RISTO SAVILAHTI

Water Damage in an Elementary School Respiratory Symptoms and Atopy among Children

One year follow-up after the renovation

■

ACADEMIC DISSERTATION
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ACADEMIC DISSERTATION
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Abstract

In this study the health effects of moisture and micro-organisms among children attending a water-damaged school (School E) were studied comparing symptoms and diseases with schoolchildren attending a school with no water-damage (School C). A follow-up questionnaire study was made at the end of the next semester. The renovation was done during the previous summer. To validate the information of questionnaire comparison with children's patients record child by child was examined.

Water damage was discovered in a school building for primary school children in early 90-ties. The staff of the school had an excess of sickness absences and visits to a physician because of respiratory infections and symptoms. The first signs of water damage and mould were found in 1993. The visible damage was repaired in the next year. In May 1995, a technical investigation of constructions revealed wide spread moisture damage in the school building.

Altogether 397 children at the age of 7-12 year attended the water-damaged school, 92% (n=365) out of them took part in the first part of this study. The longest time of exposure was 6 years among the children in the 6th grade an one year among children who finished the first grade in may 1995. The control group of this cross sectional study included 175 schoolchildren (92%) at the same age attending a school (School C) in the same suburban district. The control school was examined for this study and no water damage was found. The renovation of the damaged school was ready at the beginning of November 1995. During the renovation procedures, the area of construction was well isolated. A questionnaire was sent to the parents of the schoolchildren concerning children's health outcomes during the school year 1994-1995. The main emphasis was on respiratory symptoms and diseases. In addition, atopic diseases and the time of diagnoses were inquired. A one-year follow up study was carried out among these children from both schools. The second questionnaire for the follow-up was sent to parents in fall 1996 concerning spring semester 1996. Because of a wide spread of inflammatory diseases in autumn all around Finland, we did not include fall semester 1995 to the second questionnaire. All medical records of the children from both schools who took part of this study were examined on respiratory infections, atopy and use of antibiotics. The blood samples were drawn from randomly selected children from both schools (study groups). IgE antibodies to a mixture of 10 common environmental allergens were determined with a multi-RAST® screening test, the Phadiatop RAST®. IgG antibodies to nine microorganisms most commonly indicating water damage were analyzed by enzyme-linked immunosorbent assay (ELISA). In a cross-sectional study the incidence of common cold, respiratory symptoms and visits to a physician were significantly higher among children attending the water-damaged school. Although the incidence of respiratory infections tended to be higher also in school year 1995-1996, after the renovation of the school building, no significant differences remained, except for the visits to a physician according to the questionnaire. The elevated IgE values among the study group indicated a possible relationship between exposure and

sensitization to common environmental allergens, including micro-organisms. The occurrences of new allergic diseases after the children started the school were commoner among the exposed children, especially among those with heaviest exposure. 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. In order to validate the given information of parents about their children's health in two consecutive years, patient's records in a local health center were studied for comparison. Because over-reporting and under-reporting were about at the same level, the total number of ambulatory visits in the patients' records and questionnaires seemed to indicate good reliability. More detailed individual investigation showed poor recall validity from the questionnaires, including a high percentage of unreported visits to the local health center from both schools. Use of antibiotics had a better recall than ambulatory visits to a physician. The study indicates that information on health services in questionnaires is not reliable, at least when occurrences in a period of one year or more are evaluated. The use of patients' records of the health center as a reference of accuracy is also unreliable, if the records of all health services available to the people in the community are not covered. In conclusion, respiratory symptoms and diseases and an increased risk to allergic diseases were found among children exposed to moulds in a school building. Remediation of the building had a substantial effect to children's respiratory health. Especially concerning atopy the long-term effects of those who had been exposed to micro-organisms for many years need more follow-up studies. According to our study IgG antibodies at the group level seem to be markers of exposure also among children.

Tiivistelmä
(Abstract in finnish)

Ylöjärven keskustan koulussa esiintyneiden kosteusvaurioiden vaikutus oppilaiden terveyteen

Ylöjärven keskustan ala-asteen koulussa havaittiin laajalle levinnyt kosteusvauria. Henkilöstöllä oli runsaasti poissaoloja ja lääkärissä käyntejä. Rakennuksen ensimmäiset kosteusvauriot havaittiin vuonna 1993. Toukokuussa 1995 tehtiin rakennuksen tekninen tutkimus, jossa havaittiin laajoilla alueilla kosteusvaurioita. Käytiin keskustelut työterveyslaitoksen asiantuntijoiden kanssa, sekä päätettiin selvittää henkilöstön lisäksi myös oppilaiden terveydentilaa.

Tutkittavassa koulussa oli 397 lasta ikäryhmissä 7-12 vuotta. Vanhemmat ilmoittivat yhteensä 365 (92%) lasta tutkimukseen. Vertailuryhmänä olivat Metsäkylän ala-asteen oppilaat, joista tutkimukseen osallistui 175 (92%) lasta. Vertailuryhmän koulussa tehtiin laaja tekninen tarkastus, jossa ei löydetty kosteusvaurioita. Lasten vanhemmille lähetettiin kyselylomake joka koski sairauksia vuosina 1994-1995. Kiinnostuksen kohteena olivat hengityselin oireet ja sairaudet, sekä atopiset sairaudet ja niiden alkamisvuodet. Koulussa tehtiin mittavat tutkimukset ja korjaukset niin, että kosteusvaurioita ei ollut enää havaittavissa loppusyksyllä 1995. Koska korjaukset eivät olleet vielä valmiina lukukauden alkaessa ja lisäksi syksyllä 1995 oli koko maassa laajalle levinnyt hengityselin-sairauksien aalto, tämän lukuvuoden osalta vertailut tehtiin kevätlukukauden 1996 tietojen osalta. Molempien koulujen lapsista otettiin otannan perusteella verinäyte IgE ja IgG vasta-aineiden tutkimiseksi. IgE vasta-aineet kymmenelle tavallisimmalle ympäristössä esiintyvälle allergeenille ja IgG vasta-aineet yhdeksälle yleisimmälle kosteusvauriossa esiintyvistä mikro-organismista tutkittiin.

Tutkimukseen osallistuneiden lasten potilaskertomustiedot olivat käytettävissä vanhempien luvalla. Poikkileikkaustutkimuksen perusteella flunssa, hengityselinsairaudet ja lääkärikäynnit olivat merkittävästi vertailuryhmää yleisempiä tutkittavassa ryhmässä . Ainoana merkittävänä erona olivat lasten runsaammat lääkärikäynnit tutkittavan koulun osalta. Lisäksi uusien allergisten sairauksien ilmaantuminen koulunkäynnin aloittamisen jälkeen oli yleisempää tutkittavassa koulussa kuin vertailuryhmässä, erityisesti niillä lapsilla, joiden luokkahuoneessa oli runsaimmat kosteusvauriot. Altistuneiden ryhmässä IgG vasta-aineiden ja allergiaa ilmaisevien IgE vasta-aineiden välillä oli käänteinen korrelaatio. Vanhemmille lähetettiin kahtena peräkkäisenä vuotena kyselylomake koskien lasten hengityselinsairauksia. Koska vastauksissa oli lähes yhtä paljon ylimääräisiä lääkärikäyntejä ja liian vähän raportoituja käyntejä terveyskeskuksessa, kokonaisuus näytti hyvältä. Kun kyselylomakkeita verrattiin lapsi lapselta, vastaukset olivat usein poikkeavia terveyskeskuksen käyntitietoihin nähden. Koulun perusteellinen korjaus vaikutti huomattavasti tutkittavien koululasten terveydentilan paranemiseen.

Contents

Abbrevations

CI	confidence interval
ELISA	enzyme-linked immunosorbent assay
IgE	immunoglobulin E
IgG	immunoglobulin G
RAST	radioallerosorbent-test
SPT	skin prick test
School C	Control school
School E	Index school
Class X	Class in School E, most water damaged class
TVOC	Total Volatile Organic Combaunds
Q1	First questionnaire
Q2	Second questionnaire

List of original publications

I Savilahti R, Uitti J, Laippala P, Husman T, Roto P.
Respiratory morbidity among children following renovation of a water-damaged school. Arch Environ Health. 2000 Nov-Dec;55(6):405-10.

II Savilahti R, Uitti J, Roto P, Laippala P, Husman T.
Increased prevalence of atopy among children exposed to mold in a school building. Allergy. 2001 Feb;56(2):175-9.

III Savilahti R, Uitti J, Laippala P, Husman T, Reiman M.
Immunoglobulin G antibodies of children exposed to microorganisms in a water-damaged school. Pediatr Allergy Immunol. 2002 Dec;13(6):438-42.

IV Savilahti R, Uitti J, Husman T.
Validity and recall of information from questionnaires concerning respiratory infections among schoolchildren. Cent Eur J Public Health. 2005 Jun;13(2):74-7.

1. Introduction

Changing the air in Scandinavian buildings has been commonly accomplished by natural ventilation. Many factors have made for raised humidity inside houses, workplaces and public buildings in the past few decades At least two major changes have emphasized the important role of the indoor environment in the development of allergic diseases. Firstly due to the rise in energy prices in 1980es, insulation of buildings was increased and ventilation reduced. This lead to diminished air change and accordingly raised humidity inside buildings and this may well have created better living conditions for indoor moulds and fungi (Engvall et al. 2003 and Engvall et al. 2005, Koskinen et al.1999). Secondly, most people, including children, spend more time indoors than earlier. Most indoor time is spent at home and the rest at work or, for children, at school and daycare centers (Leickly 2003). In a study of Nevalainen et al.1998, 450 houses representing various decades were surveyed. In 80% of them, signs of current or previous moisture fault were observed; 55% were in need of repair or more thorough inspection.

