MOISTURE DAMAGE AND FUNGAL CONTAMINATION IN BUILDINGS ARE A MASSIVE HEALTH THREAT – A SURGEON'S PERSPECTIVE

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SUMMARY

Objectives: Indoor air toxicity is of major public health concern due to the increase in humidity-induced indoor mould exposure and associated health changes. The objective is to present evidence for the causality of health threats and indoor mould exposure.

Methods: PubMed search on the following keywords: dampness, mould, indoor air quality, public health, dampness, and mould hypersensitivity syndrome, sick building syndrome, and building-related illness as well as information from the health authorities of Bavaria and North Rhine-Westphalia, the Center of Disease Control (CDC), World Health Organisation (WHO), and guidelines of professional societies.

Results: The guidelines of professional societies published in 2017 are decisive for the assessment of the impact of mould pollution caused by moisture damage on human health and for official regulations in Germany. Until 2017, a causal connection between moisture damage and mould exposure could usually only be established for pulmonary diseases. The health risk of fungal components is apparent as documented in the fungal priority pathogens list (FPPL) of the WHO. Since 2017, studies, especially in Scandinavia, have proved causality between moisture and mould exposure not only for pulmonary diseases but also for extrapulmonary diseases and symptoms. This was made possible by new test methods for determining the toxicity of fungal components in indoor air. Environmental medical syndromes, e.g., dampness and mould hypersensitivity syndrome (DMHS), sick building syndrome (SBS), building-related symptoms (BRS), and building-related illness (BRI), and fungal pathogens, e.g., *Aspergillus fumigatus*, pose a major threat to public health.

Conclusion: There is evidence for the causality of moisture-induced indoor moulds and severe health threats in these buildings. According to these findings, it is no longer justifiable to ignore or trivialize the mould contamination induced by moisture damage and its effects on pulmonary and extrapulmonary diseases. The health and economic implications of these attitudes are clear.

Key words: dampness, mould, indoor air quality, dampness and mould hypersensitivity syndrome, sick building syndrome, building-related illness

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INTRODUCTION

Climate changes with heavy rain and catastrophic floods mean that water damage and mould infestation with serious health changes are becoming more and more likely in Germany. However, despite the present challenge some official regulations in Germany are inconsistent, reveal a lack of knowledge of recent scientific reports, and therefore do not provide help. This report refers to the causality between moisture damage resulting in mould infestation and serious chronic diseases, which has been established by new reports from Scandinavia. The objective is to summarize the recent developments and demonstrate a causal relationship between multiorgan diseases and moisture-induced moulds in business and private buildings.

MATERIALS AND METHODS

A PubMed search on the keywords dampness, mould, indoor air quality, public health, dampness and mould hypersensitivity syndrome, sick building syndrome, and building-related illness was performed. Personal communication from the health authorities of Bavaria and North Rhine-Westphalia (NRW) has been included as well as official open access information from the German Environment Agency (German acronym – UBA), the Robert-Koch-Institute (German National Public Health Institute – RKI), the Center for Disease Control (CDC), the World Health Organization (WHO), and guidelines of professional societies. A statistical analysis or meta-analysis of the presented studies has not been performed due to the different study characteristics and data.

Indoor Air Science

The modern indoor air science (IAS) movement started in the 1970s. It soon became clear that indoor air is of greater importance to us in terms of our health (moisture-mould-associated allergies).

Public Health and Moisture Damage-Induced Fungal Stress

The importance of IAS was recognized in Scandinavian countries and the USA. In industrialized countries, respiratory allergy

has reached an epidemiological character (1). Many volatile organic compounds (VOC) associated with industrial manufacturing cause side effects. Until recently, indoor air pollution (IAP) by biological VOC had been a less recognized serious threat to humans, causing millions of deaths every year (2). This led to integrated home and hygiene regulations to protect public health in Italy (3).

The public health system has withdrawn from private areas in some states (personal communication from the Health Department in Bavaria). However, exposure to fungi can happen at home, hospital, at leisure, or work. High numbers and concentrations of fungal elements (conidia, hyphae fragments), bioaerosols, and mycotoxins should be considered potential hazards for humans (4). Asthma is associated with indoor humidity and mould, which can also occur in medical facilities (5).

