CASE REPORT

Case Report: Antifungal Agents in the Treatment of Asthma and Allergy After Water-Damaged Building Exposure

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ABSTRACT

Damp and moisture-damaged building exposure has been linked to adverse health effects, primarily related to respiratory complications from mold spore reactions. This paper describes a case of a previously healthy man who was exposed to a home with hidden mold infestation and remained symptomatic following proper remediation. The patient presented with allergies, allergic bronchopulmonary aspergillosis, and treatment resistant asthma, as well as other non-respiratory symptoms likely related to inhalational mycotoxin exposure from his home. In this case, the addition of systemic and intranasal antifungals improved both respiratory and non-respiratory symptoms. Antifungals were used for a longer duration than customary and in combination with factors that addressed drug resistance. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Exposure to damp and/or moisture-damaged buildings increases the risk of adverse health outcomes, including allergy/atopy, eczema, asthma, and other respiratory diseases. An estimated 20% of asthma cases in the U.S. can be attributed to indoor dampness or mold exposure, with related costs of $3.5 billion annually.[1]

A July 23, 2022, paper by the Respiratory Health Division of the National Institute for Occupational Safety and Health Centers for Disease Control and Prevention (NIOSH), titled "NIOSH Dampness and Mold Assessment Tool (DMAT): Documentation and Data Analysis of Dampness and Mold-Related Damage in Buildings and Its Application"[2] outlined these salient points, in addition to acknowledging the need for updated monitoring data.

Although there are no national data on the prevalence of dampness/mold in U.S. residential buildings, the population-weighted average prevalence of dampness/mold estimated from several published studies was 47%.[3]

A study of 831 residential homes from 75 different locations in the U.S. reported that 24% of the surveyed homes had moisture or mold problems.[4]

There is also a lack of recent national data on the prevalence of dampness/mold for schools and other types of non-residential buildings. The longstanding 1995 U.S. General Accounting Office (currently, General Accountability Office) survey on school buildings indicated that 30% of schools in the U.S. had plumbing problems and 27% had roofing problems that could lead to interior or exterior water leakage.

The U.S. EPA (Environmental Protection Agency) BASE (Building Assessment Survey and Evaluation) study of 100 randomly selected public and commercial office buildings across the U.S. conducted during 1994 through 1998 showed that 85% of the buildings experienced past water damage and 45% had current leakage problems.

While these are compelling statistics, despite their dated nature, the DMAT system may be under-reporting the incidence of indoor mold due to inherent data collection methods used for building assessment, relying solely on observational assessments such as visual or olfactory detection, without environmental sampling.

Important symptomatic data was compiled for the NIOSH report from a health survey of respiratory symptoms. It states, "[from] the analyses, we found that the individual exposure index was significantly associated with building-related respiratory symptoms (wheezing, chest tightness, shortness of breath, nasal and sinus symptoms, and throat irritation that improved away from work) in an exposure–response relationship."

Table 1. Mycotoxins and their corresponding mold sources commonly found in moisture-damaged indoor environments.

Mycotoxin	Mold Source
Aflatoxin	Aspergillus flavus Aspergillus parasiticus
Chaetoglobosin A,C	Chaetomium globosum
Citrinin	Aspergillus species Monascus species Penicillium species
Enniatin B	Fusarium species
Gliotoxin	Aspergillus fumigatus Candida species
Ochratoxin A	Aspergillus ochraseus Aspergillus niger Penicillium verrucosum Penicillium nordicum Penicillium chrysogenum
Patulin	Aspergillus species Penicillium species Mucor species Fusarium species
Sterigmatocystin	Precursor of Aflatoxin Aspergillus versicolor
Trichothecenes (Roridin, Verrucarin, Nivalenol, Deoxynivalenol, Diacetoxyscirpenol, Satratoxin)	Stachybotrys chartarum Trichoderma viridae Fusarium species Myrothecium
Zearalenone	Fusarium species

The report continues, "All these findings clearly indicate that persistent dampness/mold or microbial growth is a public health hazard that should be prevented; nevertheless, if it occurs, it should be promptly remediated to minimize occupants' exposure to microbial agents before the damage becomes severe … From the perspective of preventive medicine, it is important that mold damages cannot be tolerated in indoor environments."

Water-damaged buildings host diverse populations of microbes including, but not limited to, mold spores, spore fragments, microbial volatile organic compounds (mVOCs),[5] mycotoxins, and bacteria, as well as bacterial metabolites and endotoxins. For the purposes of this paper, the focus is narrowed to aspects related to fungi, expanding beyond fungal spores to the additional health effects of indoor mycotoxin exposure, such as those shown in Table 1.