During the last 20 years, many studies have paid attention to indoor conditions in homes. When all confounding factors concerning the indoor environment are taken into account, one of the main factors related to respiratory symptoms and diseases seems to be moisture damage in the buildings (Bornehag et al. 2004b, Bornehag et al. 2005). Many offices and public buildings have been found to have water damage, among them school buildings, although in many studies, while dampness is related to symptoms, it does not seem to be the only cause of sick building syndrome (Crawford et al. 1996). In various countries there are substantial differences in the occurrence of dampness in houses, mostly depending on outdoor climate. Nevertheless, there are so many reports on the association relationship between dampness and respiratory symptoms that the relationship seems to be established (Andriessen et al. 1998, Kilpeläinen et al. 2001, Park et al. 2001). In one review, including 113 of 590 articles on dampness in buildings and health were studied (Bornehag et al. 2001). According to this study the evidence or an association between dampness and health effects is strong. Recent studies (Park et al. 2006 and Park et al. 2008) have shown an association between ergosterol and endotoxins and respiratory symptoms and asthma among adults working in water-damaged buildings.

This present study is based on a pragmatic case of moisture damage problems in a school building requiring actions on the part of the local authorities. The staff of an elementary school in a suburban area in Finland complained of respiratory and skin symptoms in 1994-95 and contacted their occupational health physician. The school building had been built in the 1950s. The first signs of water damage were found in 1993 and visible water and mould damage was repaired in1994. In May 1995, a technical investigation of the structure was undertaken and a widespread dampness was observed. Microbes indicating water damage were found in many places. Many teachers and other members of the staff were examined in the Tampere Regional Institute of Occupational Health. Because it turned out that also children experienced problems with their health, a thorough study was initiated in the fall of 1995.

A meeting with representatives from the municipal administration, local health center and center of the regional institute of occupational health was held as soon as the results of the investigation were received. The decision to renovate the building immediately during the summer vacation was made. Two meetings with the parents of the exposed children were organized and the parents accepted the study.

2. Review of the literature

2.1 Moisture damage, mould and other biological contaminants

2.1.1 Occurrence of water damage and visible mould in buildings

In most studies concerning the home environment and children's health, information on exposure is based on questionnaire studies, observations of dampness and moisture damage being subjectively evaluated (Table 1). In Finland moisture problems have been reported with increasing frequency in both family housing (Koskinen et al.1999, Nevalainen et al.1998) and workplaces (Reijula 1996, Reijula et al. 2004), including schools (Haverinen et al.1999, Immonen 2001, Patovirta et al. 2004, Taskinen 1997). Indoor air quality depends on many factors e.g. climate. In northern Europe, where winters are cold, sufficient heating and ventilation are indispendable for 6-8 months in the year and the occurrence of certain moulds in the structures of buildings is less common in winter than in summer (Pirhonen et al. 1996) by reason of dry conditions. If ventilation is insufficient, dampness may increase during the wintertime (Koskinen et al. 1999). On the other hand, people living in subtropical or tropical areas where no heating is necessary, dampness and moisture damage depend mostly on air humidity when air conditioning is not available (Li et al.1996, Yang et al.1997). Seasonal differences in respect of humidity are considerable and the prevalence of symptoms and diseases vary accordingly (Chen et al. 1998, Institute of Medicine of the National Academies 2004).

At least four major categories of causes of dampness of buildings may be identified: Outdoor sources (leakage or moisture from the ground); Indoor sources (bathing, humidifiers etc); building sources (moisture in building materials and constructions) and accidents (leakage from pipes, flooding etc) (Bornehag et al. 2001, Institute of Medicine of the National Academies 2004). The age of houses, construction faults and deficits and insufficient ventilation and condensation have their effects on the frequency of water damage (Nevalainen et al 1998).

Table 1. The prevalence of water damage in homes and studies concerning the health of children and adults

Study	Year	Studygroup / Households	Child / Adult	Questionnaire = +	Occurren. of visible mold (%)	Other signs of water-dam %	Comments
Martin C et al. England	1987	/358	Children	Surveyors	17	7	
Brunekreef B et al Netherlands	1989	4625/	8-12	+	20,9-38,1	47,5-58,2	
Platt SD et al England	1989	/597		Surveyors	45,9	23,3	
Waegemakers M Netherlands	1989	/185		+	41,6		
Dijkstra L et al Netherlands	1990	1051/876	6-12	+	9,1	14,8	
Dales RE et al Neatherland	1992	14779/14779	Adults	+	32,4	14,1	
Brunekreef B et al Canada	1991b	3334/3334	Adults	+	15,0	23,6	
Verhoeff AP et al Netherlands	1992	516/496	6-12	Investigaters	53	71 /45	Reported/ Found
Pirhonen I et al Finland	1996	1460/1460	Adults	+	3,7	22,2	
Chih Shan Li et al Taiwan	1996	/1340	8-12	+	38,3	47,8	
Chun-Yuh Yang et al. Taiwan	1997	/4164	6-12	+	30,1	43,4	
Koskinen OM et al Finland	1999	/310	--	Surveyors	27	52	
Evans J et al England	2000	/8889	18-64	+	1,2	9,1	
Chelelgo et al Finland	2001	/630		Surveyors	33	51	
Bornehag CG et al Sweden	2005a	10851/8918	1-6	+	1,5	17,8	

2.1.2 Micro-organisms and other pollutants in moisture-damaged buildings

Exposure to microorganisms has many adverse health effects. Moisture damage in constructions leads to microbial growth, and some common fungi are regarded as moisture indicative microbes. These microbes have allergenic, inflammatory and toxic properties. Among the indoor fungi Penicillinium and Aspergillus are the most important allergenic species (Verhoeff et al.1994a) and b) Outdoor moulds, for example Cladosporium and Alternaria can often be found in high levels also indoors (Hardin et al. 2003, O'Connor et al. 2004). In addition to moulds, many other outdoor allergens may be found in the indoor environment, for example pollens. Among the various kinds of biological particulate matter suspended in the atmosphere, mould spores constitute the largest population, in both indoor and outdoor environments in the summer (D'Amato et al. 1995).

A number of thorough studies have recently been published concentrating on dampness, exposure to moulds and health effects related to mould exposure and moisture indoors (Institute of Medicine of the National Academies 2004). Exposure to damp housing and indoor air pollutants has many adverse health effects, including the development of childhood asthma (Bornehag et al. 2005a, Kim et al. 2007, Stark et al. 2003). Exposure to outdoor air pollutants may have the same effects (Etzel 2003), although more rarely compared to indoor pollutants (Park et. 2006 and 2008).

The effect of moisture damage on microbiological indoor air quality has been studied according to building frame. Concentrations of viable airborne microbes were compared between 17 wooden and 15 concrete and brick school buildings. Concentrations of viable airborne fungi were more common in wooden school buildings. Water damage in a wooden school did not alter the fungal concentrations. In concrete buildings water damage was followed by increased grow of moulds, including Aspergillum versicolor, Stachybotrus and Acremonium (Meklin et al. 2003). In one review study, seven indoor air quality variables are discussed. If indoor air quality is measured using only one or a few variables, wrong conclusions concerning health effects may be drawn (Bellon et al. 2000, Brugge et al. 2003). Moisture is essential to mould growth. In a healthy house without moisture damage, the growth of fungi is prevented. Some materials, including PVC, favor on mould growth (Arundel et al 1986, Bornehag et al. 2005a). Growth on surfaces becomes visible to occupants, whereas growth within the construction frame is not usually seen (Garret et al.1998, Waegemaekers et al. 1989).

In three city schools in the USA dust mite and cat allergens were found in all schoolrooms (Abramson et al. 2006). Different species of moulds and fungi thrive in different living conditions (Husman 1996). High levels of fungi have been detected during and after a renovation of a damp building (Rautiala et al.1996).

In damp houses, exposure to many volatile organic compounds (VOC) related to moulds and fungi can affect the occupant's perceived health. Temperature, relative humidity, sources of nutrients and air movement affect the growth and dissemination of biological contaminants, including bacteria, fungi (yeast and moulds) viruses, protozoa, cockroaches and dust mites (Seltzer 1994). Airborne concentrations of viable bacteria, total volatile organic compounds (TVOC), toxins, inflammatory agents of moulds and house dust mites can be found in a damp building (Dong et al. 2008b, Flannigan et al.

1991 Hart et al.1990, Hesselmar et al. 2005, Hyvärinen et al. 2001, Malmberg 2004, Pasanen 2001, Sorenson 1999, Verhoeff et al. 1997, Wieslander et al. 1997).

The most common means of acquitting information about dampness at home is a questionnaire. In most studies examining housing and children's health, dampness has not been clearly specified. According to Table 2, in 11 (66.6%) out of 18 studies concerning the effect of the indoor environment on children's or adults' health, all the information on dampness or water damage was gathered from questionnaires only. Five studies (27.7%) included examinations of occupants and six (27.7%) a building inspection. A more approach in assessing the presence of dampness is a technical inspection of constructions and sampling of damaged materials, viable fungal particles and dust, settled dust on surfaces and indoor air for microbiological analysis and identification. Single measurement of fungal propagules in settled house dust does not provide a reliable measure of potential exposure to fungi; also the fungal propagules in house dust cannot be reliably predicted by home characteristics (Nevalainen et al. 1998, Nevalainen et al. 2004, Trudeau et al. 1994, Verhoff et al. 1994a, Verhoff et al. 1994b). One comprehensive report deals with the symptoms of different respiratory illnesses related to dampness and factor underlying different respiratory, neurological and autoimmune diseases and the mechanisms of adverse health effects induced by moisture and mould problems. In addition, the exposure to microbial metabolites in moisture damaged buildings and assessment of the effects of remedying moisture and mould damage are discussed (Majvik I recommendations 1998 and Majvik II recommendations 2006).