Investigation of European Community Offices' Contamination

In an investigation by the European Union of the offices of the EC (European OFFICAIR research project), it was found out that employees in offices with higher concentrations of volatile organic compounds suffered more from health problems. Indoor air pollution poses a major threat to humanity, causing millions of deaths every year (6). That is why the causes need to be controlled and strategies to enable an improvement in indoor air quality (IAQ) need to be designed. The following diseases are attributed to IAP: sick building syndrome (SBS), and building-related illness (BRI). To do this, new tests, sensors, and IAQ monitoring systems must be developed (7).

Several studies shed light on the negative health effects concerning indoor fungus exposure and asthma, respiratory, and allergic diseases. Consequently, the Australian Government has recognized that both older and newer homes are at risk of indoor fungal contamination (8). This must be taken into account, particularly in the case of dust-intensive renovation measures (9). Removing the exposure event has the potential to improve symptoms and spirometry results compared to continuous exposure, increasing the risk of unemployment for affected employees (10). Pandemics and the associated quarantine regulations deteriorate the quality of indoor air (e.g., SARS-CoV-2 pandemic) (11).

Public Health Recommendations in Bavaria

While in North Rhine-Westphalia the health department is responsible for water damage and mould growth in publicly accessible buildings, this is not the case according to the Bavarian health administration. In Bavaria, according to a personal communication, it is reported that even in the case of damage to medical facilities in privately owned buildings, the health department has no way of influencing the owner to control the damage. Reference is made to numerous regulations and recommendations by the local health authorities but no limit value for mould indicates the concentration at which a specific health hazard must be expected. If mould is suspected in the interior, the cause should always be clarified by an expert, eliminated, and the moisture damage repaired professionally (RKI) (12).

While this recommendation applies to interiors generally (e.g. offices and other rooms in medical facilities), the Federal Environment Agency (UBA) guidelines for the prevention, recording and elimination of mould infestations in buildings point out that hospitals and similar facilities have special hygienic requirements that are not dealt with in the UBA guidelines (13). The recommendation of the Commission for Hospital Hygiene and Infection Prevention at the RKI describes the requirements for hygiene in the medical care of immunosuppressed patients (14).

Public Health Control of Water-Damaged Buildings in North Rhine-Westphalia

The situation in NRW is regulated differently. The tasks of the lower health authorities (German acronym uGB) are regulated in the "Law on the Public Health Service of North Rhine-Westphalia (German acronym ÖGDG NRW)". The mould problem is a mandatory self-government task of the uGB. The uGB promotes the protection of the population against health-endangering or health-damaging influences from the environment. It "can" take the necessary measures to prevent damage to health or long-term effects in public buildings. The exposure of a building to mould represents a health-endangering or -damaging influence. The term "public building" (cultural and educational facilities, sports and leisure facilities, healthcare facilities, office, administration, court buildings, retail, restaurant, and accommodation facilities) is based on the concept of "publicly accessible building" used in building regulations. Physical structures are publicly accessible if and to the extent that they can be visited by persons who cannot be determined in advance according to their purpose during the period of their use. The purpose is to prevent communicable diseases in humans, detect infections at an early stage, and prevent them from spreading prevent. Fungi are among the pathogens that must be prevented and combated. The public health department can take necessary measures to avert danger (15).

Center for Disease Control Statement

The Center for Disease Control (CDC) in Atlanta, USA, states that moisture and mould exposure cause reactions in the nasal mucosa, eyes, and skin in people who are exposed to these effects. People with an allergic reaction to mould or asthma have more intense reactions. In particular, severe illness with fever and shortness of breath can follow in people who are occupationally exposed to large amounts of mould. In 2004, the Institute of Medicine found sufficient evidence to identify respiratory diseases and moisture-injury asthma to be causally related to mould (16).

WHO Statement

In 2009, the World Health Organization explained in its guidelines on damp-induced microbial loads in buildings, that there is sufficient epidemiological evidence that occupants of damp or mould-contaminated buildings (both private and public) suffer from an increased risk of respiratory symptoms, respiratory infections, and aggravation of asthma. Eliminating moisture can eliminate health disorders. There is clinical evidence that exposure to mould and other moisture-induced microbial components increases the risk of rare diseases such as hypersensitivity pneumonia, allergic alveolitis, chronic rhinosinusitis, and fungal allergic sinusitis. *In vivo* and *in vitro* toxicological evidence

was obtained that diverse inflammatory and toxic responses to exposure to microorganisms isolated in damp buildings occur.

