

Original Article

Skin test reactivity to molds in pre-school children with newly diagnosed asthma

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Abstract

Background: The aim of the present study was to evaluate the prevalence of sensitization to molds and to house dust mites (HDM) in pre-school children with newly-diagnosed asthma.

Methods: From 1996 to 2000, 122 children 1 to 6 years of age with fresh asthma treated in the Kuopio University Hospital, Kuopio, Finland, were recruited in the study; 94% attended. Skin prick tests were performed to common inhalant allergens and to 10 molds. The homes were surveyed for moisture damage.

Results: A majority of the houses had signs of dampness and moisture. One-third of the children reacted to inhalant allergens. There were 11 positive reactions to molds in five children who all reacted to at least one animal dander or seasonal pollen. *Aspergillus fumigatus*, *Botrytis cinerea*, and *Cladosporium herbarum* were the most common mold allergens. There were only two children with positive reactions to HDM, and none of them reacted to molds. No associations were found between the presence or degree of moisture problems at home and mold or HDM allergy.

Conclusion: Sensitization to molds seems to play only a minor role in pre-school children with newly-diagnosed asthma in a northern climate where the incidences of mold and HDM allergies are rather low.

Key words allergy, asthma, children, mold, skin prick test.

Asthma is the most common chronic disease that has continuously increased in children in western countries during the recent two decades.¹ Changes in indoor air quality have been speculated as one of many environmental factors, possibly influencing the increase in prevalence of asthma.^{2–5} Mold growth, as well as the presence of significant amounts of house dust mites (HDM), have been associated with dampness and moisture in buildings.^{6–8} However, mold allergy is rare in children, even among atopic ones or among those exposed to molds.^{9–15} Likewise, the incidence of HDM allergy has been reported to be rather low among children in the Nordic countries where the climate is cold and dry,^{15–18} contrary to the areas of warm climate.⁵

There is increasing evidence that exposure to moisture and molds may increase the risk of asthma in children.^{4,6,19,20} More studies investigating this possible connection are warranted,

since data on this matter, especially in pre-school children are sparse. The aim of this study was to evaluate the prevalence of sensitization to molds and to HDM focused on pre-school children with newly-diagnosed asthma.

Patients and methods

All children from 1 to 6 years of age with a fresh diagnosis of asthma at discharge, were prospectively collected according to criteria defined earlier in the Department of Paediatrics, Kuopio University Hospital, Kuopio, Finland, from October 1996 to May 2000. The children treated as inpatients ($N=64$) or outpatients ($N=58$) because of wheezing that relieved after receiving beta-agonist were eligible to the study. In addition, the children had to have had at least one previous doctor-diagnosed wheezing during the preceding 12 months; no prior (>12 months) wheezing attacks were allowed. For example, all children who had ever had a previous diagnosis of asthma or regular medication for asthma were excluded. The study is part of a large survey investigating the influence of environmental factors on the development of asthma.

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Table 1 Classification by the severity and area of moisture damages of the 114 homes

Category	Definition	Number (%; <i>n</i> =114)
C1	No damage	12 (10)
C2	Minor damage with no need for repair	10 (9)
C3	Replacement of surface covering; Drying, reglueing or repainting needed	57 (50)
C4	Opening, drying or renewing of structure needed	33 (29)
C5	Extensive damage with a need for functional elemental repair	2 (2)

Adopted from Nevalainen *et al.*²¹

Therefore, the children recruited had to have lived at least 2 years or 75% of their lifetime at their current home. The number of children fulfilling these criteria was 122, and they were recruited in the study. In total, 94% (*n*=115) of them attended.

Trained civil engineers surveyed the homes of the recruited children for the number, extent and severity of moisture damage using a structured protocol including visual observations and measurements with surface moisture recorders.²¹ The severity of the moisture damage was classified on the basis of need for repair into five categories. Category (C)1 means no damage, C2 means minor damages with no need for repair (e.g. discoloration of surface material due to current or earlier moisture), C3 means a need for repair of surfaces (e.g. detaching of floor or wall tiles), and C4 means a need for repair of structures (e.g. opening or dismantling of a floor or a wall). C5 means extensive damage with a need for large repairs, such as both wall and ceiling or floor structures. The criteria for the classification are based on both building-technical aspects of moisture damage and observations of mold growth, including rotting of wooden parts. The classification has been validated in earlier studies, where also a link between the extent of damage and health effects has been observed.^{22,23}