Table 2. Summary of studies on the association of dampness at home children's' health

	Year	Number case	Number controls	Atopy/ Respiratory. diseases.	Age	Examination of the house	Examining child	SPT	IgG/IgE	Pulmonary functions.
Starchan et al	1986	165		A	6-7	Yes	(Yes)*	No	No	No
Martin et al.	1987	24	77	R	Children	Yes	No	No	No	No
Andrea et al.	1988	4990			6kk-16v	Yes**	No	No	No	No
Strachan et al.	1988	873		A	7	Yes	Yes	No	No	Yes
Platt et al	1989	1169		R	Children	Yes	No	No	No	No
Brunekreef et al	1989	4625		A + R	8-12	No	Yes	No	No	Yes
Waegemaekers	1989	73	117	R	Children	Yes	No	No	No	No
Dales et al	1991a	13495		R	5-8	No	No	No	No	No
Dekker et al	1991	10819		A	5-8	No	No	No	No	No
Jaakkola et al	1993	2568		R	1-6	No	No	No	No	No
Strachan et al	1995	486	475	R	11-16	No	No	No	No	No
Verhoeff et al	1995	259	257	A+R	6-12	Yes	Yes	No	IgE	No
Cuijpers et al	1995	470		R	6-12	No	Yes	No	No	Yes
Li et al	1996	1340		R	8-12	No	No	No	No	No
Yang et al	1997	4164		R	6-12	No	No	No	No	No
Maier et al	1997	925		A	5-9	No	No	No	No	No
Bornehag et al	2005a	10851		R	1-6	No	No	No	No	No
Jaakkola et al	2005	1916		A	1-7	No	No	No	No	No

* Comparison to general practice consultations during previous two years
** Examination of 34 houses and 81 children for validation of questionnaire

2.2 Dampness at home or in a school building and children's' health

Although moulds and indoor moisture damage have been considered a possible trigger of allergic respiratory symptoms since the 1930s, the theory started to attract investigators in the 1980s (Munir et al. 1997b). Many confounding factors appearing simultaneously tended to make the interpretation of an effect of a single factor very difficult (Martin et al. 1987, Lannerö et al. 2002).

In a Scottish study (Platt et al. 1989), respiratory symptoms in both adults and children were ”dose-related” to the mould problem. Indoor exposure to certain fungal genera (Cladosporium and Penicillinium) has emerged as a risk factor for respiratory symptoms in children (Garret et al. 1998, Jacob et al. 2002). The same consistency was also found among adults (Strachan et al. 1989, Koskinen et al.1999). According to these studies actual measurements of indoor fungi spores predict health outcomes better than reported dampness.

2.2.1 Association of moisture damage and other factors with respiratory symptoms and infections

Mould and other fungi may adversely affect human health through four processes; infection, inflammation, allergy and toxicity (Hardin et al. 2003). Some moulds produce mycotoxins, which cause illnesses and symptoms in many organs (Kuhn et al. 2003). In numerous studies, a significant association between respiratory symptoms and respiratory infections among children and damp houses has been established (Table 2)

Respiratory and eye symptoms may reflect irritation caused by toxins and other fungal products. Irritation and damage to the epithelia may make it more vulnerable to viruses and bacteria leading to upper respiratory and eye infections (Beijer et al. 2003, Bornehag et al. 2004, Curtis et al. 2004, Hirvonen et al. 1999, Hirvonen et al. 2005, Husman 1996, Karevold et al. 2006, Kuhn et al. 2003, Munir et al. 1997b, Purokivi et al. 2001 Roponen et al. 2001, Roponen et al. 2003). Allergenic moulds growing indoors include the Penicillium and Aspergillus genera. When humidity is excessive or water damage exists, Stachybotrus, Fusarium, Trichoderma and others can grow (Husman 1996, Kim et al 2007). According to a meta-analyze (altogether 33 studies) of the association of respiratory health effects with dampness and mould in homes, building dampness and mould were associated with approximately 30-50% increases in a variety of respiratory and asthma-related health outcomes (Fisk et al. 2007). Children were more vulnerable to cough and wheeze than adults.

In a study by Rylander et al. 1998, respiratory symptoms and infections were more common among children attending a school with a mould problem than those in control schools. In this study, (1→3)-β-d-glucan was measured in both schools, the levels of -glucan being significantly higher in the problem school. However, there were no significant differences in the prevalence of asthma or other allergic diseases. According to a review by Douwes 2000 and 2005 an association of β-glucan with airway inflammation and symptoms has not been reliably shown. More and wider observations are needed to assess whether beta β-glucan exposure plays a significant role in respiratory morbidity.

In a study of eight primary schools in Uppsala, although no water damage was found and the ventilation was good, an association between respiratory symptoms and indoor TVOC was found (Kim et al. 2007).

Mould odour and water damage over a year previously has been shown to have a strong association with respiratory symptoms among pre-school children but was not associated with asthma (Jaakkola et al. 1993). Infants exposed to high levels of Penicillium are at significant risk of wheeze and persistent cough. The risk was less obvious when they were exposed to Cladosporium (Gent et al. 2002).

In one study of 806 children, 28% had an episode of otitis media before the age of 12 months. Total spore count (not including Penicillinium and Cladosporium) was significantly associated with early otitis media (Pettigrew et al. 2004). In a study by Rylander et al. 2000, mould in the house was a significant risk factor for otitis.

Adults seem to be less vulnerable to respiratory infections in damp houses than children (Martin at al. 1987, Platt et al. 1989). According to some studies the difference is not obvious (Brunekreef 1992a, Dales et al.1991, Pirhonen et al.1996).

According to a review by Bornehag (2004a), some studies show the differences in socio-economic status between study groups to be so marked that they failed to show the possible risk factor associated to mould exposure (Lannerö et al. 2002, Martin et al.1987). According to Verhoeff et al.1995 the association between dampness and diseases or symptoms is clear. These studies of indoor air point out the importance of analyzing all possible confounders one by one and clarifying their relationships to the result to establish the real risk factors. The majority of the studies had a cross-sectional study design, which limits the possibilities of drawing conclusions on causative mechanisms (Bornehag et al. 2004b).

2.2.2 Moisture damage, asthma and allergenic sensitization to moulds

Several studies have found a significant increase in the prevalence of wheezing in conjunction with respiratory symptoms, including wheezing among children living in a damp house (Table 2). The same association between wheezing and asthma also prevails among adults (Zureik et al. 2002, Björnsson et al. 1995, Kilpeläinen et al. 2001, Bornehag et al 2004). In a study of Wickman et al. (1992) among children, no association was observed between viable mould growth and sensitization to moulds. Jaakkola et al. 2005 conducted a population-based 6-year prospective cohort study of 1984 children 1-7 years of age without asthma at the beginning of the study. A total of 138 children developed asthma during the study period. A significant association was found between new cases of asthma and both parental atopy and the presence of mould odour in the home. According to Bornehag et al. (2005b) in addition to being one factor causing dampness, poor ventilation was associated with the increased prevalence of asthma among children. Elevated indoor concentrations of moulds in wintertime due to insufficient ventilation might play a role in increasing the risk of developing atopic symptoms and allergic sensitization not only to moulds but also to other common inhaled allergens (Bornehag et al. 2005a, Fisk et al. 2007, Jacob et al. 2002, and Institute of Medicine of the National Academies 2004).

Allergenic sensitization to indoor moulds is uncommon even among asthmatic patients. About 3-10% of the population with allergic symptoms have specific IgE antibodies to moulds mainly appearing outdoors (Flannigan et al. 1991, Hardin et al. 2003, Iversen et al. 1995, Ledford 1994, Reijula et al. 2003). Most individuals sensitized to fungi are also sensitized to other inhalant allergens (Munir et al. 1997b, Reijula et al. 2003 and Taskinen et al. 2001). The role of the fungal allergy responsible for an increased prevalence of respiratory symptoms in mould-damaged vs. clean houses is therefore difficult to estimate. According to Nolles et al. 2001 sensitization to fungi is prevalent in childhood with an age dependent distribution reaching maximum values at the age of 7.7 followed by a decline all fungal sensitization with increasing age. The specific agent causing asthma still remains unknown (Fisk et al. 2007).

2.2.3 Examining children's health in the context of moisture damage

In addition to the home environment, the school environment is almost equally important to the child's health. Water damaged homes or school buildings are associated with a similar spectrum of symptoms and diseases. The association between dampness in a school building and the prevalence of respiratory symptoms and infections has been established (Haverinen et al. 1999, Meklin et al. 2002, Santilli et al. 2003, Åhman et al. 2000). Respiratory symptoms, fatigue and itching were reported to a nurse in 68.5% of children attending a water damaged school building while the percentage among non-exposed children was 47.1 (Handal et al. 2004). In many studies, respiratory symptoms among children decreased significantly after the repair of a school building (Lingnell et al. 2007, Meklin et al. 2005, Åhman et al. 2000). or new cases of respiratory symptoms in excess no longer occurred (Haverinen et al. 2004). Respiratory symptoms also decreased among adult employers at the school (Patovirta et al. 2004 and Åhman et al. 2000). In a study of Meyer et al. 2005 an association between moulds in a school building and symptoms among adolescence schoolboys was shown, no association being found among teen-aged girls. More frequent symptoms of nasal and eye irritation have been found among female teachers working in a water damaged school (Ebbehoj et al. 2005).

A similar association between asthma (Taskinen et al.1997) or of wheezing and/or cough (Meklin et al.2004, Meyer et al. 2004, Taskinen et al.1999) has been observed among schoolchildren.

In a study by Taskinen et al. 1997 skin tests were made for 13 moulds in all 133 children involved. Positive reaction was observed in only six (5%) of them. Patovirta et al. 2004 found increased prevalence of asthma among teachers in a water damaged school and In a review of Mendel et al. 2005 poor indoor air quality, including water damage, has been shown in some studies to affect children's school performance.

2.3 Other indoor air factors affecting children's health

Although recently moisture damage has been one of the most thoroughly studied indoor environmental factor causing respiratory infections and symptoms, wheezing and asthma, other indoor factors also play a role in children's health. In addition to moulds, other factors in school buildings may play a part in developing asthma, for example inside temperature, humidity, irritating building material (formaldehyde), and cat allergen in settled dust (Arm et al. 2003, Ritz et al. 2002, Smedje et al. 2001a, Smedje et al. 2001b), but to pin down the effects of a single factor among them is not always possible (Smedje et al. 1997). The results of a Swedish study indicate that other environmental pollutants may act synergistically to increase the prevalence of bronchial hyper reactivity and allergy, especially among children with a positive family history of atopy (Andrea et al. 1988). In a review by Mendell (2007) chemical emissions from common indoor materials were found to be associated with a risk of asthma, allergies and pulmonary functions. Children exposed to tobacco smoke had more respiratory symptoms and infections than non-exposed (Arshad et al.1992, Austin et al. 1997, Brunekreef et al. 1989, Burr 1999, Burr et al. 1999, Cuijpers et al. 1995, Dekker et al. 1991, Dijkstra et al. 1990, Infante-Rivard et al. 1999, Maier et al. 1997, Mannino et al.2001, Neas et al.1994, Wu et al. 2007), especially during infancy (Bråbäck et al. 1995, Lindfors et al. 1995, Strachan 2000b). Children subject to environmental tobacco smoke have more absenteeism from school related to respiratory illnesses (Gilliland et al. 2003). A relationship between maternal smoking during pregnancy and childhood asthma or recurrent wheezing has been reported in studies of Gilliland et al. 2001, Lannerö et al. 2006 and Noonan et al. 2007). Jaakkola et al. 2001 showed that the presence of parental atopy and exposure to tobacco smoke had a substantial effect in both of bronchial obstruction and asthma. Arshad 1998 found marked differences in the prevalence of parents smoking inside the house in different countries. In Finland, the proportion of mothers smoking during pregnancy was 15% in 1987 and in 1997 (Jaakkola et al. 2001).

