

# Clinical Indoor dampness and mould health effects – ongoing & questions on microbial exposures and allergic versus Experimental nonallergic mechanisms

## Allergy

This editorial discusses the findings of the paper in this issue by R. A. Sharpe et al. [7], pp. 1566–1578.

J. M. Cox-Ganser

Division of Respiratory Disease Studies, National Institute for Occupational Health, Morgantown, WV, USA

For some time now, it has been apparent that living, working, or going to school in damp buildings is associated with adverse health effects. In 2004 and 2009, two major reviews were published relating to health effects and damp indoor environments. These were the Institute of Medicine (IOM) report [1] and the World Health Organization (WHO) guidelines for dampness and mould [2]. In 2011, a follow-up review to the WHO guidelines was published [3]. These three publications documented that occupants of damp indoor environments are at risk for upper and lower respiratory symptoms, onset and exacerbation of asthma, respiratory infections, hypersensitivity pneumonitis, allergic rhinitis, eczema, and bronchitis.

The IOM report covered pertinent literature published up to late 2003 on a wide range of health effects including asthma. The findings regarding asthma were that sufficient evidence existed for associating the presence of mould or other agents in damp buildings with asthma exacerbations and that limited or suggestive evidence existed for associating exposure to damp indoor environments with asthma development. The committee concluded that excessive indoor dampness is a public health problem and that prevention or reduction of this condition should be a public health goal.

The WHO guidelines report covered literature published up to July 2007 on a number of health effects

including asthma. Regarding asthma, it was concluded that there is sufficient epidemiological evidence of an association between indoor dampness-related factors and asthma development, asthma exacerbation, and current asthma. These findings were upheld in an updated review [3]. Recommendations from the WHO document included 'Persistent dampness and microbial growth on interior surfaces and in building structures should be avoided or minimized, as they may lead to adverse health effects'. The review paper by Mendell and colleagues in 2011 had as one conclusion that 'prevention and remediation of indoor dampness and mould are likely to reduce health risks'.

A 2007 meta-analysis of 33 studies estimated that exposure to dampness and mould in the home raises the risk for asthma development, ever diagnosed asthma, and current asthma by about 30–50% [4]. It has been estimated that 21 per cent of U.S. current asthma cases are attributable to dampness and mould, which translates to 4.6 million of 21.8 million U.S. current asthma cases attributable to dampness and mould [5]. This study also estimated the annual cost of asthma attributable to dampness and mould exposure at \$3.5 billion.

Another meta-analysis of 16 studies published between 1998 and 2011 found that the risk of developing asthma increases in relation to exposure to dampness and mould present in homes before the onset of the disease [6]. The 16 studies were cohort or incident case-control designs on infants (seven studies), children (seven studies), or adults (two studies). The presence of asthma in most studies was evaluated from self (or parent) reports of wheezing (in infants), doctor-diagnosed asthma, doctor-diagnosed bronchial obstruction, obstructive or asthmatic bronchitis or asthma (only asthma in infants), and asthma attacks/use of asthma medication. Two studies included the use of lung function testing. The signs of water damage, dampness, and

### Correspondence:

Jean M Cox-Ganser, Division of Respiratory Disease Studies, National Institute for Occupational Health, 1095 Willowdale Road, Morgantown, WV, 26508, USA.

E-mail: jjc8@cdc.gov

Cite this as: J. M. Cox-Ganser, *Clinical & Experimental Allergy*, 2015 (45) 1478–1482.

 This logo highlights the Editorial article on the cover and the first page of the article.

mould in the homes were reported by the occupants only (nine studies) or by inclusion of home inspection (seven studies). The overall summary of odds ratio (OR) for the relationship between onset of asthma and any sign of exposure was 1.50 (95% CI 1.25–1.80) based on the use of the highest effect estimates from 16 studies, while it was 1.31 (95% CI 1.09–1.58) based on the lowest reported effect estimates. A higher OR was found for the home inspection exposure estimates than for the self-reported exposures; 2.24 (95% CI 1.70–3.41) vs. 1.29 (95% CI 1.11–1.48), which argues against the associations being due to reporting bias. Separate analyses on the different signs of exposure found that the ORs ranged from lowest to highest for water damage (OR 1.12; 95% CI 0.98–1.27), dampness (OR 1.33; 95% CI 1.12–1.56), visible mould (OR 1.29; 95% CI 1.04–1.60), and mould odour (OR 1.73; 95% CI 1.19–2.50). This result was hypothesized to indicate that the microbial contamination causal to the health effect increases with prolonged dampness.

