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Immunol Allergy Clin N Am
28 (2008) 485–505

IMMUNOLOGY
AND ALLERGY
CLINICS
OF NORTH AMERICA

Dampness and Mold in the Indoor Environment: Implications for Asthma

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The National Institute for Occupational Safety and Health receives weekly requests to help with issues of indoor environmental quality in relation to illness in nonindustrial workplaces, such as office buildings and schools. Since the mid-1990s, there has been a marked increase in the number of these requests to the point where in 2007 they represented 57% of the total of 390 requests for evaluation of the workplace in relation to health and safety issues. As an example of requests concerning work-related asthma, from January 2007 through December 2007, there were 39 requests in relation to asthma, 34 (87%) from nonindustrial workplaces with workers concerned about indoor environmental quality. Of these 34 requests, 23 (68%) listed dampness or mold as exposures of concern. Thus, asthma in the nonindustrial environment accounts for the majority of the public's concern for possible work-related asthma, and requesters have made the association between their work-related asthma symptoms and damp/moldy environments. A recent calculation estimates that 21% (95% confidence interval [CI], 12%–29%) of current asthma in the United States is attributable to dampness/mold in homes [1].

This article presents epidemiologic findings pertinent to asthma and asthma-like symptoms in relation to exposure to dampness/mold in homes, schools, and workplaces. With regard to specific agents found in damp indoor environments that may play a role in asthma, it concentrates on mold (used synonymously with fungi) and includes some findings on bacteria. The literature on asthma in relation to dust mite or cockroach allergens is not addressed.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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0889-8561/08/$ - see front matter. Published by Elsevier Inc.
doi:10.1016/j.iac.2008.03.009

Reviews of the epidemiologic literature up to 2003

A European review (NORDDAMP) of well-designed epidemiologic studies published prior to July 1998 found that odds ratios (ORs) for cough, wheeze, and asthma associated with indoor dampness ranged from 1.4 to 2.2 [2]. A subsequent review (EUROEXPO) of studies published from 1998 to 2000 confirmed indoor dampness as a risk factor for health effects, regardless of atopic status. The investigators concluded that additional prospective studies were needed [3].

In the United States, the Centers for Disease Control and Prevention asked the Institute of Medicine (IOM) to complete a review of the scientific literature. The IOM committee reviewed studies published up to late 2003 believed influential in shaping the scientific understanding of dampness-associated health effects [4]. With respect to asthma and asthma-related symptoms, the IOM found that there was sufficient evidence for associations between exposure to damp indoor environments or mold or other agents in damp indoor environments and cough, wheeze, and asthma symptoms in asthmatic persons, and limited or suggestive evidence for associations with asthma development and dyspnea. They concluded that excessive indoor dampness is a public health problem and that prevention or reduction of this condition should be a public health goal. Among the research needs formulated by the committee were improved characterization of dampness-related microbial emissions and chemical emissions from building materials and furnishings and their roles in adverse health outcomes; studies on interaction effects of multiple exposure factors in damp indoor environments; and studies on intervention effectiveness.

Meta-analysis in 2007

A meta-analysis of 33 peer-reviewed epidemiologic studies on respiratory health outcomes and home dampness or mold included studies published from 1989 to 2006 [5]. The estimated OR for cough in adults was 1.52 (95% CI, 1.18–1.96); for cough in children 1.75 (95% CI, 1.56–1.96); for wheeze in adults 1.39 (95% CI, 1.04–1.85); for wheeze in children 1.53 (95% CI, 1.39–1.68); for current asthma 1.56 (95% CI, 1.30–1.86); for ever-diagnosed asthma 1.37 (95% CI, 1.23–1.53); and for asthma development 1.34 (95% CI, 0.86–2.10). The investigators estimated that home dampness or mold is associated with a 30% to 50% increase in respiratory health outcomes.

Dampness/mold and asthma development—recent publications

Recent research not included in the 2004 IOM report has increased the body of evidence regarding the association between dampness and asthma development (Tables 1 and 2).

Adults

In a study that investigated occupational exposures, researchers reviewed medical records at clinics in a Swedish town covering a 1.5-year period to identify cases of newly diagnosed asthma among 20 to 65 year olds [6]. Controls were randomly selected from the Swedish population registry, lived in the same town, and were matched by age and gender to cases. Response rates and study numbers for cases and controls were 90% (n = 120) and 84% (n = 446), respectively. The OR (adjusted for occupational exposure to dust, fumes, or vapors, childhood allergy symptoms, and ever smoking) for workplace exposure to building mold or moisture damage that lasted 3 or more years and occurred before the year of asthma diagnosis (for cases) or referent time (for controls) was 4.7 (95% CI, 1.5–14.3). Because this study included agricultural and maintenance workers whose exposure may differ in intensity and type from office workers in damp buildings, caution should be exercised when applying these findings to workers of nonindustrial indoor environments.

