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Adverse Health Effects of Indoor Moulds

Luke Curtis MS, CIH
Allan Lieberman MD
Martha Stark MD
William Rea
Marsha Vetter MD PhD

There is now considerable evidence in the medical literature that indoor airborne fungi exposure can cause numerous adverse health effects in multi-organ systems.

Introduction

In recent years, public attention has become increasingly focused on the very real problem of mould (fungi) inside both home and workplace and on the very real dangers posed by such mould exposure to human health. This position paper is presented by the American Academy of Environmental Medicine (AAEM) to describe the current knowledge of adverse health effects of indoor mould. There is considerable evidence in the medical literature validating the many different health effects reported in airborne mould exposed patients.

Indoor airborne mould exposure frequently causes adverse human health effects with injury to and dysfunction of multiple organs and systems including: 1) respiratory, 2) nervous, 3) immune, 4) haematological systems and 5) the skin. Indoor mould is also a common cause of life-threatening systemic infections in immuno-compromised patients.

Moulds are Common in the Indoor Environment

Fungi (or moulds) are ubiquitous in both indoor and outdoor environments. Moulds are frequently spread by airborne spores. Mould and mould spores require moisture and a food source like cellulose or decaying food to grow.[1] As mould spores swell with water and grow, they elongate, forming balloon-like protuberances (hyphae) which secrete digestive enzymes and mycotoxins. The fungus then digests the food source to support its growth.

About 100,000 fungal species have already been identified; in fact fungi are estimated to comprise an astounding 25% of the world's biomass.[2] Various surveys of homes in North America and Europe have reported that visible mould and/or water damage are found in 23% to 98% of all homes.[3-6] There are no official standards, at this time, for indoor airborne fungus concentrations. However, indoor fungal levels above a range of 150 to 1,000 colony-forming units per cubic meter of air (cfu/m^3) are considered to be sufficient to cause human health problems.[4,7-9] Numerous reports have documented that indoor air can often be contaminated with indoor fungal spore levels well in excess of 1,000 cfu/m^3.[10-17] The most common indoor fungi generally collected are Cladosporium, Aspergillus and Penicillium.[10-17] Alternaria, Stachybotrys, Rhizopus, Mucor, Wallemia, Trichoderma, yeasts, Botrytis, Epicoccum and Fusarium species are often being found indoors as well.[10-17] Foreclosures, lawsuits and insurance claims due to mould problems are common. Policyholders of America report receiving about 50 calls a week about homes with mould problems undergoing foreclosure.[18] In 2002, an estimated 10,000 mould related cases were pending in US courts.[19] In 2002, the insurance industry paid out $2 billion in mould related claims in Texas alone.[20]

Mould Related Health Symptoms are Common and Varied

Many patients have been reporting multiple ill health effects from their exposures to mould. Studies of more than 1,600 patients suffering ill effects from fungus exposure were presented at one meeting in Dallas in 2003 (21st Annual Symposium of Man and His Environment in Dallas, Texas, June 2003[19-22]).[21-25]

To cite a few studies: Lieberman[21] examined 48 mould-exposed patients who had the following health problems:

1. muscle and/or joint pain 71%
2. fatigue/weakness 70%
3. neurocognitive dysfunction 67%
4. sinusitis 65%
5. headache 65%
6. gastrointestinal problems 58%
7. shortness of breath 54%
8. anxiety/ depression/ irritability 54%
9. vision problems 42%
10. chest tightness 42%
11. insomnia 40%
12. dizziness 38%
13. numbness/ tingling 35%
14. laryngitis 35%
15. nausea 33%
16. skin rashes 27%
17. tremors 25%, and
18. heart palpitations 21%.

Rea's[23] study of 150 indoor mould-exposed patients found the following health problems:

1. fatigue 100%
2. rhinitis 65%
3. memory loss and other neuropsychiatric problems 46%
4. respiratory problems 40%
5. fibromyalgia 29%
6. irritable bowel syndrome 25%
7. vasculitis 4.7%, and
8. angio-oedema 4.0%.

These clinical reports demonstrate the multi-system adverse effects of airborne

mould. There is now considerable evidence in the medical literature that indoor airborne fungus exposure can cause numerous adverse health effects in multi-organ systems.

