

Immunoglobulin G antibodies of children exposed to microorganisms in a water-damaged school

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The aim of this study was to determine whether exposure to fungi (molds and yeasts) among children attending a water-damaged school was reflected by the children's immunoglobulin G (IgG) response to microorganisms typical of water damage and whether the presence of these IgG antibodies was associated with respiratory symptoms and morbidity. The relationships between positive IgG antibodies and atopy, described as elevated allergen-specific immunoglobulin E (IgE) antibodies, were also examined. The study population consisted of a randomly selected group of exposed children attending a water-damaged school and a group of unexposed children of the same age. Serum samples for analyses of IgG and IgE antibodies were drawn from the children. The respiratory morbidity, the number of positive IgG antibodies to nine microorganisms indicating water damage, and IgE sensitization to common environmental allergens (Phadiatop®) were studied. The mean number of positive IgG findings was significantly higher among the exposed children. The number of positive IgG antibodies did not correlate with respiratory illnesses or symptoms at the individual level even though the exposed children who had positive IgG antibodies to four or more microorganisms in the total group comparison tended to have higher respiratory morbidity. In the exposed group, a negative correlation was found between the number of positive IgG antibodies and the total value of allergen-specific IgE antibodies. As among adults exposed to microorganisms at work, IgG antibodies in children seem to be a relevant indicator of exposure to microorganisms in a water-damaged school on the group level.

**Risto Savilahti¹, Jukka Uitti²,
Pekka Laippala³, Tuula Husman⁴ and
Marjut Reiman⁵**

¹Lahti Health Center, City of Lahti, ²Tampere Regional Institute of Occupational Health, Clinic of Occupational Medicine (University Hospital), ³Tampere School of Public Health, University of Tampere, and Tampere, University Hospital, Tampere, ⁴National Public Health Institute, and ⁵Kuopio Regional Institute of Occupational Health, Kuopio, Finland

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Risto Savilahti, MD, City of Lahti, PL 116, 15101 Lahti, Finland
Tel.: +358 38102001
Fax: +358 50 5597851
E-mail: Risto.Savilahti@Lahti.fi

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Moisture damage in buildings is a potential source of microbial exposure among residents. Studies have shown an increased prevalence of respiratory symptoms and infections among children living in damp houses (1–3) and among children (4) exposed to molds in day-care centers or schools (5). Asthma and wheezing are more common among children with household water damage (6). Atopy and allergic diseases have been shown to increase among children exposed to microorganisms in a water-damaged school (7, 8). Sensitization to molds was rare among children attending a water-damaged school (9).

Children seem to be more susceptible to indoor air contaminants than adults (3).

Exposure to high concentrations of microorganisms has been found to be associated with allergic alveolitis in the work environment. Elevated counts of immunoglobulin G (IgG) antibodies have been found in exposed workers with alveolitis and also in healthy exposed workers. Thus these antibodies are considered to reflect exposure to microorganisms even without an association with related diseases (10). To our knowledge no studies of IgG antibody response have been carried out among children exposed to

microorganisms typical to water damage especially in a school environment.

The aim of this study was to determine whether exposure to microorganisms among children attending a water-damaged school was reflected by an IgG response to indicator microorganisms typical of water damage, and whether the presence of these antibodies was associated with respiratory symptoms and morbidity. Using this group of exposed children, we also examined the relationships between positive IgG antibodies and specific immunoglobulin E (IgE) antibodies to common environmental allergens.

Subjects and methods

Subjects

The personnel of a Finnish elementary school with visible water damage and mold complained of repeated respiratory and skin symptoms in 1994–95 (5). In the spring of 1995, a technical investigation of the building constructions including microbiological samples of the air (Andersen 6-stage impactor), surfaces and materials of the building revealed marked and widespread moisture damage on all three floors, the most serious damage being found on the ground floor (5). Several species of microorganisms indicating moisture damage were identified from the samples of the index school. There was visible mold growth in a class that was situated closest to the most serious moisture damage on the ground floor. Samples revealed extensive mold growth including *Penicillium*, *Aureobaculum*, *Cladosporium*, *Geotrichum*, *Aspergillus* and also mycotoxin-producing fungi (e.g. *Stachybotrys atra*).

We therefore decided to study the respiratory morbidity of the children attending the school.

The study population consisted of children between the ages of 7 and 12 years in the index school and a group of unexposed children of the same age in a control school. The investigations of the control school showed neither moisture damage nor any indication of exceptional microbial growth.