Skin prick test (SPT) results were available for 115 (94%) children. The parents of the subjects were advised to discontinue antihistamines for at least 5 days prior to the tests. The tests were performed on the volar aspect of the forearm by a qualified nurse, using the ALK (Allergologisk Laboratorium, Copenhagen, Denmark) panel of seven allergens. The panel included the seasonal allergens of birch, timothy and mugwort pollens, the animal allergens of cat and dog epithelial danders, and two HDM, *Dermatofagoides farinae* and *D. pteronyssinus*. The molds were tested by using 10 allergens: *Alternaria alternata*, *Aspergillus fumigatus*, *Aureobasidium pullulans*, *Botrytis cinerea*, *Cladosporium herbarum*, *Mucor racemosus*, *Mucor spinosus*, *Penicillium brevicompactum*, *Phoma herbarum* and *Rhodotorula species*.^{10–12} Three of these molds,

Aspergillus fumigatus, *Phoma herbarum*, and *Rhodotorula species*, are considered as indicative of a moisture problem in the building.²⁴ Histamine hydrochloride (10 mg/mL) and glycerol (50%) were used as positive and negative controls, respectively. The reactions were measured 15 min after testing, and reactions of ≥ 3 mm (the longest diameter) were regarded as positive. One child with a >3 mm reaction to the negative control was excluded.

In the statistical analysis of the data, χ^2 and Fisher's exact tests were used.

The protocol of the study was accepted by the Ethics Committees of Kuopio University Hospital and of the National Public Health Institute, Finland. A written consent was obtained from the parents of the children.

Results

In total, 92 (81%) of the 114 houses surveyed had observations of moisture that needed at least repair of surfaces; 31% of the 92 damaged houses needed structural repairs. Extensive damage was found only in two cases. The distribution of the damage categories are presented in Table 1.

One-third of the children reacted to either animal danders (29%) or seasonal pollens (21%) in SPT (Table 2). Dog dander, birch pollen and cat dander were the most common allergens. The reactions to animal danders were equally common at all ages, but reactions to seasonal pollens increased in relation to age ($P<0.05$).

There were 11 positive (≥ 3 mm) SPT responses to at least one mold in five children. The most common responsive molds were *Botrytis cinerea* with three reactions, *Aspergillus fumigatus* as well with three, and *Cladosporium herbarum* with two positive reactions. Weak (1–2 mm) responses were also recorded (Table 3).

The five children, aged from 3 to 6 years, with positive responses to molds are presented in Table 4. They all reacted to at least one animal dander or to one seasonal pollen. In contrast, none of them reacted to HDM. There were only two children who had positive reactions to HDM, neither of them reacted to molds (Table 4). The five children with positive reactions to molds all lived in moisture damaged houses with need of repairs. The respective figure was 78% for the children with no reactions to molds ($P=0.31$).

Discussion

There are three main results in the present study. First, mold allergy was rare ($<5\%$) among 1–6-year-old children with newly-diagnosed asthma, and had no association with moisture problems at home. This figure is in agreement with our previous findings, based on SPT reactions^{10–12} and/or on positive

Table 2 Skin prick test results to common animal danders and seasonal pollens among 115 children with results available

Allergens	All (n = 115)	1–2 years (n = 76)	3–4 years (n = 19)	5–7 years (n = 20)
Animal danders	33 (29%)	21 (28%)	5 (26%)	7 (35%)
Dog	26	18	4	4
Cat	20	11	2	7
Seasonal pollens	24 (21%)	8 (11%)	6 (32%)	10 (50%)
Birch	20	7	5	8
Timothy	13	2	3	8
Mugwort	1	1	0	0
Danders and pollens	17 (15%)	6 (8%)	4 (21%)	7 (35%)
Danders or pollens	40 (35%)	23 (30%)	7 (37%)	10 (50%)

Table 3 Skin prick test responses to molds

Mold	Positive (≥3 mm; n = 11)	Weak (1–2 mm; n = 14)	Total (n = 25)
<i>Alternaria alternata</i>	1	1	2
<i>Aspergillus fumigatus</i>	3	2	5
<i>Aureobasidium pullulans</i>	0	1	1
<i>Botrytis cinerea</i>	3	4	7
<i>Cladosporium herbarum</i>	2	3	5
<i>Mucor racemosus</i>	1	3	4
<i>Penicillium brevicompactum</i>	1	0	1

mold-specific IgE²⁵ in school children. Second, HDM allergy was also rare, being present in only 1–2% of the children. This low figure is in line with studies in children from Nordic countries^{15–18} but contrary to the reports from warm climates.^{5,20} Third, in disagreement with previous studies, no association was found between allergy to molds and to HDM.⁵

The rarity of mold allergy in children, including children with asthma and allergic diseases, has been observed in many previous studies.^{9–15} When assessed by SPT, 9–16% of children with asthma have been reported to be allergic to molds, most commonly to *Aspergillus*, *Alternaria*, *Penicillium* and *Cladosporium* species.^{5,9,15,20} Mold-specific IgE has been measured in 5–35% of children with asthma and/or atopy.^{9,26} In the present study, *Aspergillus fumigatus*, *Botrytis cinerea* and *Cladosporium herbarum* were the three most common positive molds.^{21,27}