A study by Gunnbjörnsdóttir and colleagues used data from the 1990–1994 European Community Respiratory Health Surveys (ECRHS) and a follow-up survey conducted in 1999–2001 [7]. Participants from four Nordic countries were 20 to 44 years old at the time of the initial survey. Response rates and study numbers for the initial and follow-up surveys were 84% (n = 21,802) and 74% (n = 16,190). New-onset asthma was defined as an asthma attack or use of asthma medications during the past 12 months on the second survey with negative responses to both of these questions on the first survey. The OR (adjusted for age, study center, gender, body mass index, rhinitis, smoking status, type of housing, age of building, and socioeconomic status) for the association between the presence of home dampness anytime between the two surveys and new-onset asthma was 1.13 (95% CI, 0.92–1.40) and thus did not quite meet statistical significance. Associations for new-onset asthma symptoms were significant. Researchers also investigated the remission of asthma-like symptoms and found that presence of home dampness in-between the two surveys significantly decreased remission of nocturnal dyspnea and nocturnal cough. Analysis of a subset (Swedish subjects, n = 1854) of second survey, also by Gunnbjörnsdóttir and colleagues, participants demonstrated significant positive associations between home dampness and dyspnea at rest, dyspnea after exertion, and nocturnal dyspnea [8].

A Finnish population-based incident case-control study compared 521 adults, who had newly diagnosed asthma (defined as reversible airways obstruction with at least one asthma-like symptom) identified over a 2.5-year period, to 932 randomly selected controls who did not have asthma [9]. Response rates for cases and controls were 90% and 80%, respectively. Cases and controls were 21 to 63 years old and lived within the same hospital district in South Finland. Workplace wall-to-wall carpeting and workplace mold independently increased the risk for new-onset asthma.

Table 1
Epidemiologic studies investigating an association between indoor dampness or mold and new-onset asthma or new-onset asthma-like symptoms that use odds ratios as a measure of risk

Reference	Study design	Environmental exposure	Health outcome	Odds ratio (95% CI)
Adults				
Flodin and Jönsson [6]	Longitudinal case-control study (20–65 years old)	Reported workplace dampness (mold or moisture damage)[a]	New-onset physician-diagnosed asthma at age 20–65 years	4.7 (1.5–14.3)
Gunnbjörnsdóttir et al [7]	Prospective study with a 7.9-year follow-up period (mean age at follow up: 40 years)	Reported dampness (water damage, leakage, or mold growth) in the home[b]	New-onset asthma attack or current use of asthma medications[c]	1.1 (0.9–1.4)
			New-onset wheeze[c]	1.3 (1.1–1.5)
			New-onset nocturnal dyspnea[c]	1.3 (1.1–1.6)
			New-onset nocturnal cough[c]	1.3 (1.1–1.4)
Jaakkola et al [9]	Population-based incident case-control study (21–63 years old)	Reported visible mold or mold odor at work[c] and – No wall-to-wall carpet at work – Wall-to-wall carpet at work	New-onset physician-diagnosed asthma with both reversible airways obstruction and a history of at least one asthma-like symptom	 1.4 (0.9–2.1) 4.6 (1.1–19.4)
Children				
Wickman et al [12]	Prospective study of a birth cohort from age 2 months to 2 years of age	Reported water damage, windowpane condensation, visible mold, or mold odor when child was 2 months of age	Three or more episodes of wheezing after age 3 months and either use of inhaled steroids or symptoms suggestive of bronchial hyper-reactivity	1.7 (1.3–2.4)
Emenius et al [13]	Nested case-control study of a birth cohort (2 years old)	One sign of dampness based on home inspection	Three or more episodes of wheezing after age 3 months and either use of inhaled steroids or symptoms suggestive of bronchial hyper-reactivity	1.3 (0.8–2.2)
		Three or more signs of dampness based on home inspection		2.7 (1.3–5.4)

Pekkanen et al [15]	Population-based incident case-control study (1–7 years old)	Mold odor based on current home inspection	New-onset physician-diagnosed asthma or new referral to hospital after two or more attacks of wheezing	4.1 (0.6–26.0)
		Visible mold based on current home inspection		1.2 (0.7–2.1)
		Visible mold in main living area based on current home inspection		2.6 (1.2–5.8)
		Water damage in main living area based on current home inspection		2.2 (1.2–4.0)

[a] Present for 3 or more years and occurred at least 3 years before year of asthma diagnosis.
[b] Present any time in between the initial and follow-up survey.
[c] Present during the past year.

Table 2
Epidemiologic studies investigating an association between indoor dampness or mold and new-onset asthma that use incidence rate ratio as a measure of risk

Reference	Study design	Environmental exposure	Incidence rate ratio (95% CI)
Adults			
Cox-Ganser et al [10]	Cross-sectional study with information on dates of hire and asthma diagnosis (mean age 46 years)	Office building with water damage and mold contamination based on building inspection	7.5 (no CI)
White et al [11]	Cross-sectional study with information on dates of hire and asthma diagnosis (mean age 48 years)	School building with evidence of water damage and mold contamination based on building inspection	8.5 (no CI)
Children			
Jaakkola et al [14][a]	Population-based cohort study with a 6-year follow-up period (1–7 years old at baseline)	Reported mold odor in the home[b]	2.4 (1.1–5.6)
		Reported visible mold in the home[b]	0.6 (0.2–1.7)
		Reported moisture on surfaces in the home[b]	0.9 (0.5–1.5)
		Reported water damage in the home[b]	1.0 (0.4–2.3)
		Any of above dampness indicators	1.0 (0.7–1.5)

[a] Cited in Fisk WJ, Lei-Gomez Q, Mendell MJ. Meta-analyses of the associations of respiratory health effects with dampness and mold in homes. Indoor Air 2007;17:284–96.
[b] Present during the past year at time of initial survey.