Atopic and allergic people are particularly sensitive to this; however, serious diseases occurred even in non-atopic people. There is an increasing prevalence of asthma and allergies in many countries due to exposure to the effects of dampness and mould. Indoor humidity affects 10–50% of the indoor environment in Europe, North America, Australia, India, and Japan. The amount of water on or in the building material is the decisive trigger for the growth of microorganisms which results in increased levels of spores, cell debris, allergens, mycotoxins, endotoxins, beta-glucan, and volatile organic compounds in indoor air. An excess of each of these components in the indoor environment has the potential to pose a serious health hazard and must therefore be eliminated. The building standards and regulations do not take this into account sufficiently. If humidity occurs due to water leakage, heavy rain, and flooding, persistent moisture and microbial growth in interior walls and building structures should be eliminated as this is what leads to adverse health effects. In case of condensation on surfaces or in structures, visible mould, odour, and water damage which are indicators of moisture and microbial growth professional damage control is warranted. Proper construction and building maintenance are fundamental for a healthy work- and living space. The WHO guidelines, e.g., fungal priority pathogens list (FPPL) serve to guide public health action and support the goal of optimal indoor air quality, covering both private and public buildings (17, 18).

Socioeconomic Burden of Moisture-Induced Mould Pollution

From 21.8 million Americans who suffer from asthma, 4.6 (2.7–6.3) million contracted the condition from dampness and mould in the home in which they live. In 2004, the economic impact of damp and mould growth was estimated at 3.5 billion ($2.1–4.8 billion). This poses a significant risk to public health and the American economy as well elsewhere in the world. Since dampness and mould growth have a significant impact on the health of Americans, the occurrence of damp damage and mould growth in new and older buildings must be controlled (19).

Water Damage and Fungal Contamination in Buildings

Dampness and mould are substantially and significantly associated with increased risks and rates of respiratory infections, bronchitis, and allergic respiratory diseases, including in children. Older buildings in Europe are more prone to mould growth from moisture (20). Water damage in buildings is associated with adverse health effects such as respiratory disease and asthma, as demonstrated by fungal infection using culture and immunochemical methods and epidemiological studies. Mould growth in a home, school, and office and certainly in medical facilities cannot be tolerated because of the dangers to humans and the decomposition of the building by fungi. In water damage in buildings, high-output sequencing can distinguish between visible and non-visible fungi and thus detect water damage in houses (21). The fraction of fungal hyphae fragments is in higher concentration than the corresponding spores in indoor air infestation. Hyphae fragments have a higher inflammatory potential and are considered the main cause of respiratory diseases in moisture mould infestation. Therefore, a better characterization of the biological components, including hyphal fragments, should be carried out to distinguish between pathogenic and non-pathogenic germs (22).

Water Damage-Induced Fungal Load in Buildings and Health Changes

Fungal contamination can cause allergies and trigger asthma. Positive associations were found with mild sensitization, asthma, and exposure to fungi, but not with environmental sensitization without fungal sensitization (23). IgE sensitization to *Aspergillus fumigatus* – a critical priority pathogen according to the WHO FPPL – means an increased risk of lung damage. Reactivity to *Aspergillus fumigatus* in asthmatic patients may worsen due to allergen exposure (24). In recent times mould exposure has been increasingly identified as the major cause of multi-organ changes and symptoms in patients unexplained by any other cause (25). There is a clear temporal relationship between water damage in home renovation and work-related asthma (26). The assessment of occupational diseases (allergic respiratory diseases, asthma, allergic rhinitis, hypersensitivity pneumonia, and increased risk of respiratory infections and bronchitis recognized) of water building damage with a fungal infestation is carried out in Germany according to the S2 guideline (2017) (27). However, there are more recent studies on test methods to prove the causality of the health changes induced by moisture damage.