Lindfors et al. (1995) found a synergistic effect on risk of developing asthma between environmental tobacco smoke and damp housing among children who had also evidenced positive SPT reactions to furred pets. Furry pets increase the risk of wheeze (Burr et al.1999). In a British study, 14% of children, 11-16 years of age with wheeze had a furry pet at home (Strachan et al.1995).

The most common allergens in the indoor air are pollens from outdoors and from furred pets. Many major allergens such as Fel d 1 (cat) and Can f 1 (dog) are present even in homes with no furry pet (Atkinson et al. 1999, Dotterud et al. 1997, Ledford 1994, Raunio et al. 1998). In studies of Arbes et al. 2004 and Hesselmar B et al 2005, Can f 1 and Fel d 1 were found in 100% in homes with furry pets and in 99,9% in homes with no pets. Animal allergens are also common in public buildings (Custovic et al. 1994, Leickly 2003, Munir et al. 2003), including schools (Dotterud et al. 1997, Munir et al. 1993) and day-care centers (Instanes et al. 2005, Munir et al. 1995). Levels of animal allergens in school classrooms correlate with number of pupils with furry pets at home (Instanes et al. 2005, Munir et al. 2003, Mussalo-Rauhamaa et al. 2001). High humidity inside the house was most often related to house dust mite (Hart et al.1990) and use of a humidifier (Dekker et al. 1991). In a study by Strachan et al. 1998, the indirect effect of temperature and humidity on the growth of moulds and mites and their effects on health were not reliably shown. The association between high humidity in houses and positive findings of house dust mite has, on the other hand been showed in many studies (Peat et al. 1998, Tham et al. 2007). Sensitization to mite allergens occurs in high percentages in temperate climates (Arshad 1998). Verhoeff et al. (1995) found positive specific IgE allergens to mites in 39% of the children living in a damp home and in 13% of children in a control group. In a Finnish study, the percentage of positive house dust mite among children who had specific IgE antibodies to moulds was 42% and 11% among those with no IgE antibodies to moulds (Taskinen et al. 2001). Mite densities in Finnish homes and workplaces were found to be mainly low, mostly because the moisture problem is not as common as in many other countries. Dust mites were the most abundant species. Storage mites were also found, mostly living in damp dwellings (Pennanen et al. 2007).

A recent study of home environmental factors and respiratory health was made among 14729 Chinese children. Doctor-diagnosed asthma and persistent cough were more common among girls (Dong et al. 2008b). According to another study by Dong et al 2008a involving 16789 children, there was a relationship between childhood asthma and pet keeping and parental asthma. Formaldehyde in the air has been shown to increase respiratory symptoms and diseases in children (Burr 1999, Daisey et al. 2003, Mendel 2007, Venn et al. 2003). Sources of formaldehyde are for instance insulating and construction materials and cleaning agents. PVC carpets also increase concentrations of formaldehyde causing respiratory symptoms (Jaakkola et al.1999, Mendell 2007, Tuomainen et al. 2004). Tuomainen et al. 2006 made an experimental test among asthmatic and non-asthmatic workers exposed to PVC. According to their findings PVC floor covering can evoke respiratory symptoms but no asthmatic reaction.

Exposure to multiple allergens was common in US homes. Of the homes surveyed, 51,5 % had at least 6 detectable allergens. Among atopic subjects a high allergen burden increased the risk of having asthma symptoms (Salo et al. 2008). Bornehag et al. (2004a and 2005) studied the association between phthalates in the indoor environment and rhinitis and asthma among 400 selected children (198 with atopic disease and 202 controls). They found an association between levels of phthalates and rhinitis and asthma. According to Venn et al. 2003, domestic volatile compounds are not a major determinant of risk or severity of childhood wheezing illness, though formaldehyde can exacerbate respiratory symptoms.

2.4 Skin prick tests and micro-organism specific antibodies

The skin prick test (SPT) is commonly used to measure allergic sensitization. There is a strong association between skin reactivity and clinical allergy, including asthma among school aged children.

Timonen et al. made SPTs on 197 schoolchildren whose parents reported asthma or dry cough. The prevalence of at least one positive skin prick test result was 79% among asthmatic children and 55% among children with dry cough only. There were no differences in serum total IgE levels between the two symptom groups.

Taskinen et al. (1997) studied 99 children exposed to dampness in a school building and 34 controls, and conducted SPT with allergen, including 13 moulds. A positive SPT reaction to moulds was registered in only six (5%) of the children, all from the three index schools. There was a significant association between positive reactions to moisture indicative moulds and the prevalence of asthma. In another study 12% of 144 children who had physician diagnosed asthma and participated in a three-year follow-up study evinced a significant (≥3mm) positive SPT reaction to moulds (Immonen et al. 2001). In this follow-up study, positive reactions developed to five children and disappeared from two. Positive reactions to moulds were most commonly found among pupils older than 14 years with multiple SPT reactions to common allergens. There was no relationship between these positive SPT findings and asthma.

Taskinen et al. (2001) measured mould specific IgE (10 moulds) in the sera of 31 children with a positive or weak SPT reaction to various aeroallergens or moulds. Mould-specific IgE antibody was elevated for at least one mould in 12 (39%) of the SPT- positive children and in two controls (3%) among children with no positive SPT reaction. Altogether most sensitized children suffered from asthma or wheezing and up to 36% of children with asthma or wheeze had IgE antibodies to moulds.

Mould specific IgE was elevated for at least one mould in 9% of 259 children with chronic respiratory symptoms and in 0.9% of among 257 children with no respiratory symptoms. No significant association with a moisture problem was found (Verhoeff et al. 1995). In a study by Wickman et al. (1992), among children no associations were observed between viable mould growth and sensitization to moulds.

Among adults, elevated IgG levels of fungi found in working place are considered to be a marker of exposure (Eduard 1995). The prevalence of elevated IgG antibodies to the moulds found in school buildings has been studied in both damp and healthy schools. No differences have emerged in prevalence of IgG antibodies in persons from a damp exposed environment compared to controls (Hyvärinen et al. 2003, Immonen et al. 2002a, and Immonen et al. 2002b, Taskinen et al. 2002). In a study by Hyvärinen et al. 2003, the mean levels of IgG were higher in their control group. The same has been observed among teachers (Patovirta et al. 2003). No association has been found between respiratory symptoms or elevated IgG antibodies specific to moulds among adults living in damp houses or houses with no water damage has been found (Hyvärinen et al.1999).

2.5 Reliability and validity of questionnaires

Self-reported utilization of health care services is important in epidemiological studies and in health care planning, policy and research, and the accuracy of information so gathered is essential.

Self-administered questionnaires on exposure, morbidity or the use of health services are commonly used in epidemiological studies. According to a review (Toren et al.1993) data concerning respiratory diseases and asthma have often been a target of questionnaire studies and many different questionnaires have been developed and applied. Some have shown good reliability and validity (Asmussen et al. 1999, Ehrlich et al. 1995, Engman et al. 2007, Jenkins et al. 1996, Pecoraro et al. 1979, Perpina et al.1998, Venables et al. 1993), some fairly good (Shiraishi et al. 1996), while some were not satisfactory (Peat et al. 1992).

Ehrlich et al. (1995) interviewed 620 parents after having had administered a questionnaire and repeated the questions in an interview. The same questions in the interview produced higher prevalence of wheeze than in the self-administered questionnaire.

Lowe et al. 2004 followed the respiratory health of 428 children from birth to the age of three. Parents' reports on wheeze were compared with physician's examination and specific airway resistance measurement. Tests were negative among children whose parents did not report wheeze and among those whose parents reported wheeze, but this was not confirmed by physician. Children with physician confirmed wheeze had significantly poorer lung function. Hoek et al. (1999) compared respiratory symptoms reported by parents, children's self-reported symptoms and pulmonary function tests. Children reported between 1.8 and 3.2 times more acute symptoms than their parents, symptoms reported by children did not agree well with parental reports. A similar association with pulmonary function suggested that self-reported symptoms were neither superior nor inferior to symptoms reported by the parents.

Peat et al. (1992) administered a questionnaire twice to parents concerning respiratory symptoms, the first being a self-report and 3 months later filled with the help of a nurse. Seven percent of children changed diagnosed asthma category, 13 percent changed to cumulative wheeze category, and 9 percent to recent wheeze category in the second questionnaire. Because the numbers of those who changed from symptom-positive to negative roughly equaled the changes from negative to positive, prevalence estimates were not affected. Hasselgren et al. (2001) studied the prevalence of respiratory symptoms, asthma and COPD. More than 40% of subjects reported respiratory symptoms. Of persons with asthma, 33% were estimated to be undiagnosed, 67% used medication and nearly 60% attended primary health care services. The epidemiological difference between the estimated prevalence of asthma and the lower detection rate in primary health care can be explained by at least three factors: persons who did not seek care, those who were not diagnosed or those who attended other health care providers.

Questionnaires have been commonly used in studies concerning damp housing and children's or adults' health. In many cases results are based solely on questionnaire data. In one study (Dales et al. 1997), 403 homes were inspected and compared to reported dampness. Respondents who reported allergy were more likely to report visible mould growth; respondents who smoked were less likely to report visible mould growth.

