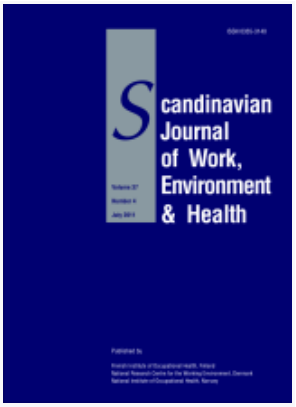
Downloaded from www.sjweh.fi on September 01, 2013



Original article

Scand J Work Environ Health 2003;29(6):461-467
doi:10.5271/sjweh.754

Nasal symptoms among residents in moldy housing

by Ruoppi PI, Husman TM, Reiman MH, Nuutinen J, Hyvärinen AM, Nevalainen AI

Affiliation: Department of Otorhinolaryngology, Kuopio University Hospital, PO Box 1777, FIN-70211 Kuopio, Finland. pirkko.ruoppi@kuh.fi

Refers to the following text of the Journal: 1996;22(1):5-13

Key terms: adult; allergy; dampness; fungi; indoor air; moisture damage; mold; moldy housing; nasal symptom; resident; rhinitis; upper respiratory symptom

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/14712854

Print ISSN: 0355-3140 Electronic ISSN: 1795-990X Copyright (c) Scandinavian Journal of Work, Environment & Health

Original article

Scand J Work Environ Health 2003;29(6):461–467

Nasal symptoms among residents in moldy housing

by Pirkko I Ruoppi, MD,[1] Tuula M Husman, MD,[2] Marjut H Reiman, PhD,[3] Juhani Nuutinen, MD,[1] Anne M Hyvärinen, PhD,[2] Aino I Nevalainen, PhD[2]

Ruoppi PI, Husman TM, Reiman MH, Nuutinen J, Hyvärinen AM, Nevalainen AI. Nasal symptoms among residents in moldy housing. *Scand J Work Environ Health* 2003;29(6):461–467.

Objectives The aim of this study was to determine whether mold allergy mediated through immunoglobulin E (IgE) was responsible for the chronic nasal symptoms experienced by residents of moldy dwellings. A secondary aim was to investigate whether nasal mucosal findings were a possible reflection of other pathological mechanisms of chronic rhinitis.

Methods Sixteen adults living in moldy housing and complaining of chronic rhinitis were compared with sixteen healthy referents without any known mold exposure. All the buildings were surveyed for visible signs of moisture and mold. Microbial measurements were performed in the damp buildings with mold problems and in half of the reference buildings. The clinical study consisted of an otorhinolaryngological examination, nasal cytology, and skin prick tests. In the study cases, nasal provocation tests with fungi cultured from the homes and nasal mucosal biopsy were performed.

Results In the housing with signs of moisture and mold, the concentrations of microorganisms were elevated, but were within the normal range of those of the reference buildings. The only positive skin reaction for molds was detected in one referent. No reactions were elicited in the nasal provocation tests with molds. Squamous metaplasia were detected in four biopsies and three cytograms of the cases but not in the nasal smears of the referents.

Conclusions In this material, the respiratory symptoms reported by occupants of moldy residences were not caused by mold allergy but were apparently related to nonspecific inflammation following irritation.

Key terms adult, allergy, dampness, fungi, indoor air, moisture damage, mold, rhinitis, upper respiratory symptoms.

The association between damp housing and respiratory symptoms has been reported for both adults (1–4) and children (1, 2, 5–9) living in different climates. Home dampness, as indicated by moisture stains, signs of water leaks, detached surface materials, mold odor, or visible mold growth, is common in modern housing, signs of moisture that require remedial work being observed in 55% of Finnish dwellings (10). In our northern climate, the most common causes of moisture damage are defects in the construction or maintenance of the dwellings (10, 11). As materials become moist, microbial growth develops, the species present and the abundance of their growth being determined by the nutrient and moisture conditions of the building (12, 13). Fungi can grow on surfaces whenever there is sufficient moisture (14). A list of so-called indicator microorganisms, which typically appear in water-damaged buildings, has been compiled (15). Exposure to fungi, bacteria, and their metabolites is a potential health risk, known to be associated with respiratory symptoms (16), which may be nonspecific irritation and common respiratory infections (17, 18). In some cases, they provoke specific allergy mediated through immunoglobulin E (IgE) (19, 20). In clinical practice, an examination of IgE-mediated allergy is the only method currently available with which to study the effects of patients' exposure in moldy residences. If allergy is not diagnosed, the association of symptoms with even visible fungal growth cannot be confirmed with the level of certainty required to determine a causal connection, for example, in cases of litigation. There is an urgent need to develop better clinical tools to verify the connection between mold exposure and health manifestations.