The indoor environmental professional (IEP) and medical industries have been slow to adopt mycotoxin surveillance. Only recently, an August 2022 study analyzing molds and mycotoxins in naturally infested indoor building materials posited that mycotoxins were one possible cause for the health issues found in residents of mold-infested buildings.[6]

Even slower has been recognition that inhalational exposure to mycotoxins can affect human health. This is due to limited epidemiological research, rather than evidence to the contrary. Mycotoxins are nanoparticle-sized chemicals produced by certain fungal species as a competitive advantage. Due to their minuscule size, variances in indoor air pressures can cause them to aerosolize from mold-affected building material even if the spores or fragments are sequestered beneath the material, thereby contaminating the indoor air. Mycotoxins are "found on particles smaller than spores that are easily respirable and can deeply penetrate the human respiratory tract."[7]

In a study of school children in Finland, multi-organ symptoms beyond the respiratory system were found in the children exposed to environmental molds with a statistically significant relative risk ratio as compared to controls, such as gastrointestinal, neurological, neuropsychiatric, or musculoskeletal symptoms, headache, fatigue, ear infections, and skin rash.[8] Mycotoxins can induce changes in the gut microbiota composition, disrupting the barrier function of the gut.[9]

Trichothecene mycotoxins have been detected in sera of individuals exposed to buildings contaminated with *Stachybotrys chartarum*, with a significant difference as compared to controls.[10] Antibodies to Satratoxin, a trichothecene mycotoxin, "were significantly greater in the [mold-exposed] patients ($P < .001$ for all measurements) than in the controls."[11]

Published literature have reported a prevalence of mycotoxins found in the urine of Myalgic Encephalitis/Chronic Fatigue Syndrome (ME/CFS) patients, including a study by Brewer, et al showing increased concentrations as compared to healthy controls.[12,13] Mycotoxins have also been reported in tissues of patients exposed to environmental molds, which were not demonstrated in healthy controls.[14]

Animal studies have reported that inhalational exposure is at least equivalent if not more toxic than dermal, ingested, or systemic exposures, depending on the mycotoxin.[15-17] For instance, a classic mouse study found that "inhalation of T-2 mycotoxin [a trichothecene] is at least 10 times more toxic than systemic administration (LD50 approximately 4.5 mg/kg) and at least 20 times more toxic than dermal administration (LD50 greater than 10 mg/kg)."[18] The respiratory tract tissue injury was minimal compared to systemic toxic effects.[19]

As seen in the case below, where many systems are impacted from a respiratory-acquired exposure, the effects of environmental mold exposure are not limited to within the respiratory tract. Non-IgE mediated reactions, generalized inflammation, immune depletion, neurological abnormalities, and toxicity also play a role.[20,21]

While mycotoxins from indoor environments have morphologic and biosynthetic diversity, they are generally found as a class to have neurotoxic, immunotoxic, dermatoxic, hepatotoxic, nephrotoxic, genotoxic, and alimentary and reproductive toxicity effects, with children being the most at risk.[22-31] Some cross the blood-brain barrier, are tremorgenic, and are found in human breast milk. In addition to being teratogenic, a June 2022 systematic review reported on the mutagenicity and carcinogenicity identifying "associations between mycotoxin-linked mutations and cancer risk."[32] A large multicenter investigation of patients with confirmed environmental exposure to mold-infested buildings found

Figure 1. Urine mycotoxin using the ELISA method.

Results:

Code	Test	Specimen	Value	Result	Not Present if less than	Equivocal if between	Present if greater or equal
E8501	Ochratoxin A	Urine	1.55300 ppb	Not Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group (B1,B2,G1,G2)	Urine	0.80500 ppb	Equivocal	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group (Macrocyclic)	Urine	0.07200 ppb	Present	0.02 ppb	0.02-0.03 ppb	0.03 ppb
E8510	Gliotoxin Derivative	Urine	1.42100 ppb	Present	0.5 ppb	0.5-1.0 ppb	1.0 ppb

a significant increased risk for autoimmunity, among other pertinent findings.[33]

More research is needed to identify the determinants of an individual's susceptibility, as not everyone exposed to the same infested environment will display the same set of symptoms. An individual's sensitivity to moisture-damaged materials appears to depend on multiple factors, including the building's unique microbial diversity, as well as the person's prior exposure, immune status, nutritional status, and genetic susceptibility.[34-36]

CASE REPORT DESCRIPTION

A 53-year-old previously healthy executive was referred with a prior diagnoses of allergies, asthma, pruritus, insomnia, and anxiety after it was discovered that he had a past exposure to a water-damaged home. Symptoms had been steadily worsening, despite treatment. At the initial appointment, he reported new onset of a persistent dull headache, bilateral tinnitus, urinary frequency, a recent development of glove-and-stocking neuropathy which further affected sleep, as well as aggravation of asthma symptoms leading to exercise intolerance.