Ritter et al. (2001) studied the accuracy of recall by comparing data obtained from another source of information, usually medical records. Visits to a physician, inpatient hospital nights and medication were studied. The authors found an exact agreement in 93% for inpatient hospital nights, 91% for ambulatory physician visits in the preceding 2 weeks, and 30% for ambulatory physician visits in the previous year. With increasing numbers of ambulatory visits to a physician during the previous year the bias to underreport grew significantly. These findings suggest that self-reported inpatient nights in the previous year and ambulatory physician visits in 2 weeks are reasonably accurate, but self-reported ambulatory physician visits in the previous year may be less accurate and likely to be biased towards underreporting at higher numbers of visits. Bellon et al. (2000) studied the validity of self-reported utilization of primary health care services according to a questionnaire and medical records. There was a tendency to over report the actual number of visits and the accuracy of self reports did not seem to decrease appreciably as the recall time was longer. In a study of Bruijnzeels et al. 1998 estimates of medical utilization rates of children were critically influenced by the method of data collection used. In this study interviews were prone to introduce a recall bias toward over reporting.

Several symptoms related to exposure to mould were statistically significant in the school with an indoor fungal problem before the problem was detected. After the situation was revealed, the perception of symptoms increased in the index school compared to the control school (Handal et al. 2004).

Daly et al. (1994) compared data from questionnaires concerning episodes of otitis media with medical records. They found that a substantial proportion of data on the age at the first episode of otitis media, occurrence of otitis the previous summer and the number of otitis bouts during past 18 months was missing. Data were significantly more likely to be missing for male children, children with siblings and those with many episodes.

In a study by Strachan et al. (1986), information on children's doctor's visits was available in addition to the questionnaire. There was disagreement between medical records and reported wheeze. There was both over reporting and underreporting. If study results are based only on reported dampness, the bias may be marked.

In a sub study of a larger study (Dampness in Buildings and Health), Bornehag et al. 2004b validated the self-reported symptoms of 400 children comparing answers to medical records. Reporting allergic diseases had good reliability compared to medical records. To study self reported home characteristics, visits were made to 390 houses. There was a remarkably low agreement on visible signs of dampness between self-reporting and observations by the inspectors (kappa 0.17-0.20). Selection bias was found among questionnaires of the total study group 14077 (children aged 1-6 years). Families were more inclined to participate if the child was reported to have more symptoms, if there was no smoking in the family, if the family had avoided pet keeping and if they belonged to a higher social group.

3. Aims of the study

The aim of this study was to characterize the effects of dampness in the school building on the respiratory health of schoolchildren and to evaluate changes in health after renovation of the school building.

The specific aims were to establish

1. whether children attending a moisture-damaged school had a higher prevalence of respiratory symptoms and infections than the reference group in a school without water damage, and whether repair of the damaged building had positive effects on children's respiratory health after one year's follow-up.

2. whether atopy (Phadiatop® positively) and/or atopic diseases were found more often among the exposed children than among the unexposed control group

3. whether the IgG antibody response to microorganisms indicating a water-damaged building was higher among exposed than unexposed children and whether IgG antibodies to molds were associated with respiratory symptoms and infections in the same children.

4. the relationship between positive IgG antibodies and sensitization (IgE) defined as positive (Phadiatop®) to common environmental allergens.

5. the validity of self-administrated questionnaires compared to documented morbidity according to patients' records among schoolchildren

4. Subjects and methods

4.1 Subjects

The study population comprised 397 children between the ages of 7 and12 years in school E (the index school), situated in a suburb community and a control group of 192 unexposed children of the same age in school C, situated 5km from the center of the same suburb. In all, 92% of parents of both study groups returned the first questionnaire in the fall of 1995 and the response rate to the second questionnaire was 81% in school E and 100% in school C. The study populations are described in the table 1 of study 1. The description and results of class X (the most exposed schoolchildren in school E) has been presented separately in the section of results.

A questionnaire was sent to all parents of the children in school E (index school) and school C in September 1995. The first questionnaire (Q1) applied to the 1994 - 1995 semester. All parents were asked for permission to take a blood sample from their child for testing. The children were selected randomly (fixed random sample) from those for whom permission was given so that each floor in school E was equally represented. In the school E 12% of the parents refused, the percentage being under 10% for school C. Blood samples were drawn from 69 children (19%) in the exposed group, including 6 children from class X and 50 children (29%) in the unexposed group.

4.2 Methods

4.2.1 Questionnaire

Our study design was a one-year follow up study among exposed and non-exposed children. The questionnaire used was divided into sections on respiratory symptoms, respiratory diseases and prescribed antibiotics; possible sources of indoor air pollution at home or in school; housing conditions; and earlier allergic diseases among the children and their first-degree relatives. The school building was renovated in the summer and early autumn of 1995. A new examination of the building showed the renovation to have been successful. A new questionnaire (Q2) was distributed at the end of the semester 1995-1996 to the parents of the pupils who responded to the first questionnaire. The question on reported allergic disease was: Has your child ever had allergic rhinitis, conjunctivitis and asthma (with the year of each diagnosis). The question on allergy in the family was limited to full siblings and biological mothers and fathers. The comparison of allergic diseases before and after the children started school, including the 1995-96 school year, and the allergic diseases in family members was based on the answers given in the second questionnaire. The questionnaire used in our study was based on MM40-questionnaire (Andersson et al.1992) used in the research projects of The Public Health Institute.

4.2.2 Medical records

In the case of children who answered the first questionnaire in both schools, a researcher (RS) studied all the medical records of the local health center from autumn 1994 to summer 1996. Visits to a physician because of a respiratory disease, the diagnoses and the number of courses of antibiotics prescribed for diseases were recorded for this study. In Finland, antibiotic medication is given only when a patient has a physician's prescription.

In order to validate the results of the questionnaires, the data from the medical records of the local health center were compared to the individual replies concerning respiratory infections in the two questionnaires from the same time period (1994-1995 and 1995-1996). Comparisons were studied at individual and school level.

4.2.3 Water damage

A technical investigation of the school building was made in April 1995. The findings were obvious and widespread. The lowest floor was totally wet. The water pipes did not function. The walls were also wet in many places on the lowest floor and especially walls against pipes. The pipes were wet because there were no covers of pipes and the current of airflow had been turned off because of mechanical airflow on the lowest floor had no compensation air. In addition water-pipes inside the walls were leaking and walls in many places were wet. There was abundant microbe growth in many places, especially on the ground floor.

4.2.4 Microbiological measurements in school buildings

In April 1995, representative microbiological samples of the air (Andersen 6-stage impactor), surfaces and materials of the building were collected from School E and also from School C in May 1995 and again after the renovation in School E in November 1995. A microbiological analysis was made, based on the identification of cultivated microorganisms. Microbes detected indicated water damage. There was a abundant microbe growth in many places, especially in the ground floor. In addition to the damage in the building, most of the water pipes under the building also leaked and the water damage inside the floor was widespread. A microbiological analysis was made based on the identification of cultivated microorganisms. Microbes indicating water damage (Acremonium, Aureobasidium, Stachypotrus, Streptomyces, Trichoderma and Wallenia. genera) were found in all air samples collected from school E (Study 3,Tbl 1),. Moisture-indicating microbes were also found in structures (Acremonium, Aureobasidium, Stachypotrus, Streptomyces) (Leivo et al.1995), There were no molds indicating water damage in school C.

4.2.5 Renovation

A decision was reached to renovate the building during the summer of 1995. The ground floor was sealed from the rest of the school. There were no drawings of the ground floor left, which made it difficult to find them. In two classes on the ground floor there was asbestos under the floor covering.

Because of the abundant water leaks under the ground floor, the floor was still wet when the semester 1995-1996 was starting. The ground floor was isolated until November 1995.

4.2.6 IgE and IgG antibodies

The responses to the first questionnaire and the patients' records showed that respiratory symptoms and diseases were markedly commoner among children in class X. Therefore, blood samples were also drawn for testing from 12 of the 14 children whose parents responded to the first questionnaire. These children were not a part of the random sample (six children from class X) of the entire school. The parents of two children refused to let their children participate in the blood test. IgE antibodies to a mixture of 10 common environmental allergens (birch, timothy, mugwort, horse, cat, dog, Dermatophagoides pteronyssinus, Cladosporium herbarum, olive tree and Paretaria judaica) were determined with a multi-RAST screening test, Phadiatop ®, Pharmacia & Upjohn Diagnostics, Uppsala (Eriksson 1990). The children with elevated IgE values ($\geq$0.4) in the Phadiatop test were then tested specifically for 8 of the 10 allergens used in the test and for 3 additional mould allergens (Penicillium notatum, Aspergillus fumigatus, Cephalosporium acremonium) (RAST, Pharmacia & Upjohn Diagnostics, Uppsala). Allergens of the olive tree and Paretaria judaica, used in the Phadiatop test, were not individually tested as they do not exist in Finland. For this study, the elevated ($\geq$0.4kU/l) total values of allergen-specific IgE antibodies were graded as moderately elevated (0.4-17.5kU/l) and markedly elevated (>17.5kU/l).

IgG antibodies to nine microorganism (moulds and yeasts) most commonly indicating water damage were analyzed by enzyme-linked immunosorbent assay (ELISA). At that time the laboratory results for IgG antibodies to each microbe were given as negative (-), slightly elevated (+), moderately elevated (++) or markedly elevated (+++) in comparison with the value given by the pooled positive reference adult serum. For defining recent exposure, an IgG antibody result was considered positive when it was either moderately or markedly elevated.

The tests were analyzed in the University of Kuopio. Results were given on a semi quantitative scale. At that time the standardizations were mainly made in each laboratory.

According to a study of Hyvarinen et al. 2003 IgG levels cannot be readily suggested as routine methods for evaluation. Elevated IgG antibodies are not always a marker of recent encounter but can also be elevated because of former exposure.

4.2.7 Statistical analysis

The statistical analysis was based on odds ratios and means supported by 95% confidence intervals. The level of significance was set at 0.05, which was used in the presentation. Because of the small numbers of children in study groups, significance at level 0.10 was used in some comparisons. Calculations were carried out using CIA software as described by Gardner and Altman (Gardner et al. 1989). As multivariate technique we applied polychromous logistic and standard logistic regressions. The statistical analysis was carried out using BMDP Statistical Software on a SUN/UNIX mainframe.