1 Department of Otorhinolaryngology, Kuopio University Hospital, Kuopio, Finland.
2 Department of Environmental Health, National Public Health Institute, Kuopio, Finland.
3 Kuopio Regional Institute of Occupational Health, Kuopio, Finland.

Reprint requests to: Dr Pirkko Ruoppi, Department of Otorhinolaryngology, Kuopio University Hospital, PO Box 1777, FIN-70211 Kuopio, Finland. [E-mail: pirkko.ruoppi@kuh.fi]

In this study, we determined whether the rhinitis experienced by 16 people living in moisture-damaged housing with visible fungal growth was an IgE-mediated allergy to the fungi found and cultured from their residences. We also examined whether, as a possible consequence of the continuous indoor exposure to molds and their metabolites, there were cytological or histological findings in the nasal mucosa that would reflect pathological mechanisms other than allergy for their symptoms.

Participants and methods

A case-referent study was carried out among 16 adults living in moldy housing and suffering from chronic rhinitis and 16 healthy referents without any known mold exposure. The symptomatic participants, the cases, belonged to seven families living in urban or suburban residences (one apartment, three terraced houses, and three single homes) with mold odor and visible fungal growth. They had been living in these homes for 2–21 (mean 10) years. The families consisted of 11 women and 5 men, aged from 17 to 59 (mean 35) years. The referents were selected from volunteering personnel of the institutes performing the study; they were 16 healthy subjects, matched with the symptomatic participants for gender and age. They were members of 15 families and had lived in their residences (two apartments, six terraced houses, and seven single-family homes) for 1–18 (mean 6) years. The referents had no respiratory symptoms nor any known moisture problems or mold in their homes nor any occupational or other mold exposure. Atopic allergy had been earlier diagnosed for four cases and two referents. There were three smokers in both groups, and likewise, in both groups, two persons kept a pet indoors.

All 7 of the complaint homes and the 15 reference homes were inspected for visible signs of moisture or mold. Microbial airborne concentrations were determined for all of the problem buildings and for seven of the reference buildings. Other than being matched according to type and age with the case homes, the seven reference homes were selected at random from the same urban or suburban area. Microbial samples were collected in situations simulating normal living conditions (such as opening the door, sweeping the floors, and changing the linen) with 6-stage impactors on 2% malt extract agar (MEA) and dichloran-18 glycerol agar (DG18) (reference buildings only) for fungi, followed by incubation for 7 days at room temperature. Samples were also collected from surfaces with sterile swabs that were then cultured on 2% MEA as a dilution series. Material samples were taken when possible. The corresponding specimens for bacterial samples were cultivated on tryptone glucose yeast agar (TGY) and incubated for 5 days. The colonies were counted, and the results expressed as colony-forming units (cfu) per cubic meter of air, per square centimeter of surface, or per gram of material. The fungal genera were identified morphologically using an optical microscope. From the samples of bacteria, the occurrence of dryish, actinomycete-type colonies was recorded. To avoid outdoor contamination, all the microbial samples were taken during the wintertime, when the ground was covered with snow.

The most common strains of fungal growth in the moisture-damaged housing were subcultivated and transferred in vessels containing malt extract (Difco®) (20 g/l), mycological peptone (Oxoid®) (10 g/l), and glucose (40 g/l). The cultures were incubated at 25°C for 1 week. The fungal colonies were then sterilized, harvested by filtering, and washed three times with phosphate-buffered saline (PBS). The fungal mass in the PBS (50% volume/volume) was disrupted mechanically with an Ultra-Turrax apparatus (Janke and Kunkel, Staufen in Breisgau, Germany) and then further homogenized with an ultrasonic disintegrator (Soniprep 150 MSE, Crawley, United Kingdom). After centrifugation at 15 000 revolutions/minute for 30 minutes and passing through a 0.45-µm filter, the supernatants were used as crude extracts in the nasal provocation testing. The protein concentration of the supernatants varied from 10 to 100 µg/ml and contained IgE-binding components detected by immunoblotting.

