

Exposure to Mould and Moisture Damage Is a Potential Risk Factor for the Development of Respiratory Diseases Opinion

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Abstract: Adverse health effects due to indoor air moisture damage has been extensively studied already for thirty years. Exposure to dampness microbiota (DM) in buildings is a risk factor for newly onset asthma and other respiratory problems. This exposure increases the rate of upper and lower respiratory tract infections because the function of the cilia cells and the integrity of mucosal layer becomes compromised. The breach of the first defense barrier of innate immunity leads to susceptibility to inhaled impurities and pathogens. Dampness and mould-associated asthma may present with several clinical peculiarities. This asthma may be resistant to treatment, the symptoms may exacerbate during periods with increased outdoor air humidity and rainfalls and this asthma may be associated with chronic obstructive pulmonary disease (COPD). It has been generally recognized that persons sensitized to DM should avoid new and repeated exposure to moldy environment. This recommendation is important especially during the current SARS-CoV2 pandemic.

Keywords: Mold Damage, Asthma, Respiratory Symptoms, COVID19, SARS-CoV2

1. Introduction

Moisture damage is a common problem worldwide. For example, in Finland, moisture damage occurs in at least 25% of school buildings, and these problems are also known to occur in individual houses, etc. Climate change and heavy rainfalls were linked to increased moisture damage in the buildings. Risky constructions, wetting and poor maintenance of building constructions, risky building materials, mechanical inadequate ventilation, too low air pressure in the buildings and switching off mechanical ventilation during weekends and holidays are known factors that cause hazardous indoor air moisture accumulation that damages the constructions [1].

According to WHO (2009), the exposure to dampness microbiota (DM) and decay products of the damaged building may result in respiratory symptoms. It has become indisputable already since the report of the WHO that the exposure to DM is associated with higher risks for upper and

lower respiratory tract infections [2].

2. Methods and Results

Here, we refer to a few selected literature reviews and meta-analyses (one per year after 2009) supporting the previous knowledge that the exposure to the components of moisture damage indeed causes a plethora of respiratory problems, and aggravation of existing asthma or its exacerbation. Moreover, it increases the incidence of respiratory infections (Table 1).

3. Findings and Discussion

On the basis of recent research several peculiarities of moisture-related asthma should be emphasized.

1) DM -associated asthma is more resistant to treatment.

Steroid resistance may be associated with the aberrant

T-cell activation, particularly in the TH2 / TH17 arm of immunity [3].

- 2) DM -associated asthma is often accompanied by COPD [4].
- 3) Patients with asthma who are sensitized to DM may experience symptom exacerbation at higher outdoor air humidity, e.g. in late summer and autumn [5].

Now, it is difficult to assess how these asthma peculiarities should be considered in the patients' management protocols. However, it seems appropriate to consider whether patients with mould-related disease might need higher doses of medication in the fall, for example.

In vitro and *in vivo* studies have shown a variety of inflammatory, cytotoxic, and immunosuppressive responses to spores, secondary metabolites such as mycotoxins, bacterial toxins, volatile organic compounds and decomposition products of construction building materials. Sensitization, histamine release by both IgE-mediated and non-mediated mechanisms, excessive or deprived immune responses, long-term production of inflammatory mediators leading to tissue damage and chronic low-grade inflammation are pathological mechanisms leading to adverse health effects. Exposure to DM can damage mitochondria and trigger autoimmune reactions. In bronchoalveolar lavage (BAL) of individuals exposed to DM who are symptomatic in moisture damaged-buildings, lymphocytosis and changes in CD8+ / CD4+ T-cell ratios have been reported [6]. Decreased CD19+ B lymphocyte counts in the blood have been observed too [7]. Changes in the CD8+ / CD4+ T-cell ratio in the BAL samples of patients with mould-related disease are typical for allergic alveolitis [reviewed 1]. DM activate and simultaneously deprive innate

and adaptive immunity. The components of DM may specifically destroy the function of the cilia cells of the epithelium. Thus, the barrier function of mucosal layer of bronchi may be impaired and inhaled impurities may not be removed properly [1, 8]. This dysfunction of the innate immunity paves the way for better pathogen entry.

From the end of 2019 the Globe has faced an unprecedented epidemiological situation, the pandemic of the SARS-CoV2 virus infection. International health authorities have issued recommendations concerning recognition of the risk groups and their protection, the policy had been adopted almost worldwide. For example, the Centers for Disease Control and Prevention warns people with chronic diseases to take special care during the COVID-19 pandemic (<https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html>). The following risk groups have been identified: the elderly, patients with immune suppression, such as medication, cancer, HIV, genetic immunodeficiencies; patients with hepatitis or chronic renal failure requiring dialysis, asthma or other chronic lung diseases.

DM-associated asthma or a pathological pulmonary condition that is not classified as asthma because not all asthma criteria may have been met, are not mentioned as a risk for COVID-19. This is partly because mould-related disease as a separate nosology has not been yet included into the International Classification of Diseases making statistics of this disease inaccurate and less visible. Therefore, due to this hurdle it is difficult to accumulate evidence that the exposure to DM is indeed a risk factor for COVID-19, but we can extrapolate this claim through the existing knowledge.