Initial respiratory issues began after a prior move into a historic home, which he updated directly upon taking ownership, including the kitchen and bathrooms. He lived in the home during the majority of the remodel. It was later discovered that the home had multiple sites of hidden water damage in the kitchen and bathrooms due to plumbing errors. The remodelers had not taken proper safety precautions when mold was found, nor did they address the sources of water intrusions. Therefore, the home was cross-contaminated from the prior molds and bacteria uncovered during remediation, and new growth returned underneath the new materials.

Previous medical management included over-the-counter antihistamines for allergies, albuterol inhaler for asthma, and doxepin for mood, pruritus, and insomnia. He was hesitant to use other medications that might dull his intellect, and occasionally used NSAIDs for headache when needed, though he reported little improvement from them.

When the possibility of mold exposure was considered, mold allergy was confirmed with IgE allergy testing. The patient hired a company to fog his home to eradicate the mold, which significantly worsened his asthma symptoms. He was then prescribed a fluticasone inhaler for allergic bronchopulmonary aspergillosis (ABPA), after which he developed oral candidiasis which responded to treatment with amphotericin B oral rinses.

He was referred to a mold specialist out of the hospital system. The mold specialist detected urinary excretion of mold mycotoxins and prescribed cholestyramine as a binder. This practitioner encouraged the patient to conduct environmental testing of his home, which indicated the continued presence of mold. Appropriate remediation was conducted including removal of affected materials with proper precautions such as containment and negative air pressurization, as well as correction of the plumbing errors. However, the patient's symptoms continued. After continued aggravation of asthmatic symptoms and the development of the new neurological symptoms, the patient was referred to our clinic.

Assessments

Prior assessments included a serum IgE mold allergy panel and a lower respiratory culture. The patient was IgE Class II or III positive to several molds, including *Penicillium chrysogenum*, *Aspergillus fumigatus*, *Alternaria alternata*, *Fusarium proliferatum*, and *Epicoccum purpur*. Lower respiratory culture was negative.

Prior assessment with the mold specialist detected urinary excretion of mycotoxins from a first-morning's sample without provocation or dietary restrictions using the ELISA method, which included Aflatoxins, Trichothecenes, and Gliotoxin Derivatives, as shown in Figure 1.

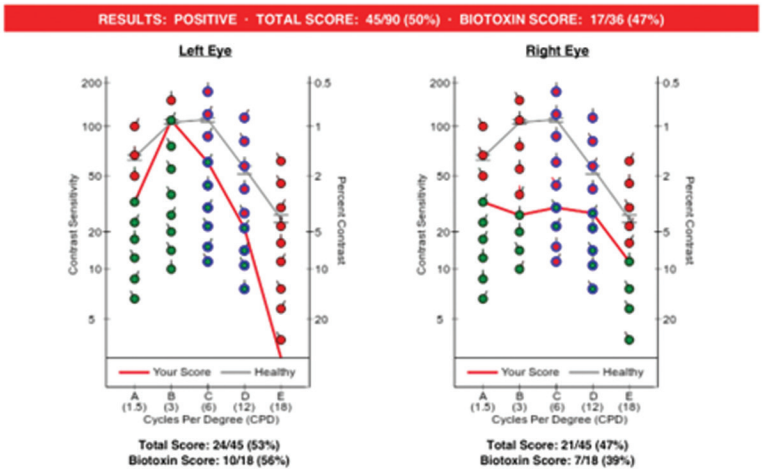
Urine mycotoxin tests are employed in research to detect human exposure to mold mycotoxins from both ingestion and inhalation.[37-41] A 2019 study in Environmental Pollution investigated mycotoxin detection from both plasma and urine. "Paired plasma and first morning urine samples were analyzed for 26 mycotoxin biomarkers…by an ultra-high-performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) method."[42] Some mycotoxins were more easily detected in urine than plasma, and some mycotoxins were the reverse, more easily detected in plasma than urine.

They also identified that sex makes a small difference for testing. "The incidence and concentration of mycotoxins in males and females were slightly different," depending on the mycotoxin and method of detection. However, there was a more significant difference in symptoms and/or timing of symptomatology, finding that women tended to have symptoms sooner than men.

Like any laboratory test, urine mycotoxin testing has its limitations and cannot be taken on its own to determine

Figure 2. Mold symptom questionnaire.