In the clinical study, an otorhinolaryngologist recorded current symptoms and made a clinical examination (anterior and posterior rhinoscopy, mirror laryngoscopy, and otoscopy). In order to reduce any biasing influence of acute respiratory infection, such as the common cold, the visits were scheduled individually. Skin prick testing (SPT) with 32 aeroallergens (ALK-Abelló A/S, Denmark) was performed and interpreted according to the recommendations of the European Academy of Allergology and Clinical Immunology (21). Histamine hydrochloride (10 mg/ml) and allergen diluent were used as positive and negative controls, respectively. A weal diameter of at least 3-mm and half of the histamine control was considered positive. The allergens used were pollen from birch, alder, seven grasses (timothy, meadow foxtail, meadow grass, meadow fescue, orchard grass, rye grass, common reed), mugwort and dandelion, six animal danders (horse, cow, dog, cat, sheep, hen) and two house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*). Thirteen of the antigens were fungi, as follows: *Alternaria alternata, Aspergillus fumigatus, Aureobasidium pullulans, Botrytis cinerea, Cladosporium herbarum, Fusarum roseum, Mucor racemosus, Mucor spinosus,*

Penicillium chrysogenum, Penicillium (glaucum) expansum, Phoma herbarum, Rhizopus nigricans, and *Rhodotorula rubra*. The allergen concentration of these commercial fungal solutions was 5 mg/ml, but, in contrast to the other allergen solutions used in this study, the allergenicity of the fungal solutions was not standardized. Two nasal cytology specimens were taken with cotton wool swabs from every participant. The samples were fixed and stained according to the routine procedure of our laboratory and were then interpreted according to the criteria of Meltzer et al (22). A biopsy from the nasal mucosa was taken from 14 cases but not from the healthy referents (two of the cases and the referents were reluctant to submit to this invasive procedure). The site of the biopsy was the middle turbinate.

Nasal provocation testing was performed on the cases during the second visit, about 3 months later. The patients were first challenged with the negative control, which was phosphate-buffered saline (the diluent of the allergen solutions). A volume of 0.05 milliliters of the test fluid was sprayed towards the inferior and middle turbinate of one nasal cavity at a time with a 1-milliliter syringe filled with air and equipped with a thin needle while the patient was holding his or her breath. If no placebo reaction occurred, the nasal challenge test was performed on the other nasal cavity with 0.05 milliliters of crude mold extract prepared from the most prominent strain of fungal growth present in the home of that individual to reflect the main domestic exposure. The fungal species used in the nasal challenges were *Penicillium* (2 species), *Aspergillus versicolor, Aspergillus terreus, Cladosporium herbarum, Cladosporium sphaerospermum* and *Rhodotorula glutinis* (representing yeasts). Nasal reactions were observed during the following 30 minutes and recorded in rhinoscopy always by the same physician. The interpretation of the test was based on the rhinoscopic findings, which were hypersecretion and mucosal edema, and on subjective symptoms (sneezing, nasal itching, and obstruction). According to the clinical routine, the test was considered positive if hypersecretion and at least one of the other two signs and symptoms were recorded. The participants were asked to report any late reactions the next day.

The results are presented as odds ratios and their 95% confidence intervals. The Ethics Committee of the University of Kuopio and the Kuopio University Hospital approved the study design.

Results

In all seven of the water-damaged dwellings, the site visit revealed visible fungal growth and the odor of mold. The concentrations of the viable fungi and the fungal genera detected are shown in table 1. The concentrations of viable fungi were elevated in most of the homes with moisture and mold damage, and they were unusually high, occasionally up to 53 600 cfu/m^3. According to the criteria for the indoor-air quality of urban dwellings in a subarctic climate, 100–500 cfu/m^3 is regarded as an elevated concentration for wintertime (23). High or elevated concentrations were found in bedrooms, living rooms, and bathrooms of the damaged homes. Some fungal genera, species, or groups were only found in the damaged homes. They were *Stachybotrys, Trichoderma, Aspergillus terreus, Alysidium,* ascomycetes, *Polyscutalum, Rhinocladiella,* and *Gliomastix.* In the 15 reference houses, there were no visible signs of dampness. The perceived indoor-air quality was assessed as good, and there was no sign of mold odor. In the seven selected reference buildings, the mold concentrations in the air were normal (23), the highest values being 90 cfu/m^3. The fungi consisted of normal flora with sporadic colonies of indicator organisms (15).

All of the symptomatic participants had suffered from continuous or recurrent rhinitis for 2–10 (mean 5) years. There were also other symptoms, for example, recurrent sinusitis (4 persons), phlegm and recurrent bronchitis (3 persons, nonsmokers), asthma (2 persons), eye irritation (1 person), and urticaria episodes (1 person). In the anterior rhinoscopy, the nose seemed healthy in three of the cases and in ten of the referents. In the others, there was prominent mucosal swelling or mucopurulent, partly crusted secretions (all cases) in the anterior part of the nose.