Members of the study groups were randomly (fixed random sample) selected for blood sampling (7). The blood samples were drawn from 69 of the 365 children in the exposed group and 49 of the 176 children in the unexposed group. The groups were comparable with regard to age, passive smoking, previous allergic diseases, and ownership of pets. There was no indication of selection with regard to allergic heredity in either group (5).

Methods

A questionnaire on respiratory morbidity was sent to all the parents of children attending the water-damaged school and the control school in September of 1995 (5,7). The data collected concerned the 1994–95 semester. In all, 92% of both the exposed and unexposed groups responded.

IgE antibodies to a mixture of 10 common environmental allergens (birch, timothy, mugwort, horse, cat, dog, *Dermatophagoides pteronyssinus*, *Cladosporium herbarum*, olive tree and *Paretaia judaica*) were determined with a multi-RAST screening test, the Phadiatop RAST® (Pharmacia & Upjohn Diagnostics, Uppsala, Sweden) (11). The IgE value in this paper refers to the Phadiatop® value. Values < 0.4 kU/l are normal. For this study, the elevated total values of allergen-specific IgE antibodies were graded as moderately elevated (0.4–17.5 kU/l) and markedly elevated (> 17.5 kU/l).

Table 1. Frequency of positive IgG findings (%) for moisture-indicating microorganisms in the index school and the control school

Microorganisms	Index school		Control school		OR (95% CI) index/control
	%	n total = 69	%	n total = 49	
<i>Phialophora bubakii</i>	70.9	49	53.1	26	2.17 (1.01–4.66)*
<i>Stachybotrys atra</i>	42	29	32.7	16	1.50 (0.70–3.21)
<i>Cladosporium cladosporioides</i>	31.9	22	12.2	6	3.35 (1.24–9.05)*
<i>Sporobolomyces salmonicolor</i>	28.9	20	12.2	6	2.93 (1.08–7.95)*
<i>Aspergillus fumigatus</i>	26.1	18	20.4	10	1.38 (0.57–3.31)
<i>Rhodotorula glutinis</i>	11.6	8	6.1	3	2.01 (0.51–8.00)
<i>Penicillium brevicompactum</i>	7.2	5	2.0	1	3.75 (0.42–33.2)
<i>Geotrichum candidum</i>	5.8	4	12.2	6	0.44 (0.12–1.66)
<i>Cephalosporium curtipiles</i>	5.8	4	6.1	3	0.94 (0.20–4.42)

*Significant at CI 95%.

n = number of children.

IgG antibodies to nine fungi (molds and yeasts) most commonly indicating water damage were analyzed by enzyme-linked immunosorbent assay (ELISA) (Table 1). The laboratory results of IgG antibodies of each microbe were given as negative (-), slightly elevated (+), moderately elevated (++) or markedly elevated (+++) in comparison with the value given by the pooled positive reference serum. In our study for the purpose of defining the recent exposure, an IgG antibody result was considered positive if it was either moderately or markedly elevated.

A physician (RS) studied the medical records of the local health center for all the children who answered the questionnaire. The visits to a physician because of respiratory diseases and the number of courses of antibiotics for these diseases were recorded (5).

The statistical analysis was based on odds ratios (OR) and means supported by 95% confidence intervals (CI) (12).

Results

IgG antibodies indicating exposure to water damage among the exposed and unexposed children

The distribution and odds ratios of the positive IgG antibody counts are shown in Table 1. In the index school, 11 children had no positive findings for the tested microbes (16%) and the corresponding number was 13 (27%) for the control school. Of the nine microorganisms tested, the average number of positive IgG antibodies per student was significantly higher for the index school (OR 2.30; 95% CI 1.90–2.71) than for the control school (OR 1.57; CI 1.27–1.89). IgG antibodies to four or more microbes were found in 16 (23%) children from the index school and in 3 (6%) children from the control school.

Respiratory symptoms and infections among the exposed children

According to the questionnaire, there were no significant (95% CI) correlations between the number of positive IgG findings and respiratory illnesses and symptoms, visits to a physician and use of antibiotics, although the prevalence of prolonged infections tended to be higher among the children who had four or more positive IgG antibodies and the average number of physician visits and use of antibiotics were more than double among these children.

There were no significant differences in respiratory infections, number of physician visits and use of antibiotics between children who had

normal IgE values compared with children with elevated IgE values.