Figure 3. Visual contrast sensitivity test.



a diagnosis of mold-related illness. One limitation is the possibility that excreted dietary exposure could amplify the results. A review article in the International Journal of Environmental Research and Public Health states that "[while] over 300 mycotoxins have been identified, six (aflatoxins, trichothecenes, zearalenone, fumonisins, ochratoxins, and patulin) are regularly found in food, posing unpredictable and ongoing food safety problems worldwide."[43]

Cooking or heating does not appreciably reduce the contamination load in food. A study in Food Chemistry aimed to replicate household cooking of commercially available pastas and found that "60% of the deoxynivalenol and 83-100% of the enniatins were retained in the cooked pasta."[44]

While the pharmacokinetics are slightly different for each mycotoxin, there is a 48-hour washout period in urine for most mycotoxins. Therefore, to minimize the limitation of dietary amplification in the urine, patients are advised to eat a low-mycotoxin diet for three days prior to urine mycotoxin testing, as will be shown later in the case. This precaution was not taken for the above sample from the previous practitioner.

Before his initial visit, the patient was asked to complete a mold questionnaire and conduct an online Visual Contrast Sensitivity (VCS) test. The patient's symptom questionnaire indicated Possible Mold, as shown in Figure 2.

The patient had decreased visual contrast sensitivity, as seen in Figure 3.

This finding added to the suspicion of neurotoxic effects, which have been correlated to water-damaged building exposures,[45] as well as other aerosolized environmental toxicant exposures.[46-48] Alterations in visual contrast sensitivity have also been reported in other biotoxin inhalational exposures, such as when mists are inhaled above aquaria during algal blooms.[49] The VCS test is used by the military as a screening tool for bioweapon exposures such as fungi and mycotoxins, including the trichothecene T-2 toxin.[50,51]

For this patient, other indoor allergens were ruled out, as well as exposures to occupational toxicants and algal blooms. Since the patient was still symptomatic despite remediation, combined with the questionnaire score and a positive VCS test, the efficacy of his home remediation was suspect.

The first priority was to rule out ongoing exposure. The patient was resistant to the idea of continued mold exposure in his home because he had invested quite a bit of money in the remediation and could no longer smell mold. Unfortunately, olfactory detection is not sufficient to rule out mold infestation in a previously exposed individual. Animal studies suggest that even though excess mucosal irritation and mucous may reduce after removal of inhaled trichothecenes, damage to the olfactory sensory neurons persists.[52]

To assess whether he was currently environmentally exposed, a serum mycotoxin antibody test was ordered. Patients with antibodies against molds also tend to have elevated antibodies against mycotoxins.[53] In addition, serum IgE mycotoxin antibody elevations may be seen for up to four weeks from exposure. If this test is positive, it raises concern about continued exposure from his home. Steroids may lead to false negative serum mycotoxin antibody results, but the patient reported that he was not using his steroid inhaler due

Figure 4. Serum IgG mycotoxin antibody.

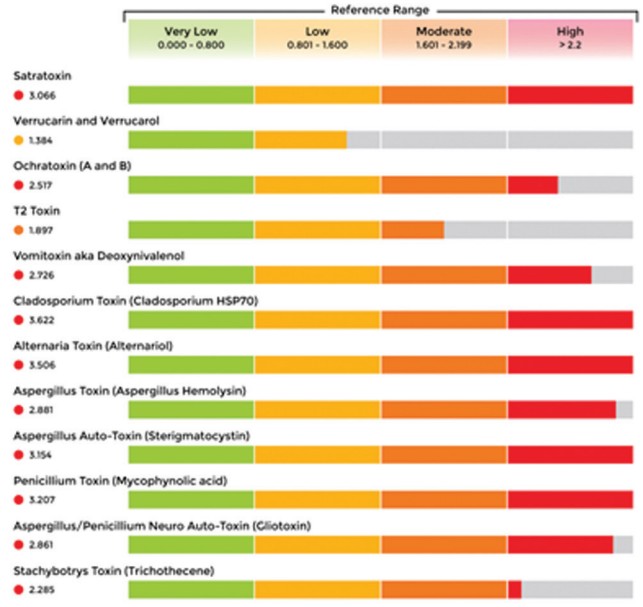
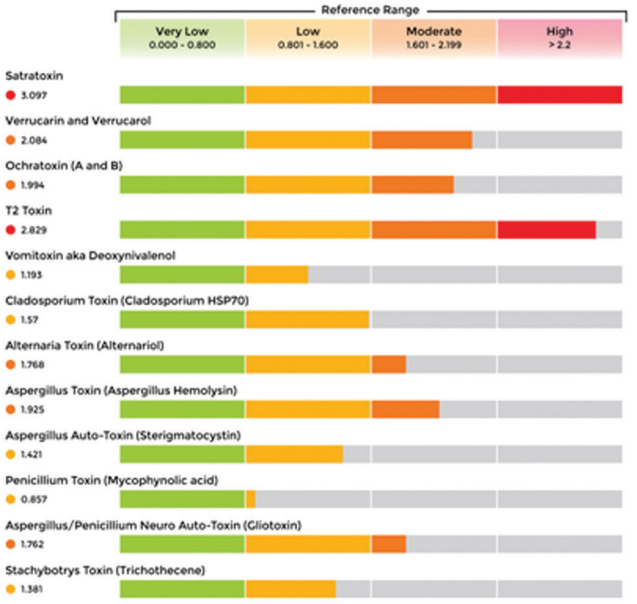


Figure 5. Serum IgE mycotoxin antibody.



to oral candidiasis recurrences whenever he would use it.