Six cases (38%) and five referents (31%) had positive skin prick tests (table 2). The only positive reactions from fungi (*Aspergillus fumigatus, Mucor racemosus*) were obtained from one referent. With respect to house dust mites, there were positive skin prick tests for three cases and one referent. A positive test to some of the dander from furry animals was detected for three cases and three referents, none of whom was directly exposed to these species. The nasal provocation testing with a negative control and a fungal strain cultured from the case's own home was done for 10 patients, the other 6 symptomatic participants refused to participate in this test. However, the challenge did not evoke any immediate or late rhinitis reaction.

The cytological examination was normal for 8 cases and 10 referents (table 3). Squamous metaplastic cells were found in the nasal smear of three cases but in none of the referents. An abundance of goblet cells was found in three cases, but we did not detect any eosinophilia indicative of immediate-type nasal allergy in either the cases or the referents. A nasal biopsy was performed on 14 participants (all cases). Five showed chronic inflammation, and four had squamous epithelial metaplasia, while the biopsy finding was normal for three cases. In

Table 1. Concentrations of viable microbes in the seven case and seven reference homes. (cfu=colony forming units; fungal genera: ACR = *Acremonium*, ACT = actinomycetes, AFUM = *Aspergillus fumigatus,* AGLA = *Aspergillus glaucus,* ALT = *Alternaria*, ALY = *Alysidium*, ANIG = *Aspergillus niger,* ASC = ascomycetes, ASP = *Aspergillus sp.,* ATER = *Aspergillus terreus,* AUR = *Aureobasidium,* AVER = *Aspergillus versicolor,* BOT= *Botrytis,* CLA = *Cladosporium,* EUR = *Eurotium*, FUS= *Fusarium*, GEO = *Geotrichum,* GLI = *Gliomastix*, GLP = *Gliocephalis,* GNT = *Gonatobotrys*, GON = *Gonatorrhoidiella,* HYA = *Hyalodendron,* MUC = *Mucor,* NON = non-sporing isolates, OID = *Oidiodendron,* PAE = *Paecilomyces*, PEN = *Penicillium*, PHI = *Phialophora,* POL = *Polyscutalum*, RHI = *Rhinocladiella*, SCO = *Scopulariopsis,* SPH = *Sphaeropsidales group,* STA = *Stachybotrys*, TRI = *Trichoderma*, ULO = *Ulocladium,* UNI = unidentified, WAL = *Wallemia* ,YEA = yeasts)

Status	Number of participating occupants, type and age of the residence	Indoor air (cfu/m^3)	Four most prevalent fungal genera in indoor air	Other genera found in the indoor environment (in alphabetic order)	Comments based on the guidelines of the Ministry of Social Affairs and Health (23)
Case					
Home 1	2 occupants, a single family house from the 1980s	139–193 (median 166), 2 samples (bedroom)	ASP, PEN, UNI, CLA	ACT[a], ALY, ASC, NON, PAE, TRI, YEA	Elevated concentrations
Home 2	1 occupant, a terraced house from the 1980s	186–386 (median 286), 2 samples (bedroom, kitchen)	NON, YEA, CLA, PEN	GEO, POL	Elevated concentrations
Home 3	2 occupants, a terraced house from the 1990s	57–761 (median 227), 6 samples (bedroom, living room, sauna)	PEN, ASP, CLA, YEA	ACR, ACT[a], ASC, AUR, GEO, HYA, MUC, NON, OID, SCO, SPH, UNI	Elevated or high concentrations, mold growth in surface and material samples
Home 4	6 occupants, a single-family house from the 1970s	43–9436 (median 311), 13 samples (bedroom, children's room, living room, sauna)	PEN, CLA, YEA, ASP	ACR, ACT[a], ALT, AUR, BOT, GEO, GON, HYA, MUC, NON, OID, PAE, RHI, SPH, STA, UNI	Elevated or high concentrations, wide variation in concentrations
Home 5	2 occupants, a terraced house from the 1980s	83–3861 (median 1420), 4 samples (living room, office)	PEN, ASP, CLA, RHI	ACR, ACT[a], GLI, MUC, NON, SCO, TRI, UNI, YEA	High concentrations, mold growth in material samples, wide variation in concentrations
Home 6	1 occupant, a single-family house from the 1970s	18 036–53 602 (median 44163), 4 samples (bedroom, living room)	ASP, GLP, PEN, CLA	ACR, ACT[a], ATER, GNT, NON, SCO, ULO, UNI, YEA	Very high concentrations, visible growth in material and surface samples
Home 7	2 occupants, an apartment from the 1990s	.	ASP, PEN, ACT [a]	.	Qualitative data [b]
Reference					
Home 1	1 occupant, a terraced house from the 1970s	31–52 (median 46), 6 samples (bathroom, bedroom, living room)	PEN, PAE, YEA, ASP	ANIG, AUR, CLA, MUC, NON, SPH	Low concentrations
Home 2	1 occupant, a single-family house from the 1980s	5–26 (median 10), 6 samples (bathroom, bedroom, living room)	PEN, ASP, YEA, CLA	ACT[a], NON	Low concentrations
Home 3	1 occupant, a terraced house from the 1980s	12–26 (median 20), 6 samples (bathroom, bedroom, living room)	PEN, ASP, CLA, YEA	ACR, ACT[a], AGLA, PAE, SPH, WAL	Low concentrations
Home 4	1 occupant, a single-family house from the 1970s	2–14 (median 11), 6 samples (bathroom, bedroom, living room)	PEN, CLA, YEA, HYA	ACR, AFUM, BOT, GEO, NON (surface samples: ALT, AVER, SPH, ULO)	Low concentrations
Home 5	1 occupant, an single-family house from the 1970s	7–90 (median 20), 6 samples (bathroom, bedroom, living room)	PEN, CLA, SCO, NON	ACT[a], AUR, PAE, SPH, YEA	Mainly low concentrations
Home 6	1 occupant, an apartment from the 1980s	7–74 (median 19), 6 samples (bathroom, bedroom, living room)	PEN, ASP, YEA, PAE	ACR, FUS, EUR, NON, PHI	Mainly low concentrations
Home 7	1 occupant, a terraced house from the 1990s	31–62 (median 47), 6 samples (bedroom, children's room, living room, sauna)	PEN, ASP, YEA, CLA	ACT[a], NON, OID, SPH, WAL	Low concentrations