Workplace wall-to-wall carpet together with workplace mold further increased the risk for new-onset asthma. Results were adjusted for gender, age, education, personal smoking, environmental tobacco smoke, water damage, and damp spots at home. It is possible that carpets acted as a reservoir for moisture and related contaminants.

Two cross-sectional studies of United States office and school employees who worked in buildings with water damage and mold contamination found postoccupancy adult-onset asthma incidence densities to be 7.5 and 8.5 times greater than preoccupancy incidence densities, respectively [10,11]. Although, incidence rate ratios (IRRs) were not adjusted for demographic variables, pre- and postoccupancy asthma incidence densities were calculated for the same group of participants. These studies support a temporal association, which is important in establishing a causal association of exposure with disease.

Children

A birth cohort study of 4089 Swedish children at 2 months old and 1 and 2 years old found a positive association between damp home environment and asthma development 1.74 (95% CI, 1.28–2.39), adjusted for gender, parental history of allergic disease, socioeconomic status, maternal age, exclusive breastfeeding, maternal smoking, pet ownership, and age of building [12]. Data on damp home environment were taken from the first questionnaire when the children were 2 months old. Asthma was defined as at least three episodes of wheezing between 3 months and 2 years of age, in combination with treatment of inhaled glucocorticoids or signs of hyperreactivity without upper-respiratory infection. In a subsequent nested case-control study of the same birth cohort, 181 children who met the case definition were compared to 359 age-matched healthy controls [13]. Information on damp indoor conditions came from the baseline questionnaire and from home inspections in the first winter season after recruitment into the case-control study. There were consistent positive associations between indicators of dampness/mold in the home and being a case. A strong finding was that there was an increasing risk for recurrent wheezing with an increasing number of indicators of dampness found during the home inspections: one indicator of dampness was associated with an OR of 1.3 (95% CI, 0.8–2.2), whereas having three or more dampness indicators was associated with an OR of 2.7 (95% CI, 1.3–5.4).

A cohort study of randomly selected children from the Finnish population registry used results from a survey at age 1 to 7 years and another survey 6 years later [14]. Response rates and study numbers for the initial and subsequent surveys were 80% (n = 2568) and 77% (n = 1984), respectively. Children were considered exposed if mold odor, visible mold, dampness, or water damage had been reported in the home prior to the baseline study. The IRR for asthma comparing children exposed (n = 384) and nonexposed

(n = 1532) to mold odor was 2.44 (95% CI, 1.07–5.60) after adjustment for age, gender, duration of breastfeeding, parental education, single parent, maternal smoking during pregnancy, environmental tobacco smoke exposure, gas cooking, presence of furry or feathery pets, and type of child care. One of the major strengths of this study was its prospective study design, which eliminated over-reporting of pre-existing home mold based on newly diagnosed asthma and provided evidence for a temporal relationship between home mold and asthma.

Other Finnish researchers conducted a case-control study of children newly diagnosed with asthma at the university hospital in Kuopio, Finland [15]. Cases were defined as children 1 to 7 years of age who had been referred to the hospital because of two or more attacks of wheezing within the past year or were newly diagnosed with asthma. Controls who did not have asthma were randomly drawn from the Finnish population registry and matched by age, gender, and municipality to cases. Cases and controls were required to have lived at least 2 years or at least 75% of their lifetime in their current homes. Participation rates and study numbers for cases and controls were 98% (n = 121) and 84% (n = 241). Homes were inspected for evidence of mold odor, visible mold, and water damage. Models adjusted for parental asthma, paternal education, number of siblings, indoor pets, and daycare attendance during the first year of life yielded significant results for water damage in the main living area (OR 2.24; 95% CI, 1.25–4.01) and visible mold in the main living area (OR 2.59; 95% CI, 1.15–5.85). The study found a trend for increased risk for newly diagnosed asthma with each additional square meter of observed home water damage (OR 1.36; 95% CI, 0.91–2.03).

Dampness/mold and dyspnea—recent publications

Recent studies have investigated associations with dyspnea, nocturnal dyspnea, dyspnea during exertion, dyspnea after exertion, and dyspnea at rest, with differing results. The findings of Gunnbjörnsdóttir and colleagues in relation to dyspnea were discussed previously. Park and colleagues developed a grading system for visible water stains, visible mold, mold odor, and moisture, which they applied in an investigation of 1231 employees (mean age 51 years) of a United States community college that had several water-damaged buildings [16]. Dampness indicators in models adjusted for age, gender, smoking, job status, year of hire, allergies, and use of latex gloves were shown to predict risk for dyspnea present during the past 12 months that improved away from the building.