Mechanisms of Mould-Related Health Effects

Fungi can exert ill health effects by 3 mechanisms: 1) infection; 2) allergy and 3) toxicity.

Serious infections by such fungi as Candida, Aspergillus and Pneumocystis are common and mostly involve severely immuno-compromised patients.[26-28] Fungi such as Candida, Histoplasmosis, Cryptococcus, Blastomyces and Coccidioides can infect internally immunocompetent people.[29] Fungi such as Trichophyton, Candida and Malasezia commonly cause minor skin infections in immunocompetent humans.[28]

At least 70 allergens have been well characterized from spores, vegetative parts and small particles from fungi (0.3 microns and smaller).[30,31] Allergies to fungal allergens are very common, with a review of 17 studies finding that 6% to 10% of the general population and 15% to 50% of atopics had immediate skin sensitivity to fungi[32].

Fungi produce a wide variety of toxic chemicals called mycotoxins.[1,33,34] Some common mycotoxins include:

1. Aflatoxins - very potent carcinogens and hepatotoxins produced by some Aspergillus species;
2. Ochratoxins - nephrotoxic and carcinogenic - produced by some Aspergillus and Penicillium;
3. Sterigmatocystin - immunosuppressive and a liver carcinogen produced by Aspergillus species especially A. versicolour; and
4. Trichothecenes are produced primarily by Stachybotrys and Fusarium species, and have been reported to inhibit protein synthesis, cause haemorrhage and vomiting.

Fungi also produce beta glucans which have immunological effects.[35] The smell of moulds come primarily from volatile organic compounds.[36]

Adverse human and animal effects from mycotoxin-contaminated foodstuffs have been well recognized since the early 20th century.[33,37] But the pathway of mycotoxin injury through inhalation is questioned.[38] In the absence of ethical, controlled studies on human inhaled mycotoxin exposure, only animal controlled exposure and human epidemiology studies can be used. The literature demonstrates that significant amounts of mycotoxins (including ochratoxin, sterigmatocystin and trichothecenes) are present in indoor dust[39-43] and in fungal spores which can be absorbed through the respiratory route.[34,37,44,45] Patients exposed to indoor Stachybotrys have been found to have measurable blood levels of the Stachybotrys haemorrhagic toxin stachylysin.[46] Levels of trichothecene mycotoxins in the urine have also been found in significantly higher levels in patients exposed to high indoor fungus levels, as opposed to a control group not exposed to high indoor fungus levels.[47] Blood ochratoxin levels have been found to be significantly higher in food industry workers exposed to airborne ochratoxin versus unexposed controls.[43] These findings clearly demonstrate an inhaled pathway for entry into the body.

Sampling for Mould Exposure

Indoor fungus sampling is most commonly performed by measuring airborne levels of viable (culturable) or total (viable and non viable) spores.[48,49] Some of the airborne viable sampling methods, such as Andersen samplers, collect air for only a few minutes.

Settle plates are an inexpensive method to get a semi-quantitative measure of indoor airborne fungus levels. Viable and non viable airborne spore counts can vary considerably over a period of minutes, so air sampling over several periods of time may be necessary to accurately characterize airborne fungal spore levels.[48,49]

However, airborne fungus measurements fail to take into consideration non-airborne mould contamination such as mould contamination in dust or surfaces (often visible to the naked eye) and mycotoxins in air, dust and on surfaces.[48,50] Therefore testing the settled dust for fungi and mycotoxins is often recommended.[48,49] In order to secure a more complete assessment, therefore, it is often recommended that airborne measurements be supplemented by testing for moulds and mycotoxins in already-settled dust or air.[48,49]

Other techniques such as PCR (Polymerase Chain reaction), ELISA (Enzyme Linked Immunosorbent Assay), and measurement of fungal volatile organic chemicals, polysaccharides, ergosterol and beta glucans can also be useful in assaying indoor environments for moulds and their allergens and mycotoxins.[48]

For a helpful overview of sampling methods, please see Pasanen[48] and Macher.[51] For an informative guide to the classification, identification and biology of common indoor fungi, see Samson.[1] Several good guides exist for prevention and remediation of indoor fungi problems.[51-53]