Correlation between the number of positive findings of tested IgG antibodies and the total values of allergen-specific IgE antibodies among the exposed children

There was a negative correlation between the positive IgG findings and the total values of the allergen-specific IgE antibodies among the exposed children. The mean IgE value of the children who had four or more positive IgG antibodies ($n = 16$) was 2.5 kU/l (CI 0–5.7), for those who had 0–3 positive IgG antibodies ($n = 53$) the mean value was 16.8 kU/l (CI 7.1–26.5). The correlation between total values of allergen-specific IgE antibodies and the number of positive IgG antibodies was -0.21 (Spearman's rank correlation, Fig. 1).

Fourteen of the children who reported an allergy in the questionnaire belonged to the randomized group. The mean IgE value of these children was 29.0, and the mean number of positive IgG findings was 1.42. For the 55 children in the randomized group who did not report allergic diseases, the mean IgE value was 9.54, and mean number of positive IgG findings was 2.53 (significant at CI 85%). Of those children ($n = 16$) who had four or more positive IgG antibodies, one reported an allergic disease and his IgE value was normal.

Discussion

In adult populations, IgG antibodies are often used at the group level as an indicator of exposure to molds and other microorganisms in the work environment. Microbial growth in

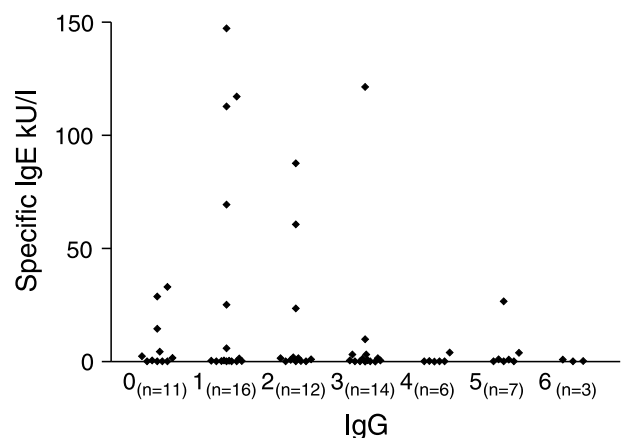


Fig. 1. The correlation between total values of allergen-specific IgE antibodies and the number of positive IgG antibodies.

an indoor environment is a dynamic process depending on environmental conditions, such as humidity, temperature and availability of nutrients, so the main species vary and differ over time. IgG antibodies reflect a longer period of exposure (months or years) and do not necessarily represent microbial species recognized from 'cross-sectionally' taken samples. The earlier findings have shown that IgG antibodies to microorganisms reflect higher exposure at the group level in an adult population (10). The IgG panel selected in our study is based on current international (13) and national knowledge and this panel covered the most frequently appearing molds in Finnish buildings with moisture damages (14). In our opinion these IgG antibodies reflect the exposure to moisture damage at group level, as our results showed.

In our earlier study, reported respiratory symptoms and illnesses, ambulatory visits to a physician and the use of antibiotics were more common among exposed children (5). These findings agree with the results of studies concerning the health effects of water damage in residences (1–3). Although statistical significance was not reached in our current study, morbidity tended to be higher among the exposed children who had four or more positive IgG antibodies. Our study indicates that the number of positive IgG antibodies is associated with higher morbidity at the group level. On an individual basis the correlation was weak. For example, a child of the exposed group who had six positive IgG antibodies had had no respiratory illnesses and a child with no IgG antibodies reported 13 respiratory illnesses.

The children with an active IgG antibody response in the exposed group had fewer IgE antibodies to common environmental allergens than the children with less active IgG production. The difference was more obvious among those who had reported an allergic disease. Because of our cross-sectional study design, we were not able to carry out additional analyses of the causal differences between IgE and IgG production among the exposed children. Nor was the comparison among the unexposed children reliable because of small number of elevated IgE values of the group. However, our study indicates that atopy does not actively produce IgG antibodies to microorganisms typical of water-damage despite exposure similar to that of non-atopics (children with normal IgE values). According to this study, children with active IgG antibody production to microorganisms tended to be more rarely sensitized to common environmental allergens. These results agree with

new theories of indicating that infections and active IgG production protect from allergy-associated IgE sensitization (15). However, according to the results of our earlier study, allergic sensitization and allergic diseases seem to increase among children exposed to microorganisms in a water-damaged school (7). Thus it seems likely that the individual susceptibility and immune response of exposed subjects is influenced by several, even controversial and unknown factors associated with microbiological exposure in a water-damaged building. The interrelationships between the IgE response, atopy and IgG antibodies to microorganisms should be evaluated further in prospective studies.

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