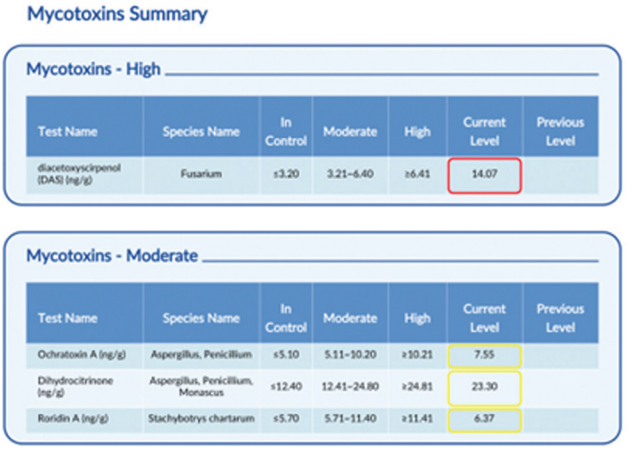
Based on findings, such as the aforementioned Environmental Pollutions study, indicating that different methods were more effective at detecting different mycotoxins, both serum and urine mycotoxin testing was ordered. For urine mycotoxin testing, care was taken to reduce the possibility of dietary exposure with a three-day low-mycotoxin diet. This is not necessary for serum testing. The removed foods were based on the aforementioned review article in the International Journal of Environmental Research and Public Health, which summarized the food contamination of the six most common food-borne mycotoxins.[54]

Provocation was not used for the urine test to increase confidence that excreted mycotoxins, if any, were from current exposure. The patient was also instructed to discontinue binders for the three-day period before the test, as they may reduce urinary excretion and therefore falsely lower the results.

Other mold-related assessments with neurological and immunological significance to mold were included. The patient had a white blood cell count at 4.1, 25-OH vitamin D at 18 ng/ml, reduced natural killer (NK) cell function at 5 lytic units, matrix metalloproteinase 9 (MMP-9) at 614 ng/ml, and a normal tryptase.[55] Due to the neuropathies, B12 deficiency was ruled out with normal serum B12 and normal methylmalonic acid. The patient had low total cholesterol and HDL, which had developed over the past 6 months. Specialized intranasal bacterial and fungal cultures reported methicillin-resistant *Staphylococcus aureus* (MRSA) and *Aspergillus fumigatus*.

The serum IgG mycotoxin antibody test in Figure 4 indicates high reactivity to Trichothecene, Ochratoxin, and Gliotoxin mycotoxins, as well as toxins from Cladosporium, Alternaria, Aspergillus, and Penicillium.

Figure 6. Urine mycotoxin using liquid chromatography, mass-spectrometry (LC-MS)



The increased serum IgE mycotoxin seen in Figure 5 suggested that he was still being exposed to moisture-damaged materials to an extent sufficient to engage his immune system.

The repeat urine mycotoxin test detected the continued presence of urinary mycotoxins from Fusarium, Aspergillus, Penicillium, and Monascus species, as well as from *Stachybotrys chartarum*, despite dietary restrictions, as seen in Figure 6. While this may occur from excretion of lipid bioaccumulation since most mycotoxins are lipophilic, the patient was not taking any measures to enhance excretion, nor had he recently lost weight.

The patient's symptoms and diagnostics taken together supported a suspicion of continued mold exposure. The patient was referred to a building biologist for an appropriate reassessment of his home. Additional areas of minor

contamination were identified, specifically in the HVAC system, as well as mild fragment and mycotoxin contamination in the kitchen, bathrooms, and master bedroom closet.

Treatments

The first rule of treatment in environmental illness is removal of the exposure. Following the guidance of the building biologist, remediation was conducted on the HVAC system as well as a meticulous particulate cleaning of the contaminated areas to address ultrafine particulates such as mold fragments and mycotoxins.

The house was cleared by the building biologist based on post-remediation environmental testing, but the patient only felt minor improvement in asthma and neuropathies. All other symptoms remained stable and he developed a new case of tinea cruris. While removal from the exposure may alleviate symptoms, removal alone is not sufficient for a number of patients once non-respiratory symptoms develop.[56] Additional treatment is often necessary, as was the case for this patient.