Tests for Detection of Microbial Load and Indoor Air Toxicity

Antibody determination in mould infections and serology are still the basis of fungal diagnostics. Living or working in a damp, fungus-infested environment increases the risk of diseases such as asthma and other respiratory diseases. Identifying the cause of the disease is to focus on those fungi that are detectable in these humid environments and are associated with moisture damage. There are new specific tests to demonstrate the toxicity and causality of mould and its volatile output components. Repeated inhalation of fungal aerosols results in significant pulmonary pathology and dynamic-specific immune changes. Specific *Aspergillus* sensitization such as *A. fumigatus* – sIgE can be detected in patients with severe asthma. Immune changes should be routinely monitored because of the risk of acute exacerbation (28). High-output sequencing and an analysis of fungal fragments, detection of toxicity (boar sperm cell motility inhibition assay), cytotoxicity tests, monocyte-derived macrophage (MDM) test, focusing on microbiota that thrives particularly well in humid environments (dampness-related microbiota), and mass spectrometer imaging (MSI) have already been successfully used to demonstrate causality between moisture-associated mould growth and health changes caused by moisture-causing microbial pathogens and their volatile output components. Indoor air toxicity determinations and the investigation of particular dampness-related microbiota sampled in classrooms were causally associated with multi-organ diseases in students and teachers (29). This supported the results of two cohort studies in terms of evidence of causality. The new toxicological methods are based on condensed water and cell culture

techniques, which are superior to previous methods in terms of correlation with clinical symptoms. Occupants of fungus-infested buildings showed complement activation, particularly in the classical pathway. This proved that these residents have an increased risk of systemic subclinical inflammation and increased health risk ($p < 0.001$) (30). Mycotoxins in indoor air are the cause of diseases in people in this environment. Indoor air cytotoxicity testing is a risk assessment method in moisture-damaged buildings (31). Monocyte-derived macrophage MDM is an experimental macrophage model to evaluate fungal-contaminated indoor air (32). The boar sperm cell motility inhibition assay is a test for detecting toxicity in the causal relationship with building-related symptoms (33).

Dampness and Mould Hypersensitivity Syndrome

Patients living or working in water-damaged buildings have a large number of non-specific findings. In the beginning, these symptoms are reversible, and mild, with irritation of the mucous membrane, increased respiratory diseases, and asthma-like symptoms. These health problems later become chronic. The determination of a dampness and mould hypersensitivity syndrome (DMHS) represents a challenge for a physician who makes the diagnosis. The diagnosis is based on the information provided by the patient and a detailed examination. Five clinical criteria exist for the diagnosis of DMHS: exposure to mould in a building with water damage; increased illness from infections; sick building syndrome; multiple chemical sensitivity; and scent sensitivity (34).

Prolonged or increased exposure to damp microbiota (DM) can make SBS life-threatening and lead to irreversible DMHS. The main feature is a dysregulation of the immune system in the direction of hypersensitivity (type I–IV) and simultaneous immunosuppression, which manifests an increased susceptibility to infections. DMHS is systemic low-level inflammation and biotoxicosis. There is evidence that DMHS is associated with autoimmune changes. DMHS is a mitochondrial disease and an endocrinopathy (35).

Indoor air dampness microbiota is a major health concern. There is ample evidence that exposure to DM causes asthma (new or worsening), dyspnoea, respiratory tract infections, and allergic alveolitis. In a recently published Finnish study examining hospital workers versus controls for health changes after exposure to dampness and mould, it was found that respiratory symptoms were significantly more common in the studied patients exposed to DM than in the controls (80% vs. 29%, $p < 0.001$). Central nervous system and peripheral nervous system symptoms were found significantly more frequently in the studied patients than in the controls (81% vs. 11%, $p < 0.001$). Fatigue (77% vs. 24%, $p < 0.001$), multiple chemical sensitivity (40% vs. 9%, $p = 0.01$), so-called brain fog (62% vs. 11%, $p < 0.001$), arrhythmias (57% vs. 2.4%; $p < 0.001$), and musculoskeletal pain (51% vs. 22%, $p = 0.02$) were found to be higher in the studied patients than in the controls. This provided evidence that exposure to DM leads to a variety of extrapulmonary disorders. This confirmed further previous study results on health impairments caused by moisture and mould at a workplace (36). The particular risk at the workplace from moisture damage (MD) was verified by the occurrence of asthma, larynx diseases, and rhinosinusitis in the studied patients, with the exclusion of atopy as a cause (37).

Sick Building Syndrome

Sick building syndrome is caused by environmental changes. With SBS, patients suffer from headaches, fatigue, lack of concentration, and irritation of the skin and mucous membranes. SBS is caused by indoor air pollution, among other causes, with bioaerosols as the main cause of respiratory and general diseases (headache 28%, allergy 20%) (38).

