl acrylate: 7; butyl acrylate: 11 (all 8 hr)
Acrylates	Evaporation warming to 40–80° C	2.5 g PFA	FA: 0.075–1.42	15–30	1.2 and 0.37 0.42 (15 min)
Formaldehyde	Evaporation warming to 40° C		GA: 0.033	25–30	1.2 and 0.37 0.42 (15 min)
Glutaraldehyde			EA: 0.055	30	FA: 1.2 and 0.37; DEA: 2.0 (8 hr); MEA: 7.6 and 2.5
Machining fluids (the main suspected agents FA and EA)	PVC warming to 200° C, mimicking work	50 mL	—	30	ND
PVC fumes	Spraying	10 mL	—	30	ND
Epoxy glue	Spraying	10 mL (3 × 3.3 mL)	—	30	Aziridine: 0.89 (15 min)
Aziridine hardeners	2 mL sprayed to the chamber with an artist's fixative nozzle and compressed air		—	15	ND
Control agent CoCaS					

*Air concentration was measured if a suitable measurement method was available.

#Estimated from concentration graph printouts.

§Sodium chloride 0.5%, phenol 0.4%, and sodium hydrogen carbonate 0.3% diluted to aqua.

>>DEA = diethanolamine; EA = ethanolamines; FA = formaldehyde; GA = glutaraldehyde; HDI = hexamethylene diisocyanate, MDI = diphenylmethane diisocyanate; MEA = monoethanolamine; ND = not declared; OEL = occupational exposure limit; PA = phthalic anhydride; PFA = paraformaldehyde; TDI = toluene diisocyanate.

PEF/FEV₁ curves of the unexposed days were reference.⁷ If IC test reaction result had been borderline positive for asthma; the histamine challenge test was in some cases repeated after the IC. The markedly increased hyperreactivity in histamine challenge confirmed the asthma in the IC test.

RESULTS

On average, three challenges were performed on each patient. Rhinitis appeared in 13% (111/829) of challenged patients. Asthmatic reactions appeared in 25% (211/829) of these patients (Table 3).

Organic agents were the most frequent causes of OR in our patients (Table 4). The most common causes of rhinitis in our study were flours. The grains inducing OR in our study were wheat, rye, buckwheat, and cornstarch. The agents most likely to produce rhinitis in inhalation tests were obeche wood dust or latex, both of which have strong allergenic potency. Other rhinitis reactions from wood dusts were caused by pine, spruce, and mahogany. Flowers and house plants triggering allergic rhinitis were Benjamin tree, tulip, daisy, and a mixture of fern, ivy, and cissus. The animal allergens causing rhinitis reactions in this study were cow (dander allergen) and fox (furs). Food ingredients causing rhinitis were potato, vanilla, and milk powder. Additives causing rhinitis in this material were cellulase and pectin. Molds causing rhinitis were *A. fumigatus* (3/98 challenges) and *A. kilience* (1/34 challenges); 28 challenges with *C. cladosporioides* did not produce rhinitis. In one patient, mixing of bacteria cultivation preparation (Todd Hewitt Broth, Difco Laboratories, Detroit, MI) produced rhinitis.

Results of exposures to inorganic agents are presented in Table 5. Acid anhydrides used as hardeners in epoxy resin systems were the main cause of OR. They were mainly MH-HPA (methylhexahydrophthalic anhydride), but also MTHPA (methyltetrahydrophthalic anhydride), phthalic anhydride, and HHPA (hexahydrophthalic anhydride) produced rhinitis. Formaldehyde was another common agent producing OR, together with glutaraldehyde. In the rhinitis cases, occupational sources releasing formaldehyde were identified in particleboards, cloths, fixatives of chemistry, and a metal machining fluid. Persulphates and thioglycolates were the most common agents producing rhinitis in hairdressers. Metacrylates and acrylates used in tooth fillings, adhesive glues, and hair sprays and diisocyanates (MDI [diphelnylmethan-di-isocyanate] and HDI [hexamethylen di-isocyanate]) used as paint hardeners and in wood coatings caused rhinitis reac-

Table 3 IC tests with 829 patients with suspected OR

Airway Findings in the Challenge Test	No. of Tests (N _{pos} /N)	%
Rhinitis in an occupational challenge test	123/1229	10
Asthma in an occupational challenge test	161/1229	13
Rhinitis in a control challenge test	19/838	2
Asthma in a control challenge test	49/838	6

Table 4 Rhinitis reactions in ICs with organic agents

Allergen or Occupational Agent	No. of Challenges	No. of Patients	Positive Specific Skin Prick (n _{pos} /n)	Positive Challenges with Rhinitis (n)	Positive Challenges with Asthma (n)	Positive Challenges with Asthma and Rhinitis (n)
Flours and fodders	115	99	51/90	31	32	12
Vegetables and spices and food ingredients	13	13	8/10	3	1	1
Animal-derived agents	17	16	2/13	2	3	2
Storage mites	5	5	3/3	0	1	0
Flowers and decorative plants	33	22	15/21	7	6	2
Obeche	9	8	4/6	4	6	4
Other wood dusts	38	37	0/30	4	4	1
Latex	7	7	3/6	3	2	1
Textiles	14	14	0/12	2	4	2
Enzymes	9	7	5/6	1	2	1
Molds	160	110	4/67	4	22	0
Peptone	1	1	0/1	1	1	1
Pectin	1	1	0/1	1	1	1