4.2.8 Ethics

The ethical board on Tampere University Hospital approved this study on 13th November 2001.

5. Results

5.1 Characteristics of study groups

Pets at home, daily exposure to tobacco smoke and visible mould were distributed evenly between the study groups. Children in school C had more siblings than the thouse in school E. There were differences between the study groups in the type of housing; 30% of the children in school E lived in apartment buildings and 70% in single-family or row houses, while all the children in school C lived in single-family or row houses. According to the questionnaires, visible mould was reported to be present in 0.2% of both apartment building and single-family or row houses (Study 1, Table 1).

5.2 Moisture damage and microbiological findings in school buildings/exposure to moulds

A technical investigation was carried out by Institution of Occupational Health. Building structures in School E revealed marked and widespread moisture damage on all three floors; the most serious damage being found on the ground floor. There were many reasons for the damage. For example, the foundation was totally wet owing to a lack of drain tiles; in many locations, walls and ceilings had been moistened by leaking pipes and roofs. The ventilation of the building was designed to function naturally. In the 1970s, tight windows replaced the old type and the natural ventilation was disturbed. The first signs of water damage were found in 1993. In April 1995 representative microbiological samples of the air (Andersen 6-stage impactor), surfaces and materials of the building were collected from the school which had sustained prolonged water damage (school E) and from the control school (school C). A microbiological analysis was made, based on identification of viable microorganisms. Several species of micro-organisms indicating moisture damage were identified in the samples from the school E. These findings completed and confirmed the investigation of the building. In school E there was visible mould growth in class X, which was situated closest to the most serious moisture damage found on the ground floor. The growth of the collected samples of moulds (Penicillium, Aureobacidium, Cladosporium, Geotrichum and Aspergillus) was most extensive in samples taken from Class X, where also growth of mycotoxin- producing moulds (e.g., Stachybotrus chartarum) was found (Leivo et al. 1997, Study3, table 1). Following the renovation we obtained new microbiological samples, and at that time only slight growth of mould species commonly appearing in the indoor environment was found (Leivo et al.1997). No observation of moisture damage or any indication of exceptional microbial growth was found in the corresponding samples from school C.

5.3 Respiratory infections and symptoms

According to the first questionnaire the mean number of common colds, visits to a physician and respiratory symptoms during the school year 1994-1995 was significantly higher among the pupils in school E, and even higher in class X, than in school C (Study1,Table 2). The group comparison after the renovation included the number of children whose parents answered both questionnaires: 303 from school E, 175 from school C and 18 from class X. The risk of common cold and bronchitis was significantly higher in school E than in school C in spring 1995, while after the follow-up the difference between the groups was no longer significant. When changes were compared, an improvement was clearly seen in the case of all the respiratory diseases except otitis media. (Study 1, Table 3)

Before the renovation the mean number of reported physician visits and the number of respiratory symptoms inquired in Q1 were significantly higher in school E than in school C (Study1, Table 4,). The use of antibiotics was also more frequent in school E (Cl 90%). Following the renovation only visits to a physician were significantly more common among children attending school E.

Boys in school E reported more visits to a doctor because of respiratory symptoms and diseases than girls according to the Q1 and patients' records, although statistical significance was not reached. The difference was less obvious after the renovation in the semester 1995-1996 among children attending school E. In school C, there was no difference between boys and girls in respect of doctor's visits during both semesters (unpublished data).

Allergic symptoms were more common among boys compared to girls in school E according to both questionnaires. The differences in symptoms in school C were not as obvious as in school E.

There have been many articles discussing differences between boys and girls in the matter of developing respiratory infections and asthma. In most studies boys in childhood were prone to asthma more often than girls. In adult age asthma is more common among women than men. (Almqvist 2008, Davis JB 1976, Postma 2007, Tollefsen et al. 2007).

5.4 Changes in the visits to the health center and in prescribed antibiotics

After the renovation there were no significant health differences between the groups with respect to any outcome variables. Changes in the numbers of visits to physicians because of respiratory infections and in prescription of antibiotics were statistically significant for school E (Study1, table 5).

5.5 Multivariate analysis of reported and recorded respiratory symptoms and diseases

In the first phase of the logistic regressions analysis visits to a physician were used as the dependent variable and classified into the three categories: no visits, one visit and two or more visits. The possible predictors were the study group, sex, age, previous allergic diseases, pets, passive smoking, moisture damage at home, number of siblings and residence in apartment building. The analysis brought out no significant difference between one visit and two or more visits. Accordingly, the final analysis used logistic regression to compare no visits with one or more visits. This showed that children in school E had a significantly increased risk of having to visit a physician (OR 1.82, 95% Cl 1.23-2.69). No other predictors proved to be significant.

5.6 IgE antibodies

Elevated IgE values were found in the Phadiatop test in 40 (58%) of the exposed children and 17 (34%) of the unexposed children. There was a significant difference when the distribution of elevated values in school E was compared with that of school C (Study 2, Table 2).

The distribution of specific IgE allergens was subsequently tested; 39% of the children in school E had antibodies to animal allergens (cat, horse or dog), 68% to pollens and 13% to house dust mite. The percentages for the children in school C were 69%, 87% and 19%, respectively.

In our study there was only one IgE finding positive to moulds in school E (A. fumigatus) and two children had IgE positive antibodies to moulds in school C, one child for three moulds (C.herbarum, A.fumigatus and C.acremonium) the other for two moulds (Cl.herbarum and A.fumigatus). IgE tests were not available at that time for all the moulds in the building (e.g. Stachybotrus chartarum)

5.7 Reported allergy

According to the questionnaire, 37% of the exposed and 39% of the unexposed children had a family history of allergy (parents or full siblings). Altogether 17% of the children (21% of the boys and 13% of the girls) in school E and 14% (14% of the boys and 13% of the girls) in school C reported current or previous allergic rhinitis, allergic conjunctivitis or asthma. Reported allergic diseases before school age were evenly distributed in the groups, 7.9% in school E and 7.6% in school C. When only new allergic diseases after school entry were compared, the occurrence in school E was higher than in school C (Study 2 Table 3).

Of the 20 children in school E and 8 in school C who reported allergies and underwent the Phadiatop test, 85% in school E and 87% in school C had elevated IgE values (sensitization).

In class X, 15 of the18 (83%) students had elevated specific IgE antibodies (Study 2, Table 2). The odds ratio for the elevated specific IgE levels was significantly higher for class X than for school E and higher than for the rest of school E. These findings suggest a relationship between different levels of exposure to microorganisms and generation of allergen specific IgE antibodies.

Altogether 34% of the children in class X had a family history of allergy, 33% were currently experiencing or had previously experienced allergic rhinitis, allergic conjunctivitis or asthma, while 11.1% had allergic diseases before school age (Study 2, Table 3). New allergic diseases after starting school were more common in class X than in the rest of school E or in school C. The difference was significant when class X was compared with school C and almost significant at level CI >90%) when class X was compared with the rest of school E.

In the logistic regression analysis, the risk of carrying an elevated level of allergen specific IgE was 17 (95% CI) times higher for the children who had reported an allergic disease vs. those without allergies and three times (95% CI) higher for those attending school E vs. those in school C. Other factors in the same model were non-significant in this logistic regression analysis.

5.8 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 study 3, Table 1. In the index school, 11 children had no positive findings for the tested microbes (16%) and the corresponding number being 13 (27%) for the control school. Of the nine microorganisms tested the average number of positive IgG antibodies per student was significantly higher (p=0.05) for the index school (mean 2.30; 95% confidence interval (CI) 1.90-2.71) than for the control school (mean 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%) from the control school.

5.9 Correlation of respiratory symptoms and infections and elevated IgG antibodies among the children in school E

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 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.

Among the children in school E there were no significant differences in numbers of visits to a physician and use of antibiotics between those who had normal IgE values compared to those with elevated IgE values.

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

There was a negative correlation between the number of positive IgG findings and the total level of the allergen-specific IgE antibodies among exposed children. The mean IgE value for the children who had four or more positive IgG antibodies (n=16) was 2.5kU/l (CI 0–5.7), while for those who had 0-3 positive IgG antibodies (n=53) the mean figure was 16.8kU/l (CI 7.1– 26.5). The correlation between total levels of allergen-specific IgE antibodies and the number of positive IgG antibodies was -0,21 (Spearman rank correlation).

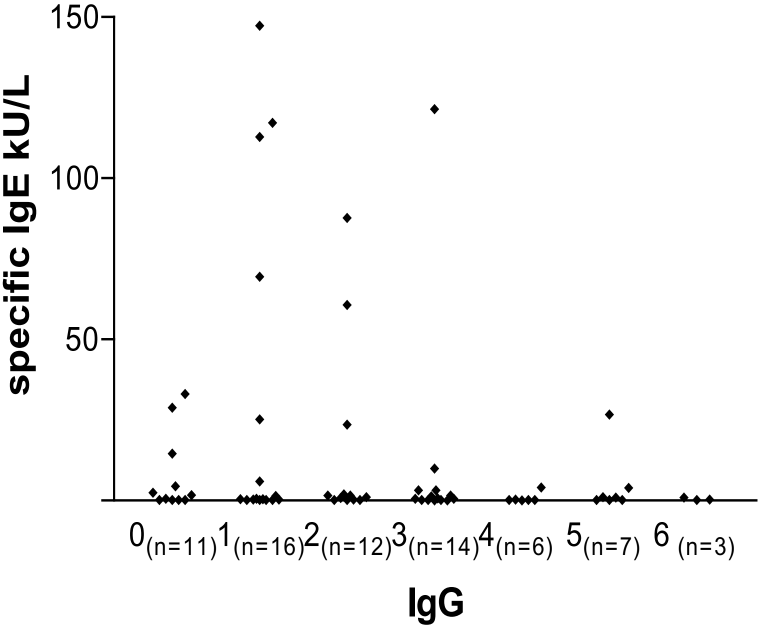

Figure1. The correlation between total levels of allergen-specific IgE antibodies and the number of positive IgG results for 9 tested antibodies

Fourteen of the children who reported an allergy in the questionnaire belonged to the randomized (blood test) group. The mean level of specific IgE antibodies among these children was 29.0kU/L., and their mean number of positive IgG titers was 1.42. For the 55 children in the randomized group who did not report allergic diseases, the mean IgE level was 9.54kU/L and the mean number of positive IgG titers was 2.53. Of those children (n=16) who had four or more positive IgG antibodies, only one reported an allergic disease and evinced no detectable level of specific IgE.