Others have compared the prevalence of work-related dyspnea among employees in water-damaged and mold-contaminated buildings to a United States survey of office workers in nonproblem buildings [10,17]. Work-related dyspnea was defined as shortness of breath that occurred 1 or more days per week in the past 4 weeks and which improved away from

work. Although analyses could not be controlled for demographic factors, researchers found significantly elevated prevalence rate ratios (2.2 to 4.6) that suggested an association between building dampness and dyspnea.

Researchers in Norway studied 2819 randomly selected adults, ages 26 to 81 years, who resided 11 years earlier (time of first survey) in the same county in Western Norway [18]. Response rate for the survey was 89%. In logistic regression models adjusted for age, gender, smoking status, educational level, pack years, and occupational exposure to dust or fumes, visible mold in the home significantly increased the risks for dyspnea when climbing two flights of stairs at an ordinary pace and of attacks of dyspnea (OR 2.3 [95% CI, 1.35–3.85] and 1.7 [95% CI, 1.06–2.72], respectively).

In summary, all nine studies (five adult studies and four pediatric studies) addressing environmental dampness and new-onset asthma published since the IOM report demonstrate some significant associations between environmental dampness and new-onset asthma or new-onset asthma-like symptoms. Additionally, all five adult studies investigating associations between environmental dampness and dyspnea found some significant associations between one or more measures of dyspnea and environmental dampness. Two of these studies showed an exposure-response relationship.

Microbial exposures in damp environments and asthma and asthma-like symptoms—recent publications

Recent research has advanced the knowledge on associations between asthma development or asthma-like symptoms and fungi and bacteria (Table 3). Limitations of sampling and analytic methods for microbial agents and lack of knowledge on which specific fungi or microbial agents are relevant measures of risk for respiratory illness have hampered exposure assessment. Such limitations include (1) lack of personal sampling methods for estimating long-term exposure to airborne microbes or microbial agents, (2) difficulty in accounting for the large temporal and spatial variability of airborne microbial agents with standard short-term sampling methods, (3) high sampling and analytic cost, and (4) lack of standardized analytic methods. Despite these limitations, measured exposure assessments are necessary to obtain evidence on possible etiologic agents of disease.

Adults

A longitudinal study of subjects who participated in the ECRHS in Melbourne, Australia, followed 360 adults (20 to 45 years old) over a 2-year period with regard to measured home exposures and the development and remission of asthma [19]. The investigators measured dust mite and cat allergens and ergosterol (the principal sterol in fungal membranes) in bedroom floor and bed dust samples and culturable fungi from bedroom air samples at the onset of the study and 2 years later. They found that

Table 3
Epidemiologic studies investigating an association between microbial agents and asthma and asthma-like symptoms

Reference	Study design	Health outcome	Odds ratios						
			Total fungi	Specific fungi	Other fungi	Fungal biomass	Endotoxin	Bacteria	MVOC
Adults									
Matheson [19][a]	Longitudinal study: home (20–45 y)	Development:							
		Current asthma	1.5 (a)	1.0 (Cla/a)	1.1 (a)	1.1 (Erg/fd)	–	–	–
		Asthma attack	1.5 (a)	**1.5** (Cla/a)	1.2 (a)	1.0 (Erg/fd)	–	–	–
		PD asthma	0.9 (a)	1.0 (a)	1.0 (a)	1.5 (Erg/fd)	–	–	–
		Remission:							
		Current asthma	1.2 (a)	1.1 (Cla/a)	0.9 (a)	1.1 (Erg/bd)	–	–	–
		Wheeze	1.0 (a)	1.0 (Cla/a)	1.0 (a)	0.8 (Erg/bd)	–	–	–
		BHR	1.0 (a)	1.0 (Cla/a)	0.9 (a)	0.9 (Erg/bd)	–	–	–
Park et al [20][b]	Case-control study: office (mean age 46 y)	Post-occupancy	1.6 (fd)	**2.2** (Hyd/fd)	0.7 (fd)	1.4 (Erg/fd)	1.4 (fd)	–	–
		PD asthma	**1.7** (cd)	**1.9** (Hyd/cd)	1.3 (cd)	1.6 (Erg/cd)	1.2 (cd)	–	–
		PD asthma or	**1.7** (fd)	**1.8** (Hyd/fd)	1.1 (fd)	**1.6** (Erg/fd)	**1.5** (fd)	–	–
		asthma symptoms	**1.6** (cd)	**1.6** (Hyd/cd)	1.3 (cd)	**1.5** (Erg/cd)	1.1 (cd)		
Park et al [21][c]	Cross sectional study: office (mean age 46 y)	WR wheeze	**2.0** (fd)	—	—	—	**2.5** (fd)	–	–
		WR chest-tightness	**1.9** (fd)	—	—	—	**2.2** (fd)	–	–
		WR shortness of breath	**2.4** (fd)	—	—	—	1.9 (fd)	–	–
		WR cough	**1.7** (fd)	—	—	—	1.3 (fd)	–	–
Salo et al [22][c]	Cross sectional study: home (73% >18 y)	Current PD asthma	–	**1.7** (Alt/sd)	–	–	–	–	–