[a] In bacterial samples.
[b] The sampling was only partly successful, and hence only qualitative information was available.

Table 2. Results of the skin prick test of the cases and referents in relation to allergens. (OR = odds ratio, 95% CI = 95% confidence interval)

Allergen group	Cases (N=16)	Referents (N=16)	OR	95% CI
Trees (alder, birch)	3	1	4.0	0.27–60
Grasses (6 most common in Finland)	5	2	7.5	0.46–120
Herbs (mugwort, dandelion)	3	–	.	.
House dust mites (2 species)	3	1	4.0	0.27–60
Animals (cat, dog, cow, horse)	3	3	0.67	0.06–7.4
Molds (13 strains)	–	1	.	.
No reactions in skin-prick test	10	11	.	.

Table 3. Nasal cytology findings for the cases and referents. (OR = odds ratio, 95% CI = 95% confidence interval)

Finding	Cases (N=16)	Referents (N=16)	OR	95% CI
Normal	8	10	.	.
Increased				
Neutrophils	2	6	0.24	0.040–1.43
Basophilic cells	1	1	1.0	0.057–17
Goblet cells	3	1	3.5	0.32 –37
Squamous epithelial cells	3	–	.	.

two cases, squamous metaplasia was found in both the cytological and the biopsy specimens. Two samples were crushed and could not be interpreted.

Discussion

It is well known that exposure to building-related moisture and mold poses a risk to health, although the underlying cellular mechanisms are still unclear. The most common symptoms are irritation of the respiratory tract and the eyes (3, 5). The first reports of serious toxic effects of indoor molds on humans have been published (24). Several molds are allergens and can cause allergic rhinoconjunctivitis and asthma (16, 19, 20). With respect to these allergenic molds, *Penicillium*, *Mucor*, *Aspergillus*, *Rhizopus*, *Alternaria*, and *Fusarium*, for example, are commonly found in the indoor air, whereas, although *Cladosporium* is common indoors, it is also the mold most frequently encountered in the outdoor air (19, 20). Estimates of the prevalence of mold allergy vary from 5% to as high as 50% in different populations (16). In Finland, nearly 30% of asthmatic children have had a positive radioallergosorbent test (RAST) to molds (25). Currently, there are major economic interests associated with moldy buildings, and thus there is also a clear need for objective clinical tests to show the causal connection between exposure and health consequences. For example, insurance companies require a positive nasal challenge test to confirm the causality between mold exposure and rhinitis. However, there is no evidence that mold-related rhinitis would specifically represent an IgE-mediated symptom.