Indoor Mould Exposure and Respiratory Problems

Many epidemiological studies have noted that residential exposure to moulds and/or chronic dampness can increase asthma/wheezing incidence or morbidity in both children and adults.[4-6,54-67] Asthma and related conditions are very common in the USA, with an overall incidence of about 5.4% among all age groups and incidences as high as 27% in inner city children.[68] Studies with infants have reported that higher fungal exposures are associated with more wheezing, coughing and respiratory illness.[69,70] Higher indoor beta glucan levels have been associated with significantly higher levels of chest tightness and joint pain[71] Non-industrial occupational mould exposure has been reported to be associated with significantly higher levels of asthma, sinusitis, irritated skin and eyes and chronic fatigue.[72-6]

One study found that patients exposed to high indoor fungus levels had significantly lower lung function than unexposed controls.[24] Higher outdoor fungal concentrations have been linked to higher asthma death rates[77] and high asthma incidence[78,79] in children or young adults. Challenge exposures with Penicillium and Alternaria extracts equivalent to high outdoor levels of fungus were noted to severely lower lung function in asthmatics.[80] Skin sensitivity to Alternaria has been linked to much higher risk of respiratory arrest.[81] Various epidemiological studies have linked skin sensitivity to common indoor fungi and higher asthma incidence or severity[82-86] and higher rates of sinusitis.[87]

Airborne fungal exposure causes sinusitis, bronchopulmonary aspergillosis and hypersensitivity pneumonitis.[88-89] An estimated 14% of the USA population suffer from rhinosinusitis and related conditions.[90]

Allergic fungal sinusitis was diagnosed on the basis of fungal growth in nasal secretions and presence of allergic mucin in 93% of 101 consecutive patients undergoing sinus surgery.[90] Another study was able to recover and culture fungi from the sinuses of 56% of 45 patients undergoing endoscopic sinus surgery for chronic rhinosinusitis.[91] A long-term cohort study of 639 patients with allergic fungal sinusitis demonstrated that remedial steps taken to reduce fungal exposure (by utilizing, for example, air filters, ionizers, moisture control and anti-microbial nasal sprays) significantly reduced rhinosinusitis and improved nasal mucosa morphology.[22] This study concluded that failure to reduce airborne fungus levels to less than 4 per hour on a settle plate failed to resolve the sinusitis.[22]

Although, historically, anti-fungal drugs have generally not been recommended for treatment of fungal sinusitis,[88,89] recent studies have found beneficial effects of oral and nasal medication for sinusitis patients.[22,92] Several studies have linked residential exposure to fungi with hypersensitivity pneumonitis.[93-95]

Stachybotrys and Haemorrhagic Effects

Exposure to high indoor levels of Stachybotrys, Aspergillus and other fungi has been epidemiologically associated with infant lung haemorrhage.[96-100] Although questions were raised after this association was discovered,[101] it meets many epidemiologic criteria for causality.[102] Acute infant pulmonary haemorrhage can be rapidly fatal; when the infant survives, lung blood vessel damage is present and deposits of haemosiderin will remain in the lung macrophages and can be seen in tissue obtained during bronchoscopy.[97]

Stachybotrys fungi produce a wide range of trichothecene mycotoxins (including satratoxins), several roridin epimers, verrucarin J and B and hemolysin.[34,99] A haemorrhagic protein called stachylysin has

been isolated from Stachybotrys collected from homes of infants with lung haemorrhage,[103,104] and from serum of patients with residential Stachybotrys exposure.[46] It is hypothesized that infants, with their rapidly growing lungs, are more susceptible to the toxic effects of Stachybotrys mycotoxins.[105] Studies with Stachybotrys-exposed adults have noted a significantly higher incidence of health problems such as lower airway problems, wheezing, skin and eye irritation, flu-like symptoms and chronic fatigue.[106] Stachybotrys has been isolated from the lungs of a child with pulmonary haemosiderosis.[107]

Immunological Changes

Fungal exposure can alter immunological parameters. Some studies have reported that indoor fungus-exposed patients have higher serum levels of IgG, IgA and IgM antibodies to common fungi, trichothecenes and satratoxins.[108-110] IgG antibodies to 9 common indoor fungi were significantly higher in subjects with sinusitis, versus non sinusitis subjects in a mouldy school.[111] Other studies note no significant increases in fungal IgG[112,113] or fungal IgE[108] in fungus-exposed patients.

Indoor fungal exposure has been associated with altered levels of T4, T8 and NK cells and higher levels of auto-antibodies.[23,114,115] Indoor glucan exposure has been associated with a lower proportion of cytotoxic T-cells (CD8+SF61+) and with secretion of tumour necrosis factor higher than from homes with lower levels of beta glucans.[116]

Studies of animals orally given such common mycotoxins as aflatoxins, ochratoxins and trichothecenes show considerable immune impairment, including depression of T cell, B cell and macrophage immunities.[117] Human cell line studies have also found that many mycotoxins can suppress T cell, B cell and NK activity at serum concentrations similar to those found in indoor mould exposed patients.[118] Thus, airborne exposure to mycotoxin is seen to cause harmful effects to the immune system.

Neurological Dysfunction

Indoor airborne mould exposure causes neurologic dysfunction and cognitive deficits. Clinical reports on large numbers of mould-exposed patients found significant fatigue and weakness in 70% to 100% of cases, and neurocognitive dysfunction, including memory loss, irritability, anxiety and depression, in over 40% of the patients.[21,23] Numbness, tingling and tremor were also found in a significant number of patients.[21,23] These signs and symptoms constitute classic manifestations of neurotoxicity.[119]

A study of 43 mould-exposed patients found they performed significantly more poorly than 202 controls on many neuropsychiatric tests including balance sway speed, blinking reflex, colour perception, reaction times and left grip strength ($P<0.0001$ in each case).[120]

Quantitative electro-encephalogram studies have also noted significant longer nerve latencies in fungus-exposed patients.[120] A triple-headed SPECT brain scan revealed neurotoxic patterns in 26 of 30 (87%) mould-exposed patients.[121]

An iriscorder study of autonomic nervous function in 60 mould-exposed patients found 95% had abnormal autonomic responses of the pupil.[23] Visual contrast sensitivity studies were often abnormal in indoor mould-exposed patients.[23]

Additional studies have reported that mould-exposed patients do significantly more poorly on tests of attention, balance, reaction time, verbal recall, concentration, memory, finger tapping.[24, 122-124] Most of these patients also experienced many health problems including chronic fatigue, headaches, insomnia and decreased balance, concentration and attention.

Studies of 10 indoor-mould-exposed children and 378 indoor-mould-exposed adults found significantly more neurophysiological abnormalities than in controls; this included abnormal EEGs and abnormal brainstem, visual and somatosensory evoked potentials as compared to 10 control children.[25,125]

The large number of objective neuropsychological findings in symptomatic patients support the findings that exposure to indoor moulds can have adverse health effects.

Renal Dysfunction

Exposure to fungi may also cause kidney dysfunction. It is well know that ochratoxin contaminated-food is nephrotoxic.[126,127] Indoor exposure to ochratoxin may also be nephrotoxic. A study was presented of a family who presented with increasing thirst and urination, lethargy, and skin rash. Considerable amounts of ochratoxin were found in the house dust. The family recovered after moving to another home.[38]

Life Threatening Fungal Infections in the Immuno-compromised

In recent years, the incidence of life-threatening infections in immuno-compromised patients from Aspergillus and other common fungi has been growing rapidly.[128,129] Invasive aspergillosis is very common among immuno-compromised patients with reported incidence rates in the following patients: lung transplants 17-26%; allogenic bone marrow transplants 5-15%; acute leukaemia 5-24%; and heart transplant 2-13%.[130,131] Even with strong anti-fungal drugs and intense hospital treatment, mortality rates from invasive aspergillosis range from 50% to 99% in the immuno-compromised.[132,133]

Environmental control plays a key role in preventing Aspergillus infections. Several studies have linked hospital construction work to increased rates of invasive aspergillosis.[134-7] Environmental controls such as using HEPA filters, sealing rooms, regular cleaning of rooms, and using anti-fungal copper-8-quionolate paint have been shown to both significantly reduce airborne levels of Aspergillus and to significantly reduce rates of invasive aspergillosis in immuno-compromised hospital patients.[135-141] Other recent research has indicated that a large number of Aspergillus spores can spread through water supplies[142] and that cleaning shower facilities can significantly lower airborne levels of Aspergillus.[143]