5.11 Validation of the questionnaire

5.11.1 Visits to a physician

If the study subjects had used the services of private physicians as frequently as recorded by the Social Insurance Institution on visits among 7 to12-year-olds of this community they should have made altogether about 140 visits to private sector because of respiratory infections, (115 in the index school and 25 in the control school) in the first school year and 112 and 32 visits in the second school year. These visits to private physicians should have been included in parents' answers in questionnaires, but not shown in the patients' records in the health center. In our study, visits to hospitals were not taken into account by reason of an agreement between the nearest hospital in the community and all surrounding communities requiring that acute respiratory diseases be treated, at least primarily, in local health centers.

There were 460 visits to a physician reported in Q1, this covering both the study and control group (Study 4, Table 2). The medical records of the health center showed 428 visits among the study and control groups resulting from respiratory illnesses (93% of reported visits) during the school year 1994-1995. The corresponding numbers in 1995-1996 were 309 reported and 271 (88%) recorded visits.

The proportion of children who reported more visits than the number found in patient's records was 21.6% in school E and 13.1% in school C in school year 1994-1995, as determined by questionnaire. The respective figures for questionnaire 2 were 19.5% and 11.4%. (Study4, Table 2).

Based on individual comparison the number of visits to a physician because of respiratory infection reported in the questionnaire equaled the number of recorded visits to a local health center for 61 percent of the children in the first questionnaire and 66 percent of the children in the second questionnaire. Eighty percent of these children had no reported visits in the first questionnaire, and the patients' records showed no visits to a physician in the health center because of respiratory infection. Corresponding percentage in the second questionnaire was 87 per cent (Study4, table 2).

According to patients' records there were 199 visits among 112 (21 percent) children that were not reported in the first questionnaire and 123 among 84 (18 per cent) in the second questionnaire. During the previous years out of the total number of visits recoded in the health center, 46 per cent for the first questionnaire and 45 per cent for second questionnaire were not reported (Study 4, table 2). The percentage of forgotten visits was higher in the control school in both questionnaires.

5.11.2 Use of antibiotics

In both schools, the reported use of antibiotic medication and the number of visits to a physician were higher when the data were compared only with information from patients' records in the local health center. The antibiotics prescribed by private physicians were reported in the questionnaires but they were not recorded in the health center. Again the over-reporting was higher in School E than in School C for both questionnaires (Study 4 Table 3).

Based on individual comparison 34 per cent of the antibiotic medication documented in patients' records was not reported in the first questionnaire for the same child, the corresponding figure being 37 per cent in the second questionnaire. The percentage of those who reported less antibiotic medication than recorded for the patient was lower than the underreporting of ambulatory visits (Study 4, Table 4). The percentage of forgotten antibiotic courses was higher in the control school in both questionnaires.

6. Discussion

The present study was a cross sectional survey of respiratory morbidity conducted with two questionnaires, two years of physician's records and one-year follow up after renovation, in respect of respiratory symptoms, infections and allergic diseases. Two sources of information were used, questionnaires and medical records. This also gave a possibility to validate the questionnaire information.

To the author´s knowledge this study in 1994-1996 was the first to examine children's health in cases where widespread water damage was found in a school. At that time there were only few laboratories able to test for IgG and IgE antibodies to moulds and microbes. Findings were shown in the different ways in different laboratories, which made it difficult to compare results to previous figures. Our tests carried out in the laboratory of Oulu University Hospital.

The study group and the control group evidenced no significant differences other than those related to school. According to the pragmatic study design the number of participants was limited, the cohort comprising all children available for this kind of study design. However, the number of the children was high enough to yield statistically significant results, even when smaller groups for were used blood testing.

The marked differences in respiratory symptoms and diseases before the renovation among most exposed children (Class X) compared to either the index group or control group were also in most variables statistically significant.

6.1 Validity aspects

6.1.1 Generalizing

According to results from a recent questionnaire sent to selected principals of finish schools, in about 80% insufficient change of air was observed and moisture damage needing repair was found in more than 20% of these schools. There are still many schools in Finland built in 1950s, in the same way as School E. The need for new schools was based on abundant numbers of children born after the war. There was a need for building material and the quality was not always as good as it should have been. These schools from fifties are in need of repairs.

Although the study was of pragmatic study design involving intervention and renovation of moisture damage and by its nature is a particular case, the results of the study may be applied to other severely damaged schools in Finland. The generalization of the results is supported by other studies of the school environment with similar findings concerning respiratory infections among school children (Taskinen et al. 1997, Meklin et al.2002, Immonen et al. 2002) and teachers (Patovirta et al. 2004).

6.1.2 Comparison

The study population consisted of a group of 365 schoolchildren between 7-12 years for School E and 176 schoolchildren from School C. Based on data from questionnaires and results of multivariate analysis, the main difference between the populations of the two schools was in terms of exposure to microorganisms in a water damaged school.

6.1.3 Relevance and reliability of methods

The study was a cross-sectional study of respiratory morbidity. Two sources of information were used, questionnaires and physician's records at the end of both semesters. This also gave the possibility to validate the questionnaire information.

The pragmatic study design and the urgency of initiation quick start of the study caused some inadequacy; on the other hand the methods used were sufficiently valid to give reliable results. The number of children, again was high enough to yield statistically significant results, even when smaller groups were used for blood testing.

The marked differences in respiratory symptoms and diseases prior to the renovation among most exposed children (Class X) compared to either index group or control group were also statistically significant in most variables.

6.2 Exposure to moulds

6.2.1 Study population

The study populations comprised unselected groups of 365 children aged 7-12 years from two schools in Ylöjärvi, a suburban community near Tampere. Based on the data from questionnaires and the results of multivariate analysis, the main difference between the populations of the two schools was in exposure to microorganisms in the water-damaged school.

6.2.2 Positive IgG and IgE antibodies among the study groups

Levels of IgE specific to multiple allergens (Phadiatop , Koivikko et al. 1991, Erikson 1990) were used to characterize atopy among the study subjects. This test had been widely used for screening purposes and is standardized, except for moulds.

For IgG antigens, we used a panel of moulds and yeast commonly used as antigens in ELISA to screen for microorganisms associated with moisture-damaged buildings at that time. (Reiman et al. 1998).

6.2.3 Respiratory symptoms and diseases related to dampness in a school building

The present study yielded two main results. Firstly, respiratory symptoms and infections were more common among schoolchildren exposed to moisture damage. Secondly, after the renovation of the school building in question no significant differences were found in all health outcomes except for visits to a doctor. However, according to patients' records these visits among children from school E had decreased subsequent to the renovation. Physician visits for any respiratory symptoms had decreased within the same group. Due to the small numbers in the study groups, significant change was shown only in the total number of respiratory infections (CL 95%) and with a CL of 90% in numbers of courses of prescribed antibiotics. Before renovation all respiratory symptoms were more common in the index school, differences being greatest in the numbers of episodes of wheezing, wheezing with cough and sore throat. In the study group all symptoms were less common after the repairs, but still more frequent than among control children. Similar changes have been recorded in other studies.

The average number of bouts of common cold, tonsillitis and bronchitis on class X was more than double that in the rest of the school E. After the renovation, there were no significant differences between class X and the rest of the school.

In a study of Meklin et al. 2005 32 schools were examined. 24 schools (index schools) had moisture problems and 8 (reference schools) had none. One of the index schools with a moisture problem was repaired and a significant decrease was observed in the prevalence of 10 symptoms out of 12 studied in another school partial repair was carried out and there was no improvement in prevalence of symptoms These finding are in agreement with our findings of that prompt and comprehensive repair of damp building reduces symptoms rapidly.

In a study of Åhman et al. 2000 336 pupils and 34 staff were interviewed immediately prior to renovation of a school building with moisture problems and 7 months after the renovation was completed. Intervention was followed by positive health effects, supporting the hypothesis that emissions from building material had contributed to the excess of symptoms.

6.2.4 Allergic diseases and atopy (Phadiatop positivity) among exposed schoolchildren

The second aim of this study was to examine whether atopic diseases were found more often among exposed children. Asthma and other allergic diseases are much more serious outcomes of indoor air impurities than respiratory infections and symptoms. Children who develop asthma or some other allergic diseases in consequence of dampness or mould in a building, whatever the mechanisms is, have a risk of life long illness. Although the mechanism is not clear, several studies have found a significant association between building dampness and asthma (Andrea et al. 1988, Brunekreef et al. 1989, Billings et al. 1998, D'Amato et al. 1995, Dekker et al. 1991, Emenius et al. 2003, Lindfors et al. 1995, Nafstad 1998, Strachan et al. 1998, Timonen et al. 1995).

In the present study, increased levels of specific IgE were found in the Phadiatop test among children randomly selected for blood tests in 40 (58%) of the exposed children and 17 (34%) of the unexposed children. Altogether 17% of the children (21% of the boys and 13% of the girls) in school E and 14% (14% of the boys and 13% of the girls) in school C reported current or previous allergic rhinitis, allergic conjunctivitis or asthma. Reported allergic diseases before school age were evenly distributed in the study groups, 7.9% in school E and 7.6% in school C. When only new allergic diseases starting after school were compared, the occurrence in school E was higher than that in school C. Our study is in agreement with many others in findings, that boys are more prone to get allergic diseases (Almqvist et al. 2008, Davis 1976, Postma 2007, Tollefsen et al. 2007). In another sub study girls had less asthma than boys but after age of 15 females carry an increased risk of asthma (Janson et al. 2001).