In this study, the growth of molds was undertaken on standard agar. It is well known that the enumeration and description of microbial flora depend on the culture media, the conditions used, and the interactions that occur between the microbes present in the sample. No single medium is capable of detecting all the microbes present, and, therefore, the selection of the culture media represents a balance between available resources and the aims of the study. The combination of culture media used in this study, 2% MEA and DG18, is considered to encompass the majority of important indoor fungi (15) since MEA is compatible with more hydrophilic fungi and DG18 encourages xerophilic strains. Fungi favoring cellulose-enriched media, such as *Stachybotrys*, can also be observed with MEA medium. If, instead, more selective media had been used, the diversity of fungi detected would probably have been smaller.

There were no positive reactions to fungal allergens in the skin-prick tests of the occupants of moldy houses, although 38% of them had shown skin reactivity to other aeroallergens tested. However, the respiratory symptoms detected for sensitized persons could not be attributable to pollen exposure because the clinical study was performed outside the pollen season. None of the persons sensitized to animal allergens had direct animal contacts, and, therefore, animal allergy did not seem to be responsible for their symptoms.

The nasal provocation testing was a simulation of a natural individual exposure. Crude mold extracts were used, on one hand, due to the poor availability of standardized allergen extracts and, on the other hand, in order to avoid false negative results possibly associated with commercially refined allergen solutions. Freezing-thawing and sonication have been used to produce crude antigens for immunologic assays (26). In quality control tests of our in-house enzyme-linked immunosorbent assay, no major difference in antibody binding proteins has been detected between sterilized and unsterilized antigens. In Finland, nasal provocation testing has been used routinely in clinical practice for confirming the diagnosis of allergic rhinitis in cases showing occupational symptoms and before allergen immunotherapy has been initiated for rhinitis. An increase in nasal secretions is one of the most prominent symptoms of an immediate allergic reaction, and experienced physicians can easily detect it in rhinoscopy, as they also can mucosal edema. If objective and measurable parameters are needed, the weighing of nasal secretion combined with acoustic rhinometry or rhinomanometry or both are recommended (27).

Since the skin prick tests showed no evidence of IgE-mediated allergy to common water-damage molds and the nasal provocation testing with individually dominant molds were negative, the symptoms were interpreted as being irritative in nature. The irritant-induced response mechanism includes both central (cholinergic) and local (axonal) neurogenic reflexes (28). Many earlier observations have indicated that IgE-mediated allergy is seldom the sole cause of the respiratory symptoms experienced by inhabitants of damp housing. Among nearly 15 000 adult Canadians, the association between exposure to home dampness and mold and respiratory symptoms was clear, but it did not seem to be an immediate allergic response (3). Positive skin tests for molds were also rare (a result in 6% of the cases only), although the occurrence of asthma and wheezing was common (32%) among 99 Finnish children exposed to a school environment with moisture problems (29). Fourteen of these children had parent-reported moisture problems also in their homes.

In addition to molds, house dust mites are associated with damp housing, and increased sensitization to mites has been reported for children (30). Also in this study, there was a tendency towards higher skin reactivity to house dust mites among people living in

moisture-damaged housing (3 of 16 skin-prick tests positive) than among the referents (1 of 16 skin-prick tests positive). House dust mites seem to be equally common in moldy and nonmoldy housing in Finland (31). The connection between house dust mites and building moisture is not very clear in northern climates, where the indoor air is generally dry even though there may be local moisture damage in some part of the building. Furthermore, in addition to dust mites, irritant chemical pollutants have been proposed as causal agents in moldy buildings. However, in our previous studies on indoor-air quality, the main differences between moisture-damaged and reference buildings have been observed in the airborne fungal concentrations and type of flora present (32).

The exposure in this study was documented as visual observations of moisture and mold in the residences of the cases, while no such findings were made in the residences of the referents. In addition, sampling and measurements of viable fungi in the homes of the cases revealed unusually high concentrations of fungi in the indoor air, on surfaces, and in material samples. Air concentrations of over 1000 cfu/m^3 are only detected in 20% of samples taken from visibly damaged homes, while half of the concentrations remain <150 cfu/m^3 (32). With respect to the microbial flora, 30 different genera, species, or groups were identified in the damaged homes, and 26 genera were found in the reference homes (ie, there was a trend towards increased diversity of the microflora in response to the elevated moisture conditions).