In this issue of Clinical and Experimental Allergy, Sharpe and colleagues [7] used existing population-based data on 2849 children aged 6–18 and 5563 adults from the U.S. National Health and Nutrition Examination Survey (NHANES) in 2005–2006. They investigated the associations between self-reported asthma, allergies, and eczema and exposures to self-reported mildew/musty odours in the home, and house dust concentrations of two species of fungi (*Aspergillus fumigatus* and *Alternaria alternata*), endotoxin (a cell wall component of gram negative bacteria), and dust mite, dog, cat, and cockroach antigens. They also examined serum levels of total IgE and allergen-specific IgE in relation to health outcomes. There were no major findings between the range of dust measures of contaminants and health outcomes, including for the two fungal species. The most consistent finding was that mildew/musty odour in the home was positively associated with childhood asthma (OR 1.60; 95% CI 1.17–2.19), adult eczema (OR 1.92; 95% CI 1.39–2.63), allergy (OR 1.59; 95% CI 1.26–2.02), and asthma (OR 1.61; 95% CI 1.00–2.57). Interestingly, there was a difference between children and adults in the association between mildew/musty odour and asthma when the models were stratified by level of total serum IgE. In children, the association was stronger in those with total IgE levels  $\geq 170$  KU/L, while in adults, the association was only found in those with total IgE levels  $< 170$  KU/L. As the authors speculate, this finding is consistent with indoor fungal contamination being associated with both allergic and nonallergic asthma depending on the age of the occupants. In contrast, adult eczema and allergy were associated with the mouldy odours, perhaps indicating complex allergic and nonallergic responses to fungal exposures in the indoor environment. In addition, the authors found

some evidence that being exposed to a higher number of different contaminants in the dust conferred a protective effect for childhood eczema and adult asthma.

Two issues of interest arising from the report by Sharpe and colleagues are the role of various indoor exposures in either causal or protective health effects and the range of allergenic and nonallergenic mechanisms involved in health outcomes. As they were using existing data, Sharpe and colleagues were limited in the microbial diversity they could assess in relation to health effects, and it is perhaps no surprise that the presence of mouldy odours, which indicates active microbial growth, was the best surrogate of exposure to fungal contamination, or at the very least a good indication of excessive dampness in the homes. It is currently not understood which specific contaminants or combinations thereof in damp indoor environments cause the various health effects, and results are inconsistent from study to study. In a recent review, Sharpe and colleagues [8] concluded there is some evidence that in indoor environments, *Penicillium*, *Aspergillus*, *Cladosporium*, and *Alternaria* species are associated with asthma outcomes, but that more work is needed on the role of fungal diversity. Earlier work in the United States by investigators from the National Institute for Occupational Safety and Health showed that in occupants of a historically water-damaged large office building asthma was associated with concentrations of water-loving (hydrophilic fungi) in floor dust [9] and that there was a synergistic effect between fungal exposure and endotoxin exposure in relation to respiratory health effects [10]. Other analyses on this same office building population found evidence for a nonallergic mechanism of building-related asthma, in that the presence of posthire onset asthma was associated with a lower prevalence of positive skin prick reactions to common aero-allergens including indoor and outdoor mould mixes [11].

Data from large cross-sectional studies of approximately 46,000, 8–12-year-old children in 20 countries during phase two of the International Study of Asthma and Allergies in Childhood (ISAAC) were analysed for associations between dampness and visible mould in homes and respiratory and allergic symptoms [12]. Both symptoms and home dampness/mould were reported by home occupants on questionnaire. There were significant and consistent associations between current exposure and wheeze (OR 1.58; 95% CI 1.4–1.79), coughing up phlegm without a cold (OR 1.90; 95% CI 1.59–2.26), rhinitis (OR 1.51; 95% CI 1.37–1.66), rhinoconjunctivitis (OR 1.61; 95% CI 1.42–1.83), and reported eczema (OR 1.52; 95% CI 1.34–1.73). There were no indications of effect modification by parental atopy and skin prick testing of the children (n = 26,967) for sensitization to house dust mites, cat dander, *Alternaria alternata*, mixed tree pollen, and mixed grass pollen. The authors

interpreted these results to indicate that the effects of dampness/mould on health were mainly due to non-allergic mechanisms.