Mold allergy seems to become more common in relation to age, being most common at the age of 7 to 10 years.²⁸ In contrast, Tariq *et al.* found *Alternaria* and *Cladosporium* as important allergens even in young children.²⁹ In accordance, allergies to *Alternaria alternata*²⁰ and *Cladosporium herbarum*, when present, were strong risk factors for asthma in children.^{26,30} In the present study, no association was found between skin reactivity to molds and newly-diagnosed asthma in pre-school age, though a third of the cases reacted to common animal danders or to seasonal pollens. Moreover, the test

Table 4 Data on moisture damage at home and skin prick test reactions to common allergens among children with allergy to molds or home dust mites

Patient	Age/gender	Category of moisture damage at home	Skin prick test responses			
			Danders	Pollens	Mites	Molds
055162	3 years/girl	3	Dog	Birch	Negative	<i>Alternaria alternata</i> , <i>Aureobasidium pullulans</i> , <i>Botrytis cinerea</i>
067198	4 years/boy	3	Cat	Timothy	Negative	<i>Botrytis cinerea</i>
089264	6 years/boy	4	Cat	Birch, Timothy	Negative	<i>Aspergillus fumigatus</i>
103306	5 years/girl	3	Cat, Dog	Birch, Timothy	Negative	<i>Aspergillus fumigatus</i> , <i>Penicillium brevicompactum</i>
118351	5 years/boy	4	Cat	Timothy	Negative	<i>Aspergillus fumigatus</i>
048141	5 years/boy	4	Negative	Negative	<i>D. farinae</i> , <i>D. pteronyssinus</i>	Negative
082243	1 year/girl	1	Cat, Dog	Negative	<i>D. farinae</i> , <i>D. pteronyssinus</i>	Negative

In addition, there were two children with weak (1–2 mm) responses to mites; they reacted to both *D. farinae* and to *D. Pteronyssinus*, to at least one animal dander and to at least one seasonal pollen, but not to molds.

panel covered as many as 10 molds. In contrast, the high proportion of SPT negatives is in line with the age distribution of the patients (2/3 were less than 3 years old), and suggest that at least part of them actually have non-permanent asthma with later improvement.

The low incidence of HDM allergy has been observed also in previous studies in Nordic countries, where winter is long and cold.^{15,16,31} Because of the climate, the houses are well insulated and provided with central heating. The heating season lasts up to 8–9 months a year, resulting in very low indoor humidity, and, therefore, unfavourable conditions for HDM proliferation. In the present study, the positive SPT reactions to HDM allergens were rare, though many children selected to the study had positive reactions to common inhalant allergens, and the test panel included two mites, *D. farinae* and *D. pteronyssinus*. There is preliminary evidence that reactions to storage mites, which our panel did not include, may be even more common than reactions to HDM, at least in adults.³² The absence of any association between SPT responses to molds and to HDM is in disagreement with previous studies in warm countries.⁵

The main shortcoming of the present study is that SPT were not performed for the controls with no asthma or asthma presumptive symptoms. Frozen serum samples were available in 102/122 cases and in 104/244 controls matched by age, gender and place of residence.³³ In these samples, IgE antibodies to the mold *C. herbarum* were determined by the fluoroenzyme-immunometric assay, UniCAP (Phadiatop combi, Pharmacia, Uppsala, Sweden), with the detection limit of 0.35 kU/L.³⁴ By this limit, the test was positive to *C. herbarum* in 4% of the cases and in 2% of the controls. IgE concentrations were low, ≤ 0.80 kU/L, in all positive assays. The result was negative in the five children with SPT responses to molds. In contrast, none of them reacted specifically to *C. herbarum*. Therefore, the children with new asthma did not differ from controls in relation to IgE specific to *C. herbarum*, and by both approaches, sensitization to molds was rare.

Currently, only non-standardized extracts of mold allergens are available for SPT and IgE assays. In addition, the commercially available test panels, though consisting of 10 extracts in the SPT of the present study, cover only a minority of molds faced in water-damaged buildings, or of the molds to which the children are normally exposed.²⁷ Moreover, no history targeting the symptoms induced by molds or by mites was obtained. Though over 100 children with asthma were tested by SPT to 10 molds, and these cases and over 100 controls were assayed for *C. herbarum* mold-specific IgE, the numbers of children with positive responses to molds or to HDM were too small for any definite statistical analyses.

We conclude that sensitization to molds seems to play only a minor role in under school-aged children with newly-diagnosed asthma in northern climate where the incidences of mold and HDM allergies are rather low. The result was

negative even though a substantial number of the children had positive SPT reactions to common inhalant allergens and had lived a long time in houses with significant moisture problems.

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