Treatment included dietary changes and supplements, as well as systemic, intranasal, and topical antifungals. Systemic and intranasal antifungals were not used immediately to allow time for the diet and supplements to preempt possible side-effects of the antifungal therapy. Many mold species will increase their production of mycotoxins when exposed to antifungals.[57,58] Certain nutraceuticals and botanicals, such as those used in this case, support the multi-organ systems affected by mycotoxins, so that antifungals may be better tolerated.

The focus of the diet and supplements was to modulate the immune system, reduce histamine sensitivity, and support organs of detoxification involved in mycotoxin excretion. The patient was given a handout of foods to avoid which were high in histamine, with particular focus on the two main categories of leftovers and fermented foods. He was also instructed to increase foods rich in quercetin bioflavonoids, such as onions, blueberries, grapes, and apples, lightly steamed kale and broccoli, as well as green tea and nettles tea.[59-66]

Vitamin D was optimized by supplementing a liposomal form of cholecalciferol (D3), dosed to a lab value of 90 ng/ml for six months to up-regulate vitamin D receptors. Some mycotoxins down-regulate vitamin D receptors in the intestine and kidneys, leading to reduced absorption of vitamin D.[67] As an immune modulator, vitamin D is indicated for asthmatics who benefit from corticosteroid therapy and may protect against particle-induced lung injury.[68-71]

Marine omega 3s are indicated for both mycotoxin injury and asthma, with one study showing that they significantly decreased the risk of non-specific bronchial hyperresponsiveness; however fish oil may have histaminic effects.[72-75] Therefore, to reduce the potential histaminic effects, anti-inflammatory compounds derived from fish oils called proresolving mediators were supplemented at a dose of 1000 mg twice daily for two weeks, then a maintenance dose of 500 mg daily.[76,77]

Turmeric (Curcuma longa) has been used in animal studies for hepatoprotection against mycotoxin exposure, and it has broad anti-inflammatory effects in humans in multiple systems, including asthmatic lungs.[78-81] The patient was given a dose of 500 mg three times daily, to be titrated over the first two weeks from a starting dose of 250 mg daily.

Resveratrol, a potent plant flavanol, attenuates allergic asthma and reduces DNA damage in bronchial epithelia, as well as enhancing NK cell cytotoxicity.[82-84] Resveratrol may reduce overactive bladder through its antioxidant activity.[85] It also addresses neuropathy by combatting known mycotoxin mechanisms, for example by activating the Nrf-2 pathway and alleviating Nf-kappa-B neuroinflammation.[86,87] To reach the desired plasma concentration, a dose of 1 gram daily was recommended.

Regarding binders, due to the patient's falling total cholesterol and HDL, a potential risk of the non-specific action of cholestyramine, the pharmaceutical binder was replaced with 2-3 Tbsp of fresh ground flax seeds daily, as bile acids are a target detoxification route for inhalational versus ingested mycotoxin exposure.[88,89]

Lastly, for the new symptom of tinea cruris reported at the appointment, topical treatment was recommended, using terbinafine hydrochloride 1% in the morning, and virgin coconut oil at night, which was added to reduce the risk of drug resistance and biofilm formation.[90,91]

While glutathione is often used to assist with hepatoprotection and mycotoxin excretion, it was not considered in this case due its risk of asthma aggravation. The patient was instructed to follow up in eight weeks.

Follow-Up

At the eight week follow up, the patient reported what he described as "measurable improvement" in his asthma symptoms, with reduced use of his albuterol inhaler by an average of 2 days per week. He was able to tolerate low-intensity exercise, though it would cause transient global pruritus.

Even though the supplements were primarily targeted to the patient's chief complaint of asthma, he saw mild improvement in glove-and-stocking neuropathy and therefore sleep, as well as faint improvement in urinary frequency and anxiety. Tinnitus and dull headache persisted. He reported that his allergies seemed to have "shrunk and come to center" on his nasal passages, noting improved eye, ear, and throat pruritus, necessitating fewer antihistamines. However, he noted slightly more nasal congestion. The patient also reported improved cognition, which he had not noticed was an issue until it improved. The tinea cruris was responding to topical treatment.

At this visit, the patient was instructed to continue the plan and add antifungal therapy, with emphatic instruction to keep his rescue inhaler close at hand in case of reactions. Before beginning any of the following antifungal therapies, he was to begin taking activated charcoal 280mg twice daily away from food. If he was still able to have regular bowel movements after one week at this dose, he could begin antifungals, and continue the charcoal for another two

Figure 7. Serum IgG mycotoxin antibody.