A 9-year prospective follow-up study for onset of asthma was conducted on 7104 young adults from 13 countries who had participated in the European Community Respiratory Health Survey (ECRHS I and II) and had not reported respiratory symptoms or asthma at baseline [13]. Dampness and mould in the homes were assessed at baseline and at the end of follow-up by questionnaire and at the end of follow-up by building inspection for a subset of 2602 homes. A participant was considered to have new-onset asthma if in the follow-up questionnaire (s)he answered 'yes' to one or more of three questions on attacks of asthma in the last 12 months, using asthma medication, or being woken by an attack of shortness of breath in the last 12 months. This definition was met by 355 (5%) of participants. A second definition included fulfilment of the first definition and evidence of bronchial hyperresponsiveness (BHR) from testing carried out at follow-up, and this was met by 56 (0.8%) of participants. Exposure variables included: baseline reports of any water damage in the last 12 months, any mould growth in the last 12 months, ever any mould growth in the bedroom, and ever any mould growth in the living room; the same questions but combined from the baseline and follow-up survey; reports on damp spots in the last 12 months (only asked at follow-up); and observed damp spots and visible mould from the home inspections. Self-reported water damage or mould was common, with 49.7% reporting water damage and 41.7% reporting mould either at baseline or follow-up. Statistically significant associations for new-onset asthma (not including BHR) were found for both self-reported (at baseline and for both surveys) with relative risks (RR) from 1.28 to 1.48 and home inspection findings of damp spots with a RR of 1.49 (95% CI 1.00–2.22). Among participants who had not moved houses over the follow-up period, new-onset asthma combined with BHR was associated with self-reported mould in the bedroom (RR 2.64; 95% CI 1.10–6.33) and self-reported mould in the living room (RR 3.79; 95% CI 1.64–8.73). Higher RRs for new-onset asthma were found for participants who were skin prick positive for *Cladosporium herbarum* and *Alternaria alternata* at baseline. For example, for water damage in the last 12 months (reported at either baseline or follow-up surveys), the RR for participants with no sensitization was 1.60 (95% CI 1.07–2.39), while for those sensitized to mould the RR was 4.57 (95% CI 2.10–9.94).

There are few published intervention studies in relation to dampness/mould and asthma in homes, and more research in this area is needed as it speaks to the efficacy of following guidelines to remediate dampness

and mould to reduce adverse health effects. A randomized controlled trial of asthmatic children in the United States examined the effects of remediation of damp and mould contaminated home environments [14]. Two- to 17-year-old children with asthma were recruited from a paediatric hospital in Cleveland, OH, and were required to be living in a home with visible mould based on an inspection. Children were randomized to remediation ( $N = 29$ ) and control groups ( $N = 33$ ), and their asthma symptoms and medical visits were tracked for 12 months. Home remediation included the removal of mould from hard surfaces, elimination of rainwater intrusion, installation of ventilation systems to exhaust water vapour from kitchens and bathrooms, and repair of plumbing leaks. There was a significant reduction in symptomatic days per month for the remediation group compared to the control group during the 10th and 12th month of the study. In addition, during the post-remediation period, there were significantly fewer emergency department visits and/or hospitalizations among children in the remediation group (4%) compared to the control group (33%).

Another randomized control trial in Britain (South Wales) studied 164 houses with dampness/mould, each with at least one occupant with asthma (232 asthma patients between 3 and 61 years old) [15]. Houses were randomly allocated to an intervention group ( $N = 81$ ) and a control group ( $N = 83$ ). Intervention consisted of visible mould removal, treatment with fungicide, and installation of a fan in the loft to improve ventilation. Health questionnaires were given, and peak flow rates were measured, at baseline, 6 months and 12 months after randomization. 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.

More recently, Takaro and colleagues studied the effects of moving into an 'asthma-friendly, Breathe-Easy home (BEH)' on asthma outcomes in children [16]. This study had a quasi-experimental design where outcomes of children in a BEH ( $n = 34$ ) were compared with those of a matched comparison group ( $n = 68$ ). The BEHs had exterior envelopes designed to avoid moisture intrusion, interior materials that minimized dust and off-gassing, and a ventilation system with filtration and continuous fresh air supply. The children who moved into the BEHs had increases in asthma-free days, from 8.6 per 2 weeks in the previous home to 12.4 per 2 weeks after 1 year in the BEH. Furthermore, the proportion of BEH children with asthma-related urgent healthcare visits in the past 3 months decreased from 62% to 21%.

In the USA, three governmental or professional bodies issued recent reports highlighting the health effects

related to the occupancy of damp indoor environments: (1) The National Institute for Occupational Safety and Health issued an Alert on Preventing Occupational Respiratory Disease from Exposures Caused by Dampness in Office Buildings, Schools, and other Nonindustrial buildings [17]. This document includes a section on current standards and recommendations in the United States. (2) The American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) released a position document on limiting indoor mould and dampness in buildings which states that: 'Credible research and cognizant health authorities have established an association between health problems and indoor dampness. A building's mechanical systems, its exterior enclosure, and its occupant activities all affect the amount of wetting and drying indoors. Therefore, ASHRAE takes the position that all policymakers, regulatory authorities, building professionals, and building occupants should be aware that indoor dampness, mould, and microbial growth are warnings of potential problems' [18]. 3) The American Industrial Hygiene Association (AIHA) released a position statement on mould and dampness in the built environment, which uses the evidence for health effects associated with

damp indoor environments to conclude that persistent dampness and mould damage in the nonindustrial workplace, including schools and residential housing, requires prevention, management and effective remediation [19].