Children										
Douwes et al [26][d]	Birth cohort study: home (1–4 y)	PD asthma by age 4	—	—	—	**0.4** (EPS/fd) 0.7 (Glu/fd)	**0.4** (fd)	—	—
		Persistent wheeze in past 4 years	—	—	—	**0.4** (EPS/fd) 0.4 (Glu/fd)	0.7 (fd)	—	—
Hyvärinen et al [27][e]	Case-control study: home (1–7 y)	Development of asthma	—	1.1 (Mes/hd) 1.1 (Xer/hd)	—	1.1 (Erg/hd)	0.7 (hd)	1.2 (Mes, Act/hd) 1.0 (Mes/hd)	—
van Strien et al [28][b]	Cross-sectional study: home (6–14 y)	PD asthma	—	—	—	—	—	1.1 (Mur/bd)	—
		Wheeze	—	—	—	—	—	0.6 (Mur/bd)	—
Kim et al [29][f]	Cross- sectional study: elementary school	PD asthma	0.94 (a)	—	—	—	—	**0.97** (a)	**2.1** (a)
		Nocturnal breathlessness	0.84 (a)	—	—	—	—	**0.92** (a)	**5.2** (a)
		Daytime breathlessness	0.94 (a)	—	—	—	—	0.97 (a)	1.8 (a)
		Wheeze	0.93 (a)	—	—	—	—	0.99 (a)	1.4 (a)

ORs in bold font are significant for $P \leq 0.05$. Underlined ORs are marginally significant for $0.05 < P \leq 0.10$.

Abbreviations: a, airborne; act, actinomycetes; Alt, *Alternaria*; bd, bed dust; BHR, bronchial hyper-reactivity; cd, chair dust; Cla, *Cladosporium*; EPS, extracellular polysaccharide of *Penicillium* and *Aspergillus* species; Erg, ergosterol; fd, floor dust; Glu, glucan; hd, house dust; Hyd, hydrophilic; Mes, mesophilic; mur, muramic acid; PD, physician-diagnosed; sd, surface dust; WR, work-related; Xer, xerophilic.

[a] ORs are for twofold increase of exposure in the second survey compared to the first survey.

[b] ORs are for IQR increase (cfu/g dust) in exposure.

[c] ORs are for highest tertile compared to lowest tertile exposure group.

[d] ORs are ratios are for high compared to low exposure group.

[e] ORs are for each 0.01 nm/mg increase of endotoxin, 10^5 cfu/g increase of mesophilic bacteria, 10^3 cfu/g increase of mesophilic actinomycetes, 10^3 pg/mg increase of ergosterol, 10^5 cfu/g increase of mesophilic fungi, and 10^5 cfu/g increase of xerophilic fungi.

[f] ORs are for each $10^2/m^3$ increase of bacteria or mold and 1 $\mu g/m^3$ increase of total MVOC.

increase in exposure to airborne *Cladosporium* over the study period significantly increased the risk for an asthma attack (OR 1.52; 95% CI, 1.08–2.13). An increase in airborne total culturable fungi over the study period also increased the risk for an asthma attack (OR 1.54; 95% CI, 0.98–2.43) and the development of asthma (wheezing in the past 12 months with bronchial hyper-responsiveness) (OR 1.53; 95% CI, 0.93–2.53). Despite the use of short-term (1-minute) air samples for fungal measurements, positive associations were found. Conversely, although ergosterol levels in dust may better represent long-term exposure, the investigators found no associations.

A case-control study was nested within the cross-sectional study (discussed previously) of 888 participants working in a large water-damaged building in the United States where there was a large increase of postoccupancy adult-onset asthma [10,20]. Fungal exposures for 49 cases of current physician-diagnosed postoccupancy asthma and 152 controls (who had no lower respiratory and systemic symptoms and no physician diagnosis of asthma, hypersensitivity pneumonitis, or sarcoidosis) were compared using logistic regression models (adjusted for age, gender, race, smoking status, and building occupancy period). Researchers found postoccupancy asthma significantly associated with dust-borne total and hydrophilic (water-loving) culturable fungi (yeasts, *Phoma herbarum*, *Chaetomium globosum*, *Mucor plumbeus*, *Rhizopus stolonifer*, and *Stachybotrys chartarum*) in a linear exposure-dependent manner. Interquartile ranges (IQRs) were calculated by subtracting the 25th percentile values from the 75th percentile values. ORs for the risk for postoccupancy onset asthma per IQR of total culturable fungi in floor and chair dust were 1.6 (95% CI, 0.96–2.53) and 1.7 (95% CI, 1.07–2.60), respectively. ORs for the risk for postoccupancy asthma per IQR of hydrophilic fungi in floor and chair dust were 2.2 (95% CI, 1.23–3.89) and 1.9 (95% CI, 1.19–2.89), respectively. In a cross-sectional analysis using all 888 participants, the same floor dust samples ($n = 338$) analyzed for culturable fungi and endotoxin (the biologically active lipopolysaccharide found in the cell walls of gram-negative bacteria) were used to establish low-, medium-, and high-exposure categories [21]. Symptoms were defined as building related if they improved when away from the building. The investigators found that fungi and endotoxin in dust were significantly associated with building-related asthma-like symptoms in an exposure-dependent manner (range of OR for wheeze, chest tightness, attacks of shortness of breath, and attacks of cough: 1.7 [95% CI, 1.02–2.77] to 2.4 [95% CI, 1.29–4.59] in the highest fungal exposure group compared to the lowest and 1.3 [95% CI, 0.77–2.19] to 2.5 [95% CI, 1.30–4.90] in the highest endotoxin exposure group compared to the lowest). The study also demonstrated that workers exposed to high levels of endotoxin and fungi showed much higher risks of building-related wheeze, chest tightness, and shortness of breath compared to workers exposed to high levels of fungi or endotoxin alone, implying a synergistic effect of endotoxin and fungi.