Building-Related Symptoms and Building-Related Illness

The causes and pathophysiological mechanisms of building-related symptoms (BRS) have been further clarified in recent studies. Classroom dust intrinsic toxicity was statistically significantly associated with the following 11 symptoms in 231 teachers: stuffy nose, runny nose, hoarseness, pharyngeal globus sensation, pharyngeal itching, shortness of breath, dry cough, weeping eyes, sensitivity to noise, difficulty falling asleep, and increased need for sleep. Toxicity tests of germ cultures were associated with 8 symptoms: headache, dry nasal mucosa, dry mouth, hoarseness, sore throat, pharyngeal congestion, weeping eyes, and increased need for sleep. The toxicity of classroom dust and the germ distribution in the interior demonstrated by the boar sperm motility inhibition assay proved to represent an increased risk of work-related respiratory and eye changes for teachers (39).

In 2010, water and moisture damage caused a massive fungal infestation in a family in a single-family home. The five family members then developed serious health changes. Symptoms, consistent with the literature, were fatigue, sleep disturbances, poor concentration, infantile nosebleeds, headaches, and recurrent respiratory infections caused by microbial volatile organic compounds released from the mould. All family members recovered after the removal of the causes after 6 years of exposure. There can therefore be no doubt that the building-related illness was caused by the massive exposure to mould (40).

CONCLUSIONS

According to IAS, indoor air is more important for our health than outdoor air. Interior building moisture and mould exposure caused by water damage are mostly caused by damage or defects in the building. Undeniably, this increases the risk of suffering from respiratory diseases and allergies. In Germany, these diseases are assessed according to the guidelines of professional societies from 2017. Recent studies, especially from Scandinavia, prove the causality between moisture-induced mould pollution in the interior and occupational respiratory diseases, but now also for extrapulmonary changes in the central nervous system and the peripheral nervous system. More diagnostic studies on mould-induced health damage are necessary. According to the study results and WHO warning on top priority pathogens, monitoring the effects of fungal VOC on human health is indispensable. The socioeconomic impact is huge. According to these more recent findings on the causality and effects of moisture-induced mould exposure, the symptoms and illnesses that arose in the temporal context of the occurrence of moisture and mould damage should no longer be ignored and trivialized. The renovation of moisture and mould damage in a publicly accessible building caused by

construction defects and poor maintenance must be declared a mandatory task due to the unacceptable health risks and the socioeconomic burden on society.