In this study, the failure to detect eosinophilia in either nasal smears or biopsies does not favor the proposal that ongoing immediate-type allergic reaction would have been the cause of the respiratory symptoms. Both cytological and histopathological findings revealed signs of metaplasia in the nasal mucous membrane of some of the participants exposed to molds, whereas no metaplasia were detected in the referents. Metaplasia can be caused by air pollution (33) and industrial chemicals such as formaldehyde (34), but also by infection (35). In this study, the nasal smears and biopsies were not taken during periods of obvious infection. Nevertheless, increased neutrophils were detected in six referents. Neutrophils are known to be present in 5% of symptom-free persons, and this prevalence probably indicates occult infection (36) or contamination from the anterior part of the nose (22). However, if no bacteria are present, this finding may reflect an irritant reaction (22). With respect to our study, the significance of these nasal neutrophils in symptom-free referents remains obscure. In symptom-free noses, squamous metaplasia are rarely detected in biopsies, and metaplastic and squamous epithelial cells appear in nasal smears only in exceptional cases (36). However, it is still too early to conclude whether nasal mucosal metaplasia can be causally linked with indoor mold exposure.

Water damage and home dampness require the elimination of the exposure (ie, prompt repairs to the building). The decision to initiate repairs should not depend on the diagnosis of mold allergy or any other mold-related disease, but, instead, it should be viewed as a preventive measure. However, there may be legal reasons for which one has to prove the causality between mold exposure and symptoms (eg, a demand for compensation from an insurance company or other litigation processes). The results of our study support previous experience that IgE-mediated allergy seldom accounts for the symptoms associated with moldy houses, and nasal challenge should not be regarded as an excluding criterion for the link between mold exposure and rhinitis. Objective tests suitable for use in clinical practice are urgently needed. The preliminary observations support the hypothesis that the symptoms are due to nonspecific inflammation following irritation. The importance of squamous epithelial metaplasia as a mold-exposure-related finding should be further verified with a larger patient material.

Acknowledgments

We thank Pirjo Halonen, MSc, for her statistical guidance.

Financial support from the Ministry of Social Affairs and Health and the Kuopio University Hospital is gratefully acknowledged.

References

1. Waegemaekers M, van Wageningen N, Brunekreef B, Boleij JS. Respiratory symptoms in damp homes: a pilot study. Allergy 1989;44:192–8.
2. Platt SD, Martin CJ, Hunt SM, Lewis CW. Damp housing, mould growth, and symptomatic health state. BMJ 1989;298:1673–8.
3. Dales RE, Burnett R, Zwanenburg H. Adverse health effects among adults exposed to home dampness and molds. Am Rev Respir Dis 1991;143:505–9.
4. Brunekreef B. Damp housing and adult respiratory symptoms. Allergy 1992;47:498–502.
5. Brunekreef B, Dockery DW, Speizer FE, Ware JH, Spengler JD, Ferris BG. Home dampness and respiratory morbidity in children. Am Rev Respir Dis 1989;140:1363–7.
6. Dales RE, Zwanenburg H, Burnett R, Franklin CA. Respiratory health effects of home dampness and molds among Canadian children. Am J Epidemiol 1991;134:196–203.
7. Brunekreef B. Associations between questionnaire reports of home dampness and childhood respiratory symptoms. Sci Total Environ 1992;127:79–89.
8. Cuijpers CE, Swaen GM, Wesseling G, Sturmans F, Wouters