A large United States cross-sectional study using a nationally representative sample of 831 residential homes (2456 residents) found that exposure to *Alternaria alternata* allergen in surface dust was associated with an increased risk for current asthma (physician-diagnosed asthma with asthma symptoms in the past year) [22]. The OR for the second tertile was 1.45 (95% CI, 0.88–2.39) and for the third tertile was 1.73 (95% CI, 1.08–2.77), in models adjusted for age, gender, race, education, smoking, sampling season, dust mite allergens, cockroach allergen, cat and dog allergens, mouse urinary protein, dust weight, and endotoxin, suggesting a linear exposure-response relationship. In models with *A alternata* in dust as a continuous variable and which adjusted for demographics, smoking, and sampling season, the risk for current asthma increased by 31% with each twofold increase in *A alternata* allergen concentration.

A United States study of 190 patients who had asthma and 36 patients who had rhinitis measured forced expiratory volume in 1 second (FEV_1) and analyzed dust samples collected from the homes of patients for (1→3)-β-D-glucan (a major carbohydrate constituent of fungal cell walls) and endotoxin [23]. In unadjusted quartile models with mean levels of bed and floor dust endotoxin and (1→3)-β-D-glucan as the exposures and FEV_1 percent predicted as the outcome, exposure to endotoxin was associated with a 3% to 6% decrease in FEV_1 percent predicted (with a nonlinear relationship). Exposure to increased levels of (1→3)-β-D-glucan had no association with FEV_1 percent predicted. A strength of this study was the use of objective pulmonary measurements. A possible limitation was that subjects who did not have asthma or rhinitis were not included for comparison.

In a Turkish case-control study, researchers collected 4-hour airborne fungal samples from living rooms during the winter and compared the levels of culturable fungi in homes with adult patients who had asthma with those in homes of controls [24]. They found that the airborne fungal levels in homes of cases and controls were not different. A limitation of this study was the single measurement per home. Considering that temporal and spatial variations of the airborne fungal concentration are large and that asthma is a chronic disease, their negative finding might have resulted from exposure misclassification.

In a cross-sectional study in Denmark of 522 teachers from 15 schools (8 wet and 7 dry), researchers estimated individual teacher exposures based on dust and air sample measurements from rooms ($n = 107$) and the number of hours spent in these rooms [25]. Using multivariate logistic regression analyses with three categories of exposure (adjusted for demographics, psychosocial work conditions, and building characteristics), they did not find any significant associations between asthma or objective pulmonary measurements (FEV_1, forced vital capacity, and methacholine challenge test results) and exposure to fungi in dust or endotoxin or other microbial agents in dust and air. Although the levels of fungi in dust from rooms in the wet and dry schools were not high, there was approximately a 150-fold

difference between the highest and lowest exposure values in the classrooms. The researchers pointed out that the study was conducted in schools with no history of excessive indoor air problems or health concerns. Therefore, these schools did not represent worst-case scenarios.

Children

In a prospective birth cohort study in the Netherlands, researchers collected dust samples from homes of 696 healthy infants at age 3 months and assessed their respiratory health 4 years later [26]. Mothers of all infants had allergy or asthma. Eighteen percent of the infants developed physician-diagnosed asthma. Dust samples were collected from living room floors and the infants' mattresses and were analyzed for endotoxin, (1→3)-β-D-glucan, and extracellular polysaccharide (carbohydrate in fungal cell walls) of *Aspergillus* and *Penicillium* species (EPS-*Pen*/*Asp*). They found that exposure to increasing levels of living room endotoxin and EPS-*Pen*/*Asp* during the first 3 months of life had significant protective effects on development of asthma during the first 4 years of life. Using models adjusted for gender, region, parental education, exposure to indoor tobacco smoke, and number of children in the household, the protective effect in the medium exposure group for endotoxin (OR 0.47; 95% CI, 0.26–0.86) was stronger than in the medium exposure group for EPS-*Pen*/*Asp* (OR 0.78; 95% CI, 0.40–1.55); and the protective effect in the high exposure group for endotoxin (OR 0.40; 95% CI, 0.21–0.77) was similar in strength to the high exposure group for EPS-*Pen*/*Asp* (OR 0.42; 95% CI, 0.18–0.99). The investigators found no associations of exposure to (1→3)-β-D-glucan with asthma development.