Conflict of Interests

None declared

REFERENCES

1. Daschner A, González Fernández J. Allergy in an evolutionary framework. J Mol Evol. 2020 Jan;88(1):66-76.
2. Inamdar AA, Morath S, Bennett JW. Fungal volatile organic compounds: more than just a funky smell? Annu Rev Microbiol. 2020 Sep 8;74:101-16.
3. Appolloni L, Dettori M, Petronio MG, Raffo M, Settimo G, Rebecchi A, et al. A proposal of hygienic and sanitary standards for the new Building Code in Italy. Ann Ig. 2020 Sep-Oct;32(5 Suppl 1):85-109.
4. Sabino R, Veríssimo C, Viegas C, Viegas S, Brandão J, Alves-Correia M, et al. The role of occupational Aspergillus exposure in the development of diseases. Med Mycol. 2019 Apr 1;57 Suppl 2:S196-S205.
5. Rollins SM, Su FC, Liang X, Humann MJ, Stefaniak AB, LeBouf RF, et al. Workplace indoor environmental quality and asthma-related outcomes in healthcare workers. Am J Ind Med. 2020 May;63(5):417-28.
6. Sakellaris I, Saraga D, Mandin C, de Kluizenaar Y, Fossati S, Spinazzè A, et al. Association of subjective health symptoms with indoor air quality in European office buildings: The OFFICAIR project. Indoor Air. 2021 Mar;31(2):426-39.
7. Tran VV, Park D, Lee YC. Indoor air pollution, related human diseases, and recent trends in the control and improvement of indoor air quality. Int J Environ Res Public Health. 2020 Apr 23;17(8):2927. doi: 10.3390/ijerph17082927.
8. Coulburn L, Miller W. Prevalence, risk factors and impacts related to mould-affected housing: an Australian integrative review. Int J Environ Res Public Health. 2022 Feb 7;19(3):1854. doi: 10.3390/ijerph19031854.
9. Kokkonen A, Väänänen M, Säämänen A, Pasanen P. The evaluation of short-term water misting of room air in reducing airborne dust after renovation work. Ann Work Expo Health. 2019 Feb 16;63(2):242-55.
10. Henneberger PK, Patel JR, de Groene GJ, Beach J, Tarlo SM, Pal TM, et al. The effectiveness of removal from exposure and reduction of exposure for managing occupational asthma: summary of an updated Cochrane systematic review. Am J Ind Med. 2021 Mar;64(3):165-9.
11. Domínguez-Amarillo S, Fernández-Agüera J, Cesteros-García S, González-Lezcano RA. Bad air can also kill: residential indoor air quality and pollutant exposure risk during the COVID-19 Crisis. Int J Environ Res Public Health. 2020 Sep 30;17(19):7183. doi: 10.3390/ijerph17197183.
12. [Mold burden of interior rooms - report of findings, health evaluation and measures. Report of the "Methods and Quality Assurance in Environmental Medicine" Committee]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2007 Oct;50(10):1308-23. German.
13. Moriske HJ, Szewzyk R, Tappler P, Valtanen K, editors. [Guide to the prevention, detection and renovation of mold infestations in buildings]. Dessau-Roßlau: Umweltbundesamt (German Environment Agency); 2017. German.
14. [Requirements for the prevention of infection in the medical care of immunosuppressed patients: recommendation of the Commission for Hospital Hygiene and Infection Prevention (KRINKO) at the Robert Koch Institute]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2021 Feb;64(2):232-64. German.
15. Justiz-online. [Public Health Service Act North Rhine-Westphalia (ÖGD NRW)] [Internet]. Düsseldorf: Department of Justice of North Rhine-Westphalia [cited 2022 Apr 24]. Available from: http://www.lexsoft.de/cgi-bin/lexsoft/justizportal_nrw.cgi?xid=146870,1. German.
16. Centers for Disease Control and Prevention. Basic facts about mold and dampness [Internet]. Atlanta: CDC; 2022 [cited 2023 Feb 19]. Available from: https://www.cdc.gov/mold/faqs.htm.
17. World Health Organization. WHO releases first-ever list of health-threatening fungi [Internet]. Geneva: WHO; 2022 [cited 2023 Feb 19]. Available from: https://www.who.int/news/item/25-10-2022-who-releases-first-ever-list-of-health-threatening-fungi.
18. Heseltine E, Rosen J, editors. WHO guidelines for indoor air quality: dampness and mould. Copenhagen: WHO Regional Office for Europe; 2009.
19. Mudarri D, Fisk WJ. Public health and economic impact of dampness and mold. Indoor Air. 2007 Jun;17(3):226-35. Erratum in: Indoor Air. 2007 Aug;17(4):334.
20. Norbäck D, Zock JP, Plana E, Heinrich J, Tischer C, Jacobsen Bertelsen R, et al. Building dampness and mold in European homes in relation to climate, building characteristics and socio-economic status: The European Community Respiratory Health Survey ECRHS II. Indoor Air. 2017 Sep;27(5):921-32.
21. Sylvain IA, Adams RI, Taylor JW. A different suite: the assemblage of distinct fungal communities in water-damaged units of a poorly-maintained public housing building. PLoS One. 2019 Mar 18;14(3):e0213355. doi: 10.1371/journal.pone.0213355.
22. Holme JA, Øya E, Afanou AKJ, Øvrevik J, Eduard W. Characterization and pro-inflammatory potential of indoor mold particles. Indoor Air. 2020 Jul;30(4):662-81.