The prevalence of asthma and other atopic diseases has increased markedly during the recent decades. This is especially true among children in developed, highly hygienic Western countries. In a recent study comparing asthma, rhinitis and eczema among randomly selected schoolchildren aged 6-16 and their mothers from Finland (n=344 children, 344 mothers) and Russia (427 and 284 respectively) participated SPT's and measurements of IgE to common inhalant and food allergens were performed. Also a questionnaire for was used. The rate of positive IgE results was significantly higher in Finland among both mothers and children. In all atopic diseases the reported rate of allergic diseases was about 50% higher in Finnish children (Pekkarinen et al. 2007). According to the current "hygiene hypothesis" there are many elements affecting the incidence of atopic diseases; exposure to endotoxins, the number of siblings, earlier infections, exposure to pets, growing up on a farm and helminth infection (Platts-Mills 2005 and Strachan 2000).

A significant difference emerged when the distribution of elevated IgE values in school E was compared with that in school C. In logistic regression analysis the risk of yielding an elevated IgE value was 17 times higher for the children who had reported an allergic disease and 3 times higher for those attending school E compared to school C.

Another significant difference between the study groups was the occurrence of new cases of allergies after starting school. The water-damage had been recognized in the index school for several years and minor repairs had been made (Leivo et al.1997). The oldest children had been exposed for six years. The children in the worst damaged class had been exposed for 2 years when the first questionnaire was sent. Before going to school, the percentage of children having allergic diseases was 8%. At the time of the second questionnaire the percentages were 17.2% among the study group and 13.7% in the control school and 33% in children in the worst damaged class. Wheezing was reported 2.2 times more often among children in the study group.

6.2.5 IgG to micro-organisms and IgE antibodies to common environmental allergens among exposed schoolchildren

One aim of this study was to establish whether there was an IgG response among exposed children to microorganisms commonly found in Finnish water-damaged buildings and whether the presence of IgG antibodies was associated with respiratory symptoms and morbidity

In adult populations IgG antibodies are often used at group level as an indicator of exposure to moulds and other microorganisms in the work environment. Microbial growth in an indoor environment is a dynamic process depending on environmental conditions such as humidity, temperature and availability of nutrients, the main species thus varying and differing over time. IgG antibodies reflect a longer period of exposure (months or years) and do not necessarily correspond microbial species recognized from samples taken "cross-sectionally" (Verhoeff et al.1994a). Eduard (1995) showed that IgG antibodies to microorganisms reflect higher exposure at group level in an adult population. In our study, IgG antibodies reflected the exposure to moisture damage at group level. There was a negative correlation between the level of specific IgE antibodies and the number of positive IgG titers. Children with active production of IgG antibody to microorganisms tended to be more seldom sensitized to common environmental allergens. According to the results of the study it seems that atopics do not produce IgG antibodies to microorganisms typical of water-damage while similar exposure of non-atopics (children with negative findings for allergen specific IgE) results in antibody production. In studies among adults (Hyvärinen et al. 1999, Makkonen et al. 2001),a positive association between water damage and levels of specific IgG antibodies among adults were found.

In infants, IgG levels and information on mould exposure correlated well. Children from farming families had higher IgG levels. In schoolchildren, IgG and current exposure information do not correlate equally well (Korppi et al. 2003).

In a three-year follow-up study of school children, the presence of positive levels of specific IgE antibodies was associated with clinical atopy and positive SPT reactions to common allergens. No association between positive IgE findings and moisture problems was found. Mould specific IgE antibodies were positive mostly in atopic children with no association with exposure in the school. (Hyvärinen et al. 2003).

We found detectable levels of IgE antibodies to moulds in a single child in the study group, and in two in the control group. The average level of IgE antibodies in the Phadiatop test (9 allergens) was 13.3 kU/L in the study group and 27.8 kU/L among children in class X (worst water-damaged classroom) and 4.1kU/L in the control group. Levels were undetectable in 50% in the study group, in 66% in the control group and in 11% among class X.

Exposure to indoor moulds increased the appearance of both allergic symptoms and IgE sensitization and this response was even dose-dependent, being most distinct among the most heavily exposed subpopulation in the material. Whether this was an acceleration of immune deviation towards atopy or whether the regulatory mechanisms were so severely disturbed as a result of mould exposure, that even those not prone to develop atopy were affected. This may only be speculated in the risk of our findings in this cross sectional study. Fungal exposure may have an allergen-specific effect on sensitization, but also a non-specific effect on immune system facilitating sensitization to other allergens, possibly via mycotoxins and ß-glucans (Woodcock et al. 2000, Rylander et al. 1998).

The negative correlation between IgE and IgG responses to mould favour the conception that those capable of IgG response to the antigen have more securely established Th1 predominant immunity protecting them from atopy under the study circumstances, while sensitization and allergy development is provoked among those already prone to Th2. If so, a later follow-up should show a similar rate of atopy in study group and controls. There has been much debate on the hygiene hypothesis first proposed in the late 1980s, not all have been certain about the roles of Th1 and Th2 (McGeady 2004, Holt P 1999, Pitrez et al. 2005, Sheikh et al. 2003,Strachan 1999 and Varner 2002, von Hertzen et al. 2006).

6.3 Renovation

The rapid and thorough renovation of the water-damaged school building and simultaneous decrease in the prevalence of respiratory symptoms and infections confirmed that exposure to moulds and other irritants found in damp buildings were the most important factors affecting to the health of the children. This intervention study showed the importance of proper renovation procedures for moisture damage in improving respiratory health.

After the renovation new microbiological samples were taken, and only slight growth of mould species commonly appearing in this kind of environment was found (Leivo et al. 1997). Mechanical ventilation was started at the beginning of November 1995 when the ground floor was dry. No observation of moisture damage or any indication of exceptional microbial growth was found in the respective samples of school C. The policy-maker and authorities of the community made prompt decisions for fast actions concerning of the renovation of the school building. Although the decisions of renovation procedures were fast, the longest time of exposure to moulds among schoolchildren was six years.

6.4 Reliability and validity of questionnaires

The questionnaire used in this study has been applied in many other studies in Finland (Immonen et al. 2001, Meklin et al. 2002, Timonen et al. 1995, Taskinen et al.1999). In studies using a questionnaire as the only source of information on many variables there is always a risk of bias. In many of the earlier studies both variables, children's health and dampness in their house are based on parents' opinion and are thus prone to under-reporting and over-reporting (Table 2 in review of the literature).In many studies possible bias has been suspected and found to exist (Bornehag et al. 2004, Dales et al. 1997 and Handall et al. 2004).

The fifth aim was to test the reliability of self-reported symptoms and diseases and to establish possible recall biases among the study groups. Self-administered questionnaires on exposure, morbidity or the use of health services are commonly used in epidemiological studies. In simple terms, in a typical epidemiological study causes for outcomes are being solved. The outcome is usually clearly defined. In most early studies referred to a review of literature, both effector (dampness in some form) and outcome (children's' health) are reported and conclusions drawn without further study. Technically, by the multivariate technique, results within accepted and significant limits may be obtained. However, if variables are not defined correctly and in a way that comparisons can be made at group level among both causes and outcomes and even between different studies, a technically satisfactory outcome of a study is unreliable. Bornehag et al. 2004 studied a selection bias in their study on home dampness and symptoms among children. Families were more inclined to participate if the child had many symptoms, if a family member smoked, if they had avoided pet-keeping and belonged to a higher social group. In some cases (Andrea et al.1988), validation constitutes part of the study.

When our first questionnaire was sent, the water damage at school E was obvious, and the parents were aware of it, and this situation could have caused bias and weakened the comparability of the questionnaire between school E and school C. The strength of our study was the availability of use data from both questionnaire and medical records. In this study information from questionnaires was thus compared with patients' records from the local health centre. From September 1994 to September 1996, all visits because of respiratory infections or allergic diseases were recorded for this study. However, the findings based on patient records at the health center gave the same results as the questionnaires in respect of occurrences of respiratory infections, antibiotic medication and number of visits to a physician, and statistically significant results were found from both sources.

With the possibility of comparing information from questionnaires and patients' records, we could estimate reliability concerning visits to a doctor and use of antibiotics. Although there was some under-reporting of visits to a doctor and use of antibiotics in the control group, the accuracy among the study group was better. The possibility of recall bias, especially among the study group was inclined toward over-reporting. When accuracy was considered using data from patients' records as a comparison to data from questionnaires, no over- reporting of visits to a doctor or use of antibiotics was found on a group level although individual variations were found in both groups.

This inconsistency does not thus disturb our study setting or jeopardize accurate and valid results and conclusions.

7. Summary and conclusions

1. Children in the moisture-damaged school evinced significantly more respiratory symptoms and infections than controls. There was also a significant difference when comparison was made between the children using the worst damaged classroom with visible mould and the rest of the index school, this indicating dose-response. Common colds, respiratory symptoms and visits to a doctor were significantly more common (Cl 0.05) and respiratory symptoms and use of antibiotics tended to be (CI 0.10) more common among exposed than among unexposed children. In view of the small numbers of children results were also tested using Confidence interval 0.10.
2. After the repair of the school building the only significant difference in the spring term 1996 was found when visits to a doctor among exposed children were compared to those of unexposed children. The changes were also compared based on the information from the patients' records. Among the exposed children visits to doctors and the use of antibiotics decreased significantly (CI 0.1) when spring terms were compared. No significant change was found among unexposed children.
3. The number of IgG findings positive to moulds per child was higher among the exposed children. Accordingly, IgG findings at group level seemed to indicate recent exposure to moulds and hence moisture damage at school. There was no correlation between the number of elevated IgG findings and respiratory symptoms or diseases at the individual level.
4. Levels of allergen-specific IgE antibodies (Phadiatop) were measured among randomly selected groups from both schools in order to test for athopy and sensitization to common environmental allergens. There was a clear correlation between positive findings in elevated Phadiatop tests and exposure to moulds. The differences were significant when the study group was compared to the control group and when the most severely exposed group was compared to the control group or to the rest of the index school.
5. Later, in addition to levels of allergen specific IgE, values for antibodies found in Phadiatop and IgE specific to two more moulds were also measured. We found detectable levels of mould-specific IgE in only one index case and 2 controls.
6. The level of allergen-specific IgE had a negative correlation with the number of positive IgG titers among the index group. This may simply infer to the established immune balance, favouring either Th1 or Th2 type of response. That exposed sensitized (with increased levels of allergen specific IgE in Phadiatop test) children do not actively produce IgG antibodies to the moulds in the indoor environment further emphasizes this dichotomy.

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