A case-control study in Finland investigated home characteristics and levels of various microbial agents, including endotoxin, 3-hydroxy fatty acids (a biomarker of lipopolysaccharide), ergosterol, fungi, and actinomycetes (a large group of gram-positive bacteria), in house dusts of 36 children who had newly diagnosed asthma or who were referred to a hospital because of a history of two or more attacks of wheezing and 36 control children (age range 1 to 7 years old) [27]. Researchers found an increased risk for developing asthma with exposure to higher concentrations of mesophilic actinomycetes, mesophilic and xerophilic fungi, and ergosterol (adjusted OR range 1.08–1.18). In this study, ORs were small and statistical significance was marginal, possibly because of small sample size.

A cross-sectional study performed in rural areas of three countries in Europe collected dust samples from the mattresses of children and analyzed these samples for endotoxin and muramic acid (a sugar in the peptidoglycan layer of bacterial cell walls) [28]. They studied 241 farm and 311 non–farm school children through a questionnaire and a skin test for a mixture of aeroallergens (grass pollen, birch pollen, mugwort pollen, Der p1, cat dander, dog dander, and *Cladosporium herbarum*). In an analysis stratified by sensitization, they found that muramic acid had a protective effect on

wheeze in the past 12 months and on physician-diagnosed asthma in a linear exposure-dependent manner among nonsensitized children. Among the sensitized children, however, no linear exposure-response relationship was found. In this analysis, they adjusted for age, gender, study area, family history of asthma or hay fever, educational level of parents, number of older siblings, living on a farm, and mattress dust endotoxin concentration. Thus the effect of muramic acid was independent of endotoxin and farming environments. This study suggests that the effect of exposure to specific microbial agents on asthma and asthma symptoms in children may be modified by sensitization status.

A cross-sectional study of 1014 primary school children in Sweden analyzed culturable fungi and bacteria, microbial volatile organic compounds (MVOCs), plasticizers, and total fungal and bacterial counts in air samples collected from 23 classrooms in eight schools [29]. Researchers used school-specific mean values of each analyte as an average exposure for all participants in each school. In logistic regression models adjusted for age and gender, they found significant positive associations between exposure to several individual MVOCs and wheeze, nocturnal dyspnea, and physician-diagnosed asthma (OR range 1.03–3.41); total MVOCs and nocturnal dyspnea (OR 5.25; 95% CI, 1.82–15.18) and physician-diagnosed asthma (OR 2.07; 1.09–3.93); and a plasticizer (2,2,4-trimethyl-1,3-pentanediol diisobutyrate) and wheeze, daytime dyspnea, nocturnal dyspnea, and physician-diagnosed asthma (OR range 1.85–5.71). One study limitation was the assumption that measured volatile organic compounds were of microbial origin. Significant but small protective effects were found for total fungal counts on wheeze in the past 12 months (OR 0.98; 95% CI, 0.96–1.00), total bacterial counts on nocturnal dyspnea in the past 12 months (OR 0.92; 95% CI, 0.87–0.98), total culturable bacteria on nocturnal dyspnea (OR 0.92; 95% CI, 0.87–0.98), and total culturable bacteria on physician-diagnosed asthma (OR 0.97; 95% CI, 0.94–1.00). The investigators questioned these protective effects and discussed that exposure misclassification bias may have occurred due to restrictions on opening of windows during the sampling period; however, how this misclassification produced the small protective effects of fungal and bacterial exposure is not clear.

A 1-year study followed 17 children who had asthma and rhinitis and two children who had rhinitis alone who had a positive skin test for one or more fungal allergens (*Cladosporium, Alternaria, Penicillium,* or *Aspergillus*) [30]. Over a 1-year period, researchers collected monthly air samples for culturable fungi from the homes of the children. The researchers did not find significant correlations between total or individual airborne culturable fungi and daily asthma score (based on symptoms, daily medication use) and morning or evening peak expiratory flow. Only simple correlations between mold levels and health outcomes were performed, however. Longitudinal data analysis accounting for correlations among

repeated measurements adjusted for demographics and other potential confounding factors may have provided more reliable and complete results.

These studies present evidence that exposures to specific microbial agents in damp indoor environments are associated with development of asthma and asthma-like symptoms in adults. In contrast, studies among infants and young children have found adverse and protective effects. This duality of response in infants and children to microbial exposures has been a topic of much discussion in the literature since the effects of unhygienic conditions in relation to the development of allergic illnesses were first published [31]. A recent editorial expands on the complexities of exposure characteristics and genetic factors that may influence health outcomes [32].

Intervention studies in relation to asthma and asthma-like symptoms

Three damp/moldy building remediation health studies with some aspects pertinent to asthma or asthma-like symptoms were reviewed by the IOM; two were among children in Finnish schools [33,34] and one was among office workers [35]. All three studies reported some decrease in respiratory symptoms after remediation. Among the office workers, there was no new asthma after relocation or after return to the remediated building. Prevalences of chest tightness, shortness of breath, cough, and wheeze among office workers were not reduced by 4 months after relocation but were lower 4 years after relocation. Eight newer studies are discussed.

Workplace intervention studies

A Danish study of employees of a damp/moldy swimming pool complex (which included an office building), before and after remediation, indicated drops in irritative and nonspecific symptoms, but lower respiratory symptoms were not studied [36]. Remediation included replacement of the roof and damp insulation materials below the roof, replacement of portions of the ceiling that were water damaged or contaminated with mold, cleaning of the inner building surfaces, and cleaning of the ventilation system. Researchers were able to document a significant decline in peak flow variability (20% to 15%) based on 2-week peak flow monitoring results before and 6 months after remediation, indicating intervention effectiveness.