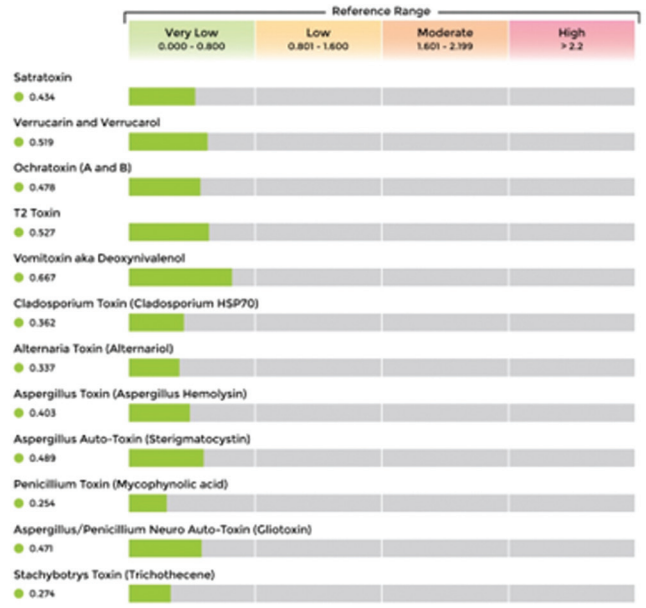


Figure 8. Serum IgE mycotoxin antibody.

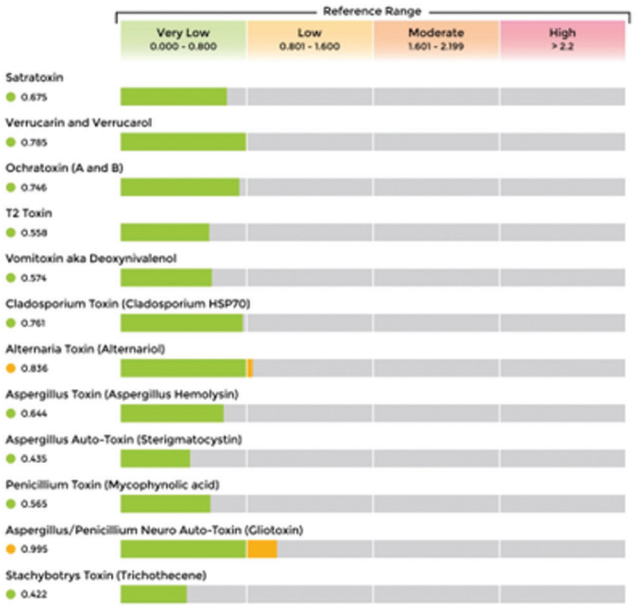
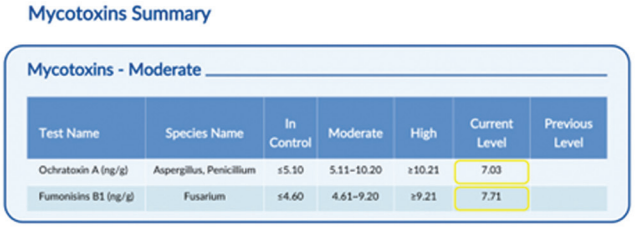


Figure 9. Urine mycotoxin using liquid chromatography, mass-spectrometry (LC-MS)



weeks. If not, he was instructed to contact the clinic for an adjustment to the plan.

For systemic antifungals, he began itraconazole 200 mg, given once daily to account for the significant first-pass effect of the triazoles. He was to take this dose continuously for 60 days, then pulsed for 2 consecutive days per week until follow-up. Liver enzymes were monitored at 30 days and were normal.

Drug resistance is an emerging problem, possibly made worse in the presence of mycotoxins.[92] For instance, the mycotoxin Gliotoxin is involved in the pathogenesis of its parent mold, *Aspergillus fumigatus*.[93] Therefore, to combat drug resistance to itraconazole, he was co-administered a garlic supplement with concentrated allicillins at a dose of 200mg allicillins twice daily with food.[94,95]

For intranasal antifungal treatment, he was to atomize a compounded nasal solution of nystatin 50 000 IU/10ml saline once daily, alternated twelve hours apart with an intranasal colloidal silver nasal spray.[96,97] He could add Nasalcrom daily as needed for breakthrough nasal allergy symptoms.

RESULTS

Seven months after his initial visit, and five months after initiating antifungal therapy, his daily asthma symptoms were significantly improved, requiring his albuterol inhaler only one time in the past 4 months after moving mulch in his yard, which he suspected was moldy. This was also one of the only times in that same timeframe that he required antihistamines for allergic symptoms.

Other symptoms of headache, glove-and-stocking neuropathy, pruritus, urinary frequency, and tinea cruris had resolved and he was back to his regular exercise routine. Sleep had improved to such a degree that the patient self-withdrew the doxepin during this time, and used a combination product containing melatonin 3 mg, L-theanine 200 mg, and GABA 100 mg as needed for sleep, which he reported averaged one night weekly (usually Sunday) based on high demands of his job. He discontinued the topical antifungals but was continuing all supplements. Residual symptoms were low-grade tinnitus and rare situational anxiety, which he began to attribute to mold exposures at restaurants and hotels.