Table 1. A selection of meta-analyses and literature reviews one/year after 2009 providing additional evidence that residential moisture and mould damage are independent risk factors for adverse respiratory health effects and respiratory infections in particular.

Publication type and the publication year	Study design and main conclusions	Reference
Quantitative meta-analysis, 2010	Twenty-three original publications were included. Residential moisture and mould damage are associated with a significant risk for respiratory infections and bronchitis. Odds ratios (95% confidence interval): bronchitis 1.45 (1.32-1.59); respiratory tract infections 1.44 (1.31-1.59); respiratory tract infections excluding nonspecific upper respiratory tract infections 1.50 (1.32-1.70); respiratory tract infections in children and neonates 1.48 (1.33-1.65). Review of publications in peer-reviewed journals by November 2009; Total for references less than 148 because studies may have reported multiple findings.	9
Updated, comprehensive review of the epidemiological evidence collected from original studies and meta-analyses, 2011	Evident dampness or mould had consistent positive associations with multiple allergic and respiratory effects. Epidemiologic studies and meta-analyses showed indoor dampness or mould to be associated consistently with increased asthma development and exacerbation, current and ever diagnosis of asthma, dyspnoea, wheeze, cough, respiratory infections, bronchitis, allergic rhinitis, eczema, and upper respiratory tract symptoms. Associations were found in allergic and nonallergic individuals. Evidence strongly suggested causation of asthma exacerbation in children.	10
Systematic review and quantitative meta-analysis, 2012	Sixteen studies: 11 cohort and 5 incident case-control studies. The summary effect estimates (EE) based on the highest and lowest estimates for the relation between any exposure and onset of asthma were calculated. The evidence indicates that residential dampness and moulds are determinants of developing asthma. The association of the presence of visible mould and especially mould odour are risk factors for asthma and points towards mould-related causal agents.	11
Review of the literature and quantitative meta-analysis, 2013	Thirty-one studies on rhinitis, allergic rhinitis, or rhinoconjunctivitis were included. The largest risk was observed in relation to mould odor (rhinitis: 2.18 [95% CI, 1.76-2.71]; allergic rhinitis: 1.87 [95% CI, 0.95-3.68]). The risk related to visible mould was also consistently increased (rhinitis: 1.82 [95% CI, 1.56-2.12]; AR: 1.51 [95% CI, 1.39-1.64]; rhinoconjunctivitis: 1.66 [95% CI, 1.27-2.18]). In addition, exposure to dampness was related to increased risk of all types of rhinitis. Remediation of moisture and mold damage is	12

Publication type and the publication year	Study design and main conclusions	Reference
Mini review of the literature, 2014	likely to prevent chronic rhinitis. The review summarizes the available data on the low-molecular-weight toxins reliably known from fungi common on damp building materials, the toxins that have been measured on mouldy building materials and the new understanding of the role that they play in the documented health effects of individuals living and working in damp and mouldy buildings.	13
Summing-up the reviews and meta-analyses since 2004 on microbial exposures and allergic versus nonallergic mechanisms, 2015	All reviewed studies on adults and children point to the fact that staying in a moisture-damaged building puts an occupant at risk for upper and lower respiratory symptoms, such as the onset and exacerbation of asthma, and increased rate of respiratory infections, hypersensitivity pneumonia, allergic rhinitis, allergic rhinoconjunctivitis, eczema, and bronchitis.	14
Original paper estimating the costs of allergic rhinitis, acute bronchitis and asthma are due to moisture and mould damage, 2016	The total annual cost to society attributable to dampness and mould is estimated to be \$3.7 (2.3-4.7) billion for allergic rhinitis, \$1.9 (1.1-2.3) billion for acute bronchitis, \$15.1 (9.4-20.6) billion for asthma morbidity, and \$1.7 (0.4-4.5) billion for asthma mortality.	15
Review of the literature to find metrics for defining unhealthy levels of residential dampness and mould 2017	Visible mould, and odour indicative for hidden residential moisture and mould is associated with a significantly increased risk of adverse respiratory health.	16
Review of the literature to search studies of quantified building moisture and occupant health effect 2018	3 eligible studies. Water damage of building materials is an underestimated problem. Moisture in the walls of a building is linked to the development of asthma. Moisture damage is associated with respiratory health problems and allergies, as well as severe and moderate atopic dermatitis. Analyses were performed using data from adults and children combined, using only data from children, and using data from adults and children after excluding two studies	17
Meta-analysis, 2019	The odds ratios of 1.32 for cough and 1.68 for wheeze suggest moderate increases in health risk. Studies not included in the meta - analyses provide additional evidence that dampness and mould in schools are associated with adverse health outcomes.	18
Review of the the main methods for detection and characterization of fungal aerosols and in vitro research to study mould toxicity and extrapolation on airway exposure 2020	Hyphal fragments of prevalent mould species with strong pro - inflammatory potential may be particularly relevant candidates for respiratory diseases associated with dampness and mould - contaminated indoor air.	8

4. Conclusions

We suggest that recognition of DM-associated asthma and preceding respiratory problems due to DM exposure is important during the COVID-19 pandemic. Avoidance of moldy environment should be highly recommended.

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