Table 5 Rhinitis reactions in ICs with inorganic agents

Allergen or occupational agent	No. of Challenges	No. of Patients	Specific Skin Prick (n_{pos}/n)	Positive Challenges with Rhinitis (n)	Positive Challenges with Asthma (n)	Positive Challenges with Asthma and Rhinitis (n)
Acid anhydrides	41	28	18/27	14	2	2
Persulphates	82	72	1/67	8	11	3
Thioglycolates	38	36	0/8	5	5	1
Paraphenylenediamine	12	11	0/3	3	1	1
Methacrylates	65	59	0/35	6	5	0
Acrylates	21	21	0/21	1	1	0
Formaldehyde	122	95	2/83	7	10	3
Glutaraldehyde	9	9	0/6	3	2	1
Machining fluids (contain e.g. ethanalamines and formaldehyde)	18	16	—	1	1	0
Isocyanates	70	53	2/50	3	6	0
Welding fumes	23	20	—	2	2	1
Colophony fumes	43	40	1/38	1	2	0
Chloramine T	15	15	7/12	2	1	0
PVC fumes	6	6	1	1	0	0
Epoxy	14	13	1/8	1	4	1
Aziridine (ethylene imine)	13	4	0/4	2	3	2

Table 6 Description of rhinitis reactions in control challenges

Control Agent	No. of Challenges	Positive Challenges with Rhinitis (n)	Positive Challenges with Asthma and Rhinitis (n)
Lactose	341	11	1
Coca solution	299	4	1
ALK diluting liquid	94	1	0
Black iron welding fumes	23	3	1
Total (also other control agents)	838	19	3

tions as well. Some reactions also were induced by a disinfectant, chloramine-T. Rare causes of rhinitis found were aziridine in leather finishing work, fumes of PVC plastic, and use of epoxy glue.

Welding caused rhinitis symptoms both in the occupational and in the control challenge tests. In the control tests, welding of black steel caused rhinitis as a result of what was considered an unspecific irritation mechanism. In one case, welding of painted metals produced acid anhydride gas that caused OR, as described elsewhere.⁸ Another welder was diagnosed with OR due to a late reaction (2–6 hours, both rhinorrhea and excess of mucosal swelling, repeatedly and in biopsy, degranulation of mast cells) in connection with welding of both black iron and stainless steel. We don't know such cases from the literature.

Compared with the general atopy propensity of Finnish adults at that time (34%),⁹ our patients showed an elevated amount of atopy, with 268/715 (37%) of patients tested having some positive result to common environmental allergens. In most patients with rhinitis reaction in the IC, sensitization to these agents was shown in a specific SPT. Similarly, agents with negative SPTs seldom induced rhinitis in IC (Tables 4 and 5).

Altogether, 838 placebo or nonoccupational control challenges were conducted (Table 6). The placebo tests gave 2% positive rhinitis reactions, although in the lower airways the figure was 6%.

DISCUSSION

A challenge test may be valuable when there is uncertainty about whether the patient should change jobs. OR may cause inability to work in the present job or obligate the employer to reduce the exposure in the workplace. IC can clarify and confirm the state of the disease to the employer and insurance companies. However, if challenge tests are required, simultaneous evaluation of both upper and lower airways is effective. Combining upper and lower airway follow-up sometimes causes some delay in nasal evaluation compared with individual nasal challenges. In our clinic the main criteria for OR is a runny nose, nasal blockage being of lesser importance. We consider our method an efficient and repeatable way to assess runny nose and nasal allergy caused by occupational agents, even though the exact timing for follow-up varies slightly more than with nasal challenges.

Compared with local nasal challenges, the evaluation of possible pulmonary reactions requires a follow-up of at least 6 hours after the exposure.¹⁰ In our clinic the subjects are admitted as inpatients for the follow-up. The examinations

usually last for 1–2 weeks, while local nasal challenge tests are typically done in 2 days. Organic agents rarely produce isolated late-phase asthmatic response, although this is not uncommon for low molecular weight chemical sensitizers.¹⁰ It has been estimated that chamber challenge reactions may cause asthmatic symptoms to exacerbate for a few days after the challenge with $\leq 5\%$ of asthmatic patients.¹¹ Most asthmatic reactions resolve with inhalation drugs; only a few reactions have been i.v. treated. No anaphylactic reactions have ever appeared in our tests. The main cause for the cancellation of a planned IC is unstable asthma. In our clinic, sick leaves required before challenge tests are determined individually after considering both the time frame and the severity of symptoms.