A retest of the IgE mold spore allergy panel showed only one Category 0/I reaction to *Aspergillus fumigatus*; all others were normal. The following lab results were also taken in time for the appointment. As seen in Figures 7 and 8, both the IgG and IgE reactions to mold mycotoxins came into normal range. The patient was instructed to discontinue the itraconazole and maintain the Garlic for one additional month as he monitored symptoms. Assuming no increase in prior symptoms, he could discontinue the Garlic as well.

The intranasal nystatin and colloidal silver were then discontinued one at a time, two weeks apart, beginning with the nystatin. The patient was instructed to monitor for and report any return of symptoms. The patient was given a photobiomodulation device to use in the nares as needed for allergic symptoms.[98]

The repeat urine mycotoxin test in Figure 9 detected moderate presence of two mycotoxins with overall reduced

excretion as compared to the previous test. It's common for different mycotoxins to excrete at different timeframes and from different metabolic detoxification routes. Continued excretion above controls despite dietary avoidance indicated that he would benefit from continued detoxification support. He was instructed to continue the resveratrol and turmeric at half the dose for 2-3 more months, with flexibility to increase if any previous symptoms returned.

He could discontinue the proresolving mediators as desired, and reduce the vitamin D 25-OH blood test target to 60 ng/ml. He chose to continue the diet and flax seeds as he felt that the combination improved his energy and bowel movement consistency.

DISCUSSION

The challenge with the treatment of mold-related illness is the paucity of research, resulting in limited evidence to guide treatment. Due to medical ethics, we tend to avoid purposefully exposing humans to known mutagens, carcinogens, and teratogens, such as mycotoxins, in order to test treatments—especially when the first rule of treatment in toxin-based conditions is to remove the patient from the exposure.

The consistent immunosuppressive effects of toxins from molds have produced some commonly used medications, such as penicillin from Penicillium species molds, as well as mycophenolate (Cellcept) from both *Aspergillus* and *Penicillium* species, and in oncology, chaetoglobosin-A from *Chaetomium globosum*. Some previous attempts to adopt mycotoxins as medical treatments were fraught with complications, such as in the case of the mycotoxin citrinin, previously used as an antibiotic and investigated as a hypolipidemic, but discontinued due to nephrotoxicity. Their toxicity cannot be debated.

Not only are epidemiological studies limited to identify the human health effects of mycotoxins, but it is difficult to find randomized controlled trials in the treatment of the non-respiratory adverse health effects resulting from exposure to a moisture-damaged building. We are left with case reports such as this one to stimulate collaborative discussion.[99,100] As previously discussed, moisture-damaged building environments host a diversity of microbes. Once a person who has been exposed to this milieu develops both respiratory and non-respiratory symptoms, removal of the patient from the exposure may not be sufficient in improving health.

The evolving evidence of non-respiratory health effects obliges the conversation to expand beyond the respiratory system, beyond the single species of Aspergillus, and beyond the narrow focus on spores alone. For instance, this patient had treatment-resistant asthma and allergic bronchopulmonary aspergillosis (ABPA), as his symptoms continued to worsen despite treatment and despite removal from the exposure verified by an IEP. Antihistamines, inhalers, and binders did not resolve the problem for this patient. His condition was, however, resolved with antifungal therapy.

The mechanisms behind why some patients have persistence of symptoms despite removal from the exposure are debated and require further study. One hypothesized mechanism is colonization of the respiratory tract, leading to changes in the sinonasal microbiome.[101,102] Another is infection, owing to the ability of indoor molds to compromise the immune system.[103-105] And yet another is biofilm, which may complicate treatment due to resistance factors and may be associated with comorbid asthma.[106-108] Once mechanisms are appreciated through more research, treatments may be more targeted.

In this case, working within the three hypotheses mentioned, the target of treatment was alteration of the gut and sinonasal microbiome using long-term systemic and intranasal antifungals, administered alongside methods to combat resistance. Before antifungal therapy was initiated, support was given to those systems related to the reported non-respiratory symptoms.

The patient's improvement appeared to be related to re-establishing microbial balance. He was able to discontinue all medications related to allergies, sleep, and asthma, except for retaining a rescue inhaler for occasional use, which the patient had linked to incidental environmental mold exposures.

Before concluding, the management of the building requires caution for doctors and patients. The use of foggers is not considered industry standard for mold remediation, and as discussed in this case, often aggravates respiratory symptoms due to the aerated substances. Even after the gold standard remediation was done, particulates remained which may have aggravated the patient's respiratory passages. Patients are encouraged to hire an Indoor Environmental Professional (IEP), preferably one with BBEC credentials.

CONCLUSIONS

In conclