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 to human health posed by such mould exposure. 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. 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. 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. 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 metre of air (cfu/m³) are considered to be sufficient to cause human health problems. Numerous reports have documented that indoor air can often be contaminated with indoor fungal spore levels well in excess of 1,000 cfu/m³. The most common indoor fungi generally collected are Cladosporium, Aspergillus and Penicillium. Alternaria, Stachybotrys, Rhizopus, Mucor, Wallemia, Trichoderma, yeasts, Botrytis, Epicoccum and Fusarium species are often being found indoors as well.

Foreclosures, lawsuits and insurance claims due to mould problems are common. Policyholders of America reports receiving about 50 calls a week about homes with mould problems undergoing foreclosure. In 2002, an estimated 10,000 mould-related cases were pending in US courts. In 2002, the insurance industry paid out US$2 billion in mould-related claims in Texas alone.

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, Dallas, Texas, June 2003). To cite a couple of studies...

Lieberman 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 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 three 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 immuno-competent people.19 Fungi such as *Trichophyton, Candida* and *Malassezia* commonly cause minor skin infections in immuno-competent humans.20

At least 70 allergens have been well characterised 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%–10% of the general population and 15%–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 Penicillum* species;

3) Sterigmatocystin: immuno-suppressive and a liver carcinogen produced by *Aspergillus* species, especially *A. versicolour*; and

4) Trichothecenes: produced primarily by *Stachybotrys* and *Fusarium* species, and reported to inhibit protein synthesis and cause haemorrhaging and vomiting.

Fungi also produce beta glucans which have immunological effects.35

The smell of moulds comes primarily from volatile organic compounds.36

Adverse human and animal effects from mycotoxin-contaminated foodstuffs have been well recognised 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 dust39–43 and in fungal spores which can be absorbed through the respiratory route.44–46 Patients exposed to indoor *Stachybotrys* have been found to have measurable blood levels of the *Stachybotrys* haemorrhagic toxin stachylysin.44 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 in unexposed controls.48 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.44,49 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 characterise airborne fungal spore levels accurately.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.46

For a helpful overview of sampling methods, please see Pasanen44 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.52–53

**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.1,6,54–57 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. Higher outdoor fungal concentrations have been linked to higher skin sensitivity to common indoor fungi and higher asthma death rates in children or young adults. One study found that patients exposed to high indoor fungus levels had significantly lower lung function than unexposed controls. Higher outdoor fungal concentrations have been linked to higher asthma death rates and high asthma incidence in children or young adults.

Studies with infants have reported that higher fungal exposures are associated with more wheezing, coughing and respiratory illness. Higher indoor beta glucan levels have been associated with significantly higher levels of chest tightness and joint pain. Non-industrial occupational mould exposure has been reported to be associated with significantly higher levels of asthma, sinusitis, iritated skin and eyes, and chronic fatigue.

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

Airborne fungal exposure causes sinusitis, bronchopulmonary aspergillosis and hypersensitivity pneumonitis. An estimated 14% of the US population suffers from rhinosinusitis and related conditions.

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

Although, historically, antifungal drugs have generally not been recommended for treatment of fungal sinusitis, recent studies have found beneficial effects of oral and nasal medication for sinusitis patients. Several studies have linked residential exposure to fungi with hypersensitivity pneumonitis.

### Stachybotrys and Haemorrhagic Effects

Exposure to high indoor levels of Stachybotrys, Aspergillus and other fungi has been epidemiologically associated with infant lung haemorrhage. Although questions were raised after this association was discovered, it meets many epidemiologic criteria for causality. 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.

Stachybotrys fungi produce a wide range of trichothecene mycotoxins (including satratoxins), several roridin epimers, verrucarin J and B and haemolysin. A haemorrhagic protein called stachylysin has been isolated from Stachybotrys collected from homes of infants with lung haemorrhage and from serum of patients with residential Stachybotrys exposure. It is hypothesised that infants, with their rapidly growing lungs, are more susceptible to the toxic effects of Stachybotrys mycotoxins.

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. Stachybotrys has been isolated from the lungs of a child with pulmonary haemosiderosis.

### 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. IgG antibodies to nine common indoor fungi were significantly higher in subjects with sinusitis versus non-sinusitis subjects in a mouldy school. Other studies note no significant increases in fungal IgG or fungal IgE 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. Indoor fungal 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.
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. 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.

Thus, airborne exposure to mycotoxins 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%–100% of cases, and neurocognitive dysfunction including memory loss, irritability, anxiety and depression in over 40% of the patients. Numbness, tingling and tremor were also found in a significant number of patients. These signs and symptoms constitute classic manifestations of neurotoxicity.

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).

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

An iriscorder study of autonomic nervous function in 60 mould-exposed patients found 95% had abnormal autonomic responses of the pupil. Visual contrast sensitivity studies were often abnormal in indoor-mould-exposed patients. Additional studies have reported that mould-exposed patients do significantly more poorly on tests of attention, balance, reaction time, verbal recall, concentration, memory and finger tapping. 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; these included abnormal EEGs and abnormal brainstem, visual and somatosensory-evoked potentials as compared to 10 control children.

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 known that ochratoxin-contaminated food is nephrotoxic. 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.

**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. 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 transplants, 2%–13%.

Even with strong anti-fungal drugs and intense hospital treatment, mortality rates from invasive aspergillosis range from 50% to 99% in the immuno-compromised. Environmental control plays a key role in preventing *Aspergillus* infections. Several studies have linked hospital construction work to increased rates of invasive aspergillosis. Environmental controls such as using HEPA filters, sealing rooms, cleaning rooms regularly and using anti-fungal copper-8-quinolate paint have been shown to significantly reduce airborne levels of *Aspergillus* and significantly reduce rates of invasive aspergillosis in immuno-compromised hospital patients.

Other recent research has indicated that a large number of *Aspergillus* spores can spread through water supplies and that cleaning shower facilities can significantly lower airborne levels of *Aspergillus*.
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. 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 has been developed to test for:

1. antibodies to moulds and mycotoxins in the sera of these patients
2. immunological factors
3. mycotoxins in urine and blood
4. several important parameters (including electrolytes, blood sugar and kidney status) using a basic metabolic panel.

Use of pulmonary function tests is also useful for patients with respiratory symptoms.

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

Other common indoor environmental exposures should also be considered as a potential source of health problems. Common non-fungal indoor environmental factors include poor ventilation, carbon monoxide from faulty heat sources, pesticides, second-hand tobacco smoke, petrochemicals such as those found in cleaners, building materials and 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 allergens and viral infections can also have a synergistic effect with fungal exposure to worsen asthma and rhinitis.

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. HEPA air filters can also significantly reduce indoor airborne fungus concentrations. For clean-up 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.

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

1. detoxification (sauna, massage, exercise);
2. correction of identified immune deficiencies;
3. use of topical, nasal or oral antifungal 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.

Summary

Indoor airborne mould and/or mycotoxin exposures cause many multi-system 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 the potential adverse health effects of moulds and mycotoxins, 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 three mechanisms: infection, allergy and toxicity.

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