As discussed by Sharpe and colleagues in their report in this issue, there is much to learn about the role of exposure to microbial agents from diverse microbiomes in both the natural and built environment in relation to development and adaptation of our immune systems and how we cope with changes in such exposures at all stages of our lives. While research in these areas continues, it is prudent from a public health standpoint to recognize that damp and mouldy indoor environments are unhealthy and should be remediated or prevented in the first place with appropriate building design and maintenance.

### Disclaimer

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

### References

- 1 IOM (Institute of Medicine). *Damp indoor spaces and health*. Washington, DC: The National Academies Press, 2004.
- 2 World Health Organization (WHO). *WHO guidelines for indoor air quality: dampness and mould*. Geneva: WHO Regional Office for Europe, 2009.
- 3 Mendell MJ, Mirer AG, Cheung K, Tong M, Douwes J. Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence. *Environ Health Perspect* 2011; **119**:748–56.
- 4 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.
- 5 Mudarri D, Fisk WJ. Public health and economic impact of dampness and mold. *Indoor Air* 2007; **17**:226–35.
- 6 Quansah R, Jaakkola MS, Hugg TT, Heikkinen SAM, Jaakkola JJK. Residential dampness and molds and the risk of developing asthma: a systematic review and meta-analysis. *PLoS ONE* 2012; **7**:e47526.
- 7 Sharpe RA, Thornton CR, Tyrrell J, Nikolaou V, Osborne NJ. Variable risk of atopic disease due to indoor fungal exposure in NHANES 2005–2006. *Clin Exp Allergy* 2015; **45**:1566–78.
- 8 Sharpe RA, Bearman N, Thornton CR, Husk K, Osborne NJ. Indoor fungal diversity and asthma: a meta-analysis and systematic review of risk factors. *J Allergy Clin Immunol* 2015; **135**:110–22.
- 9 Park J-H, Cox-Ganser JM, Kreiss K, White SK, Rao CY. Hydrophilic fungi and ergosterol associated with respiratory illness in a water-damaged building. *Environ Health Perspect* 2008; **116**:45–50.
- 10 Park J-H, Cox-Ganser J, Rao C, Kreiss K. Fungal and endotoxin measurements in dust associated with respiratory symptoms in a water-damaged office building. *Indoor Air* 2006; **16**:192–203.
- 11 Cox-Ganser JM, White SK, Jones R et al. Respiratory morbidity in office workers in a water-damaged building. *Environ Health Perspect* 2005; **113**:485–90.
- 12 Weinmayr G, Gehring U, Genuneit J et al. the ISAAC Phase Two Study Group. Dampness and moulds in relation to respiratory and allergic symptoms in children: results from Phase Two of the International Study of Asthma and Allergies in Childhood (ISAAC Phase two). *Clin Exp Allergy* 2013; **43**:762–74.
- 13 Norback D, Zock J-P, Plana E et al. Mould and dampness in dwelling places, and onset of asthma: the population-based cohort ECRHS. *Occup Environ Med* 2013; **70**:325–31.
- 14 Kercsmar CM, Dearborn DG, Schluchter M et al. Reduction in asthma morbidity in children as a result of home remediation aimed at moisture sources. *Environ Health Perspect* 2006; **114**:1574–80.
- 15 Burr ML, Matthews IP, Arthur RA et al. Effects on patients with asthma of eradicating visible indoor mould: a randomized controlled trial. *Thorax* 2007; **62**:767–72.
- 16 Takaro TK, Krieger J, Song L, Sharify D, Beaudet N. The breathe-easy home: the impact of asthma-friendly home construction on clinical outcomes and trigger exposure. *Am J Public Health* 2011; **101**:55–62.
- 17 NIOSH Alert: Preventing Occupational Respiratory Disease from Exposures Caused by Dampness in Office Buildings, Schools, and Other Non-Industrial

Buildings. Principal contributors: Martin M, Cox-Ganser J, Kreiss K, Kanwal R, Sahakian N. National Institute for Occupational Safety and Health, Department of Health and Human Services, DHHS (NIOSH) November 2012. Publication Number 2013-102.

18 ASHRAE. *Position document on limiting indoor mold and dampness in buildings*. 2012. <https://www.ashrae.org/about-ashrae/position-documents>

19 American Industrial Hygiene Association (AIHA). *Position statement on mold and dampness in the built environment*. 2013. <https://www.aiha.org/government-affairs/Pages/Position-Statements-and-White-Papers.aspx>