Diagnosis and Treatment of Mould Related Health Problems

A careful environmental and medical history is an essential first step in evaluating a patient for mould-related health problems.[52,144-6] Particular attention should be paid to any history of exposure to visible mould and/or water damage at the home or workplace. Environmental sampling for viable spores, total spores, and mycotoxins in the air and dust can provide important exposure information. For patients suspected of having substantial fungal exposure, a battery of sophisticated laboratory tests have been developed to:

1. test for antibodies to moulds and mycotoxins in the sera of these patients,[108,109]
2. other immunological tests,[115]
3. urine and blood testing for mycotoxins,[47]; and
4. a basic metabolic panel to test for several important parameters (including electrolytes, blood sugar and kidney status).

Visual contrast sensitivity tests should be done on all mould-exposed patients. The use of standard neuropsychological tests batteries[23,122-4] as well as autonomic nerve testing, EEG and brain imaging techniques like SPECT and MRI can be very helpful tools in documenting mould-related neurological damage.[25,120,121,125,144] Use of pulmonary function tests is also useful for patients with respiratory symptoms.[24,120]

If patient symptoms or a review of systems suggests involvement of ears, nose throat, gastrointestinal system, the eyes or the heart, then consultation with physicians knowledgeable about environmental exposures (be the doctor an ENT specialist, a gastro-enterologist, and ophthalmologist or a cardiologist) may be very useful. Failure to perform objective evaluations for accessing system or organ dysfunction account for the presently accepted position that airborne mould exposures have no significant adverse health effects.[38]

Other common indoor environmental exposures should also be considered as a potential source of health problems.

Common non-fungal indoor environ-mental factors include poor ventilation, carbon monoxide from faulty heat sources, pesticides, second hand tobacco smoke, petrochemicals such as cleaners/building materials/solvents, formaldehyde from outgassing carpets and building materials, bacteria, and allergens from the fur, feathers and saliva of common household animals like cockroaches, dust mites, cats, dogs, caged birds, and pigeons. Exposure to ozone, second-hand tobacco smoke, formaldehyde, cockroach allergen and

viral infections can also have a synergistic effect with fungal exposure, to worsen asthma and rhinitis.[147-151]

The most important part of treatment for mould-exposed patients is avoidance of fungal exposure and remediation of mould contamination in the home and workplace. Any water leaks, and flooded or damp areas should be rectified immediately. Non-porous surfaces like floors and walls which have visible mould growth should be cleaned. Porous waterlogged materials like carpet and furniture should be thrown out. Control of humidity is important to control mould growth.

The use of air conditioners and dehumidifiers can significantly reduce summertime indoor airborne mould concentrations.[10,152] HEPA air filters can also significantly reduce indoor airborne fungus concentrations.[141] For cleanup of severe indoor water or mould problems, use of protective equipment like face masks and/or use of a professional remediation firm may be essential.[50-2]

Some studies with laboratory animals suggest that a high-quality diet with adequate anti-oxidant vitamins, selenium, phyto-chemicals, methionine and total protein, can reduce the harmful effects of food mycotoxins

Use of sublingual or injective fungal immunotherapy has been shown to be beneficial to some patients sensitized to common indoor moulds such as Alternaria and Cladosporium herbarium.[153,154] Other therapies found helpful include:

1. detoxification (sauna, massage, exercise);
2. correction of identified immune deficiencies;
3. use of topical, nasal or oral anti-fungal drugs when indicated.

Some studies with laboratory animals suggest that a high quality diet with adequate anti-oxidant vitamins, selenium, phytochemicals, methionine and total protein can reduce the harmful effects of food mycotoxins.[155, 156]

Summary

Indoor airborne mould and/or mycotoxin exposures cause many multisystem adverse human health effects, as indicated by the more than 100 references cited. Healthcare professionals, building managers, home owners and the general public need to be much more aware of their potential adverse health effects, the need for proper building remediation and the need for appropriate patient diagnosis and treatment. There is sufficient data from the medical literature and the large number of clinical reports to substantiate the reported adverse health effects of indoor airborne mould. Indoor mould and mycotoxin exposure absorbed through the respiratory route can be a major pathway of injury by all 3 mechanisms: infection, allergy, and toxicity.

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