EF. Adverse effects of the indoor environment on respiratory health in primary school children. Environ Res 1995;68:11–23.
9. Li C-S, Hsu L-Y. Home dampness and childhood respiratory symptoms in a subtropical climate. Arch Environ Health 1996;51:42–6.
10. Nevalainen A, Partanen P, Jääskeläinen E, Hyvärinen A, Koskinen O, Meklin T, et al. Prevalence of moisture problems in Finnish houses. Indoor Air 1998; Suppl 4:45–9.
11. Nevalainen A, Pasanen A-L, Niininen M, Reponen T, Kalliokoski P, Jantunen MJ. The indoor air quality in Finnish homes with mold problems. Environ Int 1991;17:299–302.
12. Grant C, Hunter CA, Flannigan B, Bravery AF. The moisture requirements of moulds isolated from domestic dwellings. Int Biodeter 1989;25:259–84.
13. Pasanen A-L, Juutinen T, Jantunen MJ, Kalliokoski P. Occurrence and moisture requirements of microbial growth in building materials. Int Biodeter 1992;30:273–83.
14. Pasanen A-L, Kalliokoski P, Pasanen P, Jantunen MJ, Nevalainen A. Laboratory studies on the relationship between fungal growth and atmospheric temperature and humidity. Environ Int 1991;17:225–8.
15. Recommendations. In: Samson RA. Flannigan B, Flannigan ME, Verhoeff AP, Adan OC, Hoekstra ES, editors. Health implications of fungi in indoor environments. Air quality monographs, vol 2. Amsterdam: Elsevier Publications; 1994. p 529–38.
16. Husman T. Health effects of indoor-air microorganisms [review]. Scand J Work Environ Health 1996;22:5–13.
17. Pirhonen I, Nevalainen A, Husman T, Pekkanen J. Home dampness, moulds and their influence on respiratory infections and symptoms in adults in Finland. Eur Respir J 1996;9:2618–22.
18. Koskinen OM, Husman TM, Meklin TM, Nevalainen AI. The relationship between moisture or mould observations in houses and the state of health of their occupants. Eur Respir J 1999;14:1363–7.
19. Gravesen S. Fungi as a cause of allergic disease. Allergy 1979;34:135–54.
20. Güneser S, Atici A, Köksal F, Yaman A. Mold allergy in Adana, Turkey. Allergol Immunopathol (Madr) 1994;22:52–4.
21. Sub-committee on Skin Tests of the European Academy of Allergology and Clinical Immunology. Skin tests used in type I allergy testing: position paper. Allergy 1989;44 Suppl 10:1–59.
22. Meltzer EO, Orgel HA, Jalowayski AA. Cytology. In: Mygind N, Naclerio RM, editors. Allergic and non-allergic rhinitis. Copenhagen: Munksgaard; 1993. p 66–81.
23. Sosiaali- ja terveysministeriö [Ministry for Social Affairs and Health]. Sisäilmaohje: sosiaali- ja terveysministeriön oppaita 1997:1 [Directions for indoor air: a guide of the Ministry of Social Affairs and Health 1997:1] Helsinki: Sosiaali- ja terveysministeriö; 1997.
24. American Academy of Pediatrics, Committee of Environmental Health. Toxic effects of indoor molds. Pediatrics 1998;101:712–4.
25. Koivikko A, Viander M, Lanner Å. Use of the extended Phadebas RAST panel in the diagnosis of mold allergy in asthmatic children. Allergy 1991;46:85–91.
26. Priest JW, Kwon JP, Moss DM, Roberts JM, Arrowood MJ, Dworkin MS, et al. Detection by enzyme immunoassay of serum immunoglobulin G antibodies that recognize specific *Cryptosporidium parvum* antigens. J Clin Microbiol 1999;37:1385–92.
27. Pirilä T, Nuutinen J. Acoustic rhinometry, rhinomanometry and the amount of nasal secretion in the clinical monitoring of the nasal provocation test. Clin Exp Allergy 1998;28:468–77.
28. Bascom R, Shusterman D. Occupational and environmental exposures and the upper respiratory tract. In: Naclerio RM, Durham SR, Mygind N, editors. Rhinitis: mechanisms and management. 1st ed. New York, Basel, Hong Kong: Marcel Dekker Inc; 1999. p 65–94.
29. Taskinen T, Meklin T, Nousiainen M, Husman T, Nevalainen A, Korppi M. Moisture and mould problems in schools and respiratory manifestations in schoolchildren: clinical and skin test findings. Acta Paediatr 1997;86:1181–7.
30. Verhoeff AP, van Strien RT, van Wijnen JH, Brunekreef B. Damp housing and childhood respiratory symptoms: the role of sensitization to dust mites and molds. Am J Epidemiol 1995;141:103–10.
31. Hyvärinen A, Reponen T, Husman T, Nevalainen A. Comparison of the indoor air quality in mould damaged and reference buildings in a subarctic climate. Cent Eur J Public Health 2001;9:133–9.
32. Hyvärinen A. Characterizing moisture damaged buildings—environmental and biological monitoring [dissertation]. Kuopio: National Public Health Institute and University of Kuopio; 2002.
33. Calderon-Garciduenas L, Osorno-Velazquez A, Bravo-Alvarez H, Delgado-Chavez R, Barrios-Marquez R. Histopathologic changes of the nasal mucosa in southwest metropolitan Mexico City inhabitants. Am J Pathol 1992;140:225–32.
34. Edling C, Hellquist H, Ödkvist L. Occupational exposure to formaldehyde and histopathological changes in the nasal mucosa. Br J Ind Med 1988;45:761–5.
35. Ohashi Y, Nakai Y. Functional and morphological pathology of chronic sinusitis mucous membrane. Acta Otolaryngol 1983;Suppl 397:11–48.
36. Holopainen E. Nasal mucous membrane in atrophic rhinitis with reference to symptomfree nasal mucosa [dissertation]. Helsinki: University of Helsinki; 1967.

Received for publication: 22 January 2003