23. Kespohl S, Liebers V, Maryska S, Meurer U, Litzenberger C, Merget R, et al. What should be tested in patients with suspected mold exposure? Usefulness of serological markers for the diagnosis. Allergol Select. 2022 Mar 29;6:118-32.
24. Kalayci O, Miligkos M, Pozo Beltrán CF, El-Sayed ZA, Gómez RM, Hossny E, et al. The role of environmental allergen control in the management of asthma. World Allergy Organ J. 2022 Mar 8;15(3):100634. doi: 10.1016/j.waojou.2022.100634.
25. Rea WJ. A large case-series of successful treatment of patients exposed to mold and mycotoxin. Clin Ther. 2018 Jun;40(6):889-93.
26. Hyvönen S, Syrjala H. Asthma case cluster during renovation of a water-damaged and toxic building. Microorganisms. 2019 Dec 3;7(12):642. doi: 10.3390/microorganisms7120642.
27. Wiesmüller GA, Heinzow B, Aurbach U, Bergmann KC, Bufe A, Buzina W, et al. Abridged version of the AWMF guideline for the medical clinical diagnostics of indoor mould exposure: S2K Guideline of the German Society of Hygiene, Environmental Medicine and Preventive Medicine (GHUP) in collaboration with the German Association of Allergists (AeDA), the German Society of Dermatology (DDG), the German Society for Allergology and Clinical Immunology (DGAKI), the German Society for Occupational and Environmental Medicine (DGAUM), the German Society for Hospital Hygiene (DGKH), the German Society for Pneumology and Respiratory Medicine (DGP), the German Mycological Society (DMykG), the Society for Pediatric Allergology and Environmental Medicine (GPA), the German Federal Association of Pediatric Pneumology (BAPP), and the Austrian Society for Medical Mycology (ÖGMM). Allergo J Int. 2017;26(5):168-93.
28. Goh KJ, Yii ACA, Lapperre TS, Chan AK, Chew FT, Chotirmall SH, et al. Sensitization to Aspergillus species is associated with frequent exacerbations in severe asthma. J Asthma Allergy. 2017 Apr 21;10:131-140.
29. Hyvonen SM, Lohi JJ, Rasanen LA, Heinonen T, Mannerstrom M, Vaali K, et al. Association of toxic indoor air with multi-organ symptoms in pupils attending a moisture-damaged school in Finland. Am J Clin Exp Immunol. 2020 Dec 15;9(5):101-13.
30. Atosuo J, Karhuvaara O, Suominen E, Vilén L, Nuutila J, Putus T. Indoor-related microbe damage induces complement system activation in building users. Innate Immun. 2021 Jan;27(1):15-22.
31. Vaali K, Tuomela M, Mannerström M, Heinonen T, Tuuminen T. Toxic indoor air is a potential risk of causing immuno suppression and morbidity-a pilot study. J Fungi (Basel). 2022 Jan 21;8(2):104. doi: 10.3390/jof8020104.
32. Øya E, Solhaug A, Bølling AK, Øvstebø R, Steensen TB, Afanou AKJ, et al. Pro-inflammatory responses induced by A. fumigatus and A. versicolor in various human macrophage models. J Toxicol Environ Health A. 2019;82(8):483-501.
33. Salin JT, Salkinoja-Salonen M, Salin PJ, Nelo K, Holma T, Ohtonen P, et al. Building-related symptoms are linked to the in vitro toxicity of indoor dust and airborne microbial propagules in schools: A cross-sectional study. Environ Res. 2017 Apr;154:234-9.
34. Valtonen V. Clinical diagnosis of the dampness and mold hypersensitivity syndrome: review of the literature and suggested diagnostic criteria. Front Immunol. 2017 Aug 10;8:951. doi: 10.3389/fimmu.2017.00951.
35. Tuuminen T. The roles of autoimmunity and biotoxicosis in sick building syndrome as a "starting point" for irreversible dampness and mold hypersensitivity syndrome. Antibodies (Basel). 2020 Jun 22;9(2):26. doi: 10.3390/antib9020026.
36. Hyvönen S, Lohi J, Tuuminen T. Moist and mold exposure is associated with high prevalence of neurological symptoms and MCS in a Finnish hospital workers cohort. Saf Health Work. 2020 Jun;11(2):173-7.

37. Nynäs P, Vilpas S, Kankare E, Karjalainen J, Lehtimäki L, Numminen J, et al. Clinical findings among patients with respiratory Symptoms Related to Moisture Damage Exposure at the Workplace-The SAMDAW Study. Healthcare (Basel). 2021 Aug 27;9(9):1112. doi: 10.3390/healthcare9091112.
38. Kumar P, Singh AB, Singh R. Comprehensive health risk assessment of microbial indoor air quality in microenvironments. PLoS One. 2022 Feb 25;17(2):e0264226. doi: 10.1371/journal.pone.0264226.
39. Salin J, Ohtonen P, Andersson MA, Syrjälä H. The toxicity of wiped dust and airborne microbes in individual classrooms increase the risk of teachers' work-related symptoms: a cross-sectional study. Pathogens. 2021 Oct 21;10(11):1360. doi: 10.3390/pathogens10111360.
40. Kramer A, Wichelhaus TA, Kempf V, Hogardt M, Zacharowski K. Building-related illness (BRI) in all family members caused by mold infestation after dampness damage of the building. GMS Hyg Infect Control. 2021 Dec 7;16:Doc32. doi: 10.3205/dgkh000403.

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