A double-blind multiple crossover study in office workers in three Canadian office buildings investigated the effect of ultraviolet (UV) germicidal lights installed in the heating, ventilation, and air conditioning (HVAC) systems on symptoms [37]. Despite noninclusion of buildings with known outbreaks of building-related illness or which were known to have substantial microbial contamination, researchers found that the use of UV lights lowered the prevalence of cough, chest tightness, and difficulty breathing. This effect was seen most strongly among never-smokers. The UV lights led to a 99%

reduction of microbial contamination on exposed surfaces within the HVAC system but had no effect on airborne microbial concentrations.

School intervention studies

A study of a Swedish school with moisture problems found a decrease in lower respiratory symptoms (including dyspnea and cough) among the staff 7 months after remediation. Remediation consisted of ventilation of the damp concrete slab foundation and replacement of interior walls that had sustained water damage during repair of a prior roof leak. There was no change in lower respiratory symptoms among pupils but there was a decrease in some upper respiratory symptoms [38].

A 3-year follow-up of Finnish teachers in a damp/moldy school with a cluster of eight asthma cases (26%) and a reference school found that before and after remediation wheezing and dyspnea was higher in the damp/moldy school and that the asthma cases were still on similar asthma medication after remediation [39]. Remediation included replacement of mold-contaminated materials and repair of water leaks. The study did find some beneficial effects in regards to no new diagnosis of asthma and significant decreases in conjunctivitis, bronchitis, and sinusitis in the teachers after remediation.

A 5-year follow-up study of Finnish children in a damp/moldy school that underwent remediation found mixed results in terms of improvement in health after remediation [40]. Remediation included an improved rainwater drainage system, improved water barrier on the basement walls, replacement of water-permeable materials with non–water-permeable materials in building locations prone to high moisture loads, improved ventilation in crawl spaces, replacement of damaged materials, and extensive cleaning and disinfection of all surfaces after remediation. There were decreasing trends over time for sinusitis, nocturnal cough, and asthma in all students and in a smaller group of students who participated in all three surveys. There was no clear trend in other respiratory or nonspecific symptoms. Prevalences of symptoms in students who first occupied the school after remediation were lower than in the students who had occupied the school before remediation.

Another Finnish study of elementary students in a damp/moldy school and a reference school found that symptoms were higher in students in the damp/moldy school compared to the reference students before but not during remediation [41]. Researchers surmised that there could have been some over-reporting during the preremediation surveys. Remediation included correction of moisture problems, installation of a mechanical exhaust and supply ventilation system to replace the natural ventilation system, and thorough cleaning after remediation. After remediation, study symptoms prevalence at the two schools were similar (including lower respiratory symptoms of cough, wheeze, and dyspnea) indicating that remediation may have been effective in improving health.

Home intervention studies

A randomized controlled trial in the United States recruited children (2 to 17 years old) who had asthma from a pediatric hospital in Cleveland, Ohio. All children lived in a home with visible mold based on an inspection [42]. Children were randomized to remediation (n = 29) and control groups (n = 33). Home remediation included removal of mold from hard surfaces, elimination of rainwater intrusion, installation of ventilation systems to exhaust water vapor from kitchens and bathrooms, and repair of plumbing leaks. The two groups had a standardized treatment regimen and measures were taken to minimize treatment barriers. There was a significant reduction in symptomatic days per month for the remediation group compared to the control group during the 10th and 12th months of the study. In addition, there were significantly fewer emergency department visits or hospitalizations among children in the remediation group (4%) compared to the control group (33%).

A randomized control trial in South Wales studied 164 houses with dampness/mold, each with at least one occupant who had asthma [43]. Asthmatic subjects (n = 232) ranged in age from 3 to 61 years. Houses were randomly allocated to an intervention group or control group. Intervention consisted of visible mold removal, treatment with fungicide, and installation of a fan in the loft to improve ventilation. Over the 12 months of the study, asthma symptoms and asthma medication use declined in the intervention group, but no difference was found between intervention and control groups in changes in variability of peak flow.

Summary

Based on their review of the literature up to late 2003, the IOM concluded that there was sufficient evidence for associations between exposure to damp indoor environments or mold or other agents in damp indoor environments and asthma-like symptoms, and limited or suggestive evidence for associations with asthma development and dyspnea. They suggested that respiratory effects be studied through additional prospective and intervention studies. Recent epidemiologic studies not included in their report provide additional evidence for an association between damp indoor environments and asthma development and dyspnea. There is some evidence that remediation reduces respiratory health effects, but lower respiratory symptoms may take some time to resolve and dampness-related asthma among occupants may not completely resolve. Exposure to specific microbial agents, such as total fungi, hydrophilic fungi, *Cladosporium, Alternaria*, and endotoxin, in damp indoor environments is associated with development of asthma and asthma-like symptoms in adults; however, both adverse and protective effects have been identified in studies of infants and children.

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