In our data, flours, especially wheat and rye, were the main allergens causing OR, reflecting their position as the leading cause of OR in Finland. Similarly, flours also are major causes of occupational asthma. Other potent inhalant allergens in the food industry and chemistry are enzymes. The small number of enzymes in our material most likely reflects improved awareness and efficient protection against such hazards in Finland. Storage mites also can be found in the chain of food processing, although they did not induce rhinitis reactions in this study.

Animal allergens, especially cow dander, are the second largest cause of OR in Finland. In this respect, our study does not represent the whole country's situation, because our patients were mostly urban and laboratory animal allergies were examined as workplace challenges.

Flowers and decorative plants were the prevalent causes of rhinitis and lower airway symptoms among florists. SPT was useful to identify the sensitization to plants before the IC.

Molds were often suspected to cause nasal symptoms in the 1990s, which can be seen in the high number of such patients in this material. Although IgE-mediated sensitization to some molds recently has been identified as a risk factor for adulthood asthma,¹² this evaluation supports the previous conclusion that the majority of the nasal symptoms in moisture-damaged buildings are other than immediate IgE-mediated allergy.¹³

In this material positive ICs appeared also without IgE sensitization to pine, spruce, and mahogany dusts. Obeche has strong allergenic potential. Specific allergens in pine and spruce dusts are not considered as main causes of the symptoms found in the woodworking industry.^{14,15} In most workplaces where wood is handled, the inhaled air contains a high amount of wood dust. Pine terpenes (α -pinene) have been reported to be involved with complaints of airway irritation.¹⁶

In rhinitis and asthma, atopy has been reported as one important modifier with wood-dust reactions.¹⁷ In critical reviews, the lack of standardization of challenge tests has been put forward as one possible explanation for some positive nasal reactions to wood dusts. In this study lactose was most often the control agent of wood dusts. Unspecific hypersensitivity, mechanical irritation of the nasal mucosa, and, perhaps, cross-reactive IgE are possible causes of the rhinitis of these patients.¹⁸

Chemical allergens are small molecular mass agents that usually cause more asthma and lower airway symptoms than distinct rhinitis, although they may cause irritation to upper airways as well. Acid anhydrides were shown to be the main chemicals inducing OR in Finland in our evaluation. They act as haptens and induce IgE-mediated sensitization and asthma and/or rhinitis.

Persulphates were found as another important chemical group causing rhinitis OR, although the mechanisms of the symptom remain unknown.¹⁹ Hairdressers' OR is caused by mostly persulphates in bleaching agents and less by thioglycolates in perm agents. Other agents causing rhinitis to hairdressers are paraphenylenediamines and other hair dyes.²⁰ Our material included one case with rhinitis from hairspray containing acrylate polymers. Possible imprecision in this material may consist of insufficient standardization of the amount of oxidant used in these chemicals and the exact method of exposure.²¹

The third prevalent chemical group causing rhinitis in Finland between 1997 and 2003 were formaldehydes and, to a smaller amount, glutaraldehyde. Our results support that clinical IgE-mediated allergy to gaseous formaldehyde does not exist, or if it does exist, it is extremely rare.^{22,23} One person, with unspecific rhinitis also, had positive challenge test conducted with machining fluids of workplace machinery work.²⁴ Machining fluids contain and release some formaldehyde, and they also contain ethanolamines, diethanolamines, and triethanolamines. The concentration of formaldehyde in the challenges with machining fluids is low compared with gaseous formaldehyde exposures.

Acrylates and methacrylates can cause rhinitis reactions. The occupational sources of acrylates and methacrylates in our rhinitis patients were dentists' tooth filling materials and glues and hairdressers' hairsprays. The OR caused by methacrylates have diminished since this evaluation in Finland, because of the spread of information on the risk of allergy to dentists. Allergic reactions to latex also have become rare, as the amount of latex contained by gloves has been reduced since the 1980s and 1990s.

Colophony fumes as work-related exposures are formed from solder fluxes during soldering and are known causes of OR.²⁵ Often, they were suspected but rarely caused OR in our study.

In painting, coating, and finishing work, diisocyanates are important occupational causes of airway reactions. Diisocyanates are one of the leading causes of occupational asthma worldwide. Only a small minority of the reactions are connected with IgE.^{26,27}

IC with a placebo agent produced rhinitis reactions in 2% of the challenges in our study, and 10% of the occupational challenges triggered rhinitis reactions (Table 3). In the nasal challenge test, we have previously described a higher propor-

tion of rhinitis reactions, both from occupational (39%) and placebo challenges (10%).⁴ We believe the difference is caused mainly by the different patient materials. The challenges with inorganic agents in this study produced less rhinitis than the organic protein challenges. In a nasal challenge, the local concentration of the allergen used becomes higher, without the fear of serious reactions. Because challenge tests with chemicals can irritate airways, careful control of the test agent's concentration as well as patient selection and optimal treatment is important. Based on our experience we encourage cooperation between rhinologists, chest physicians, and specialists of occupational medicine in evaluations of both nasal and bronchial reactions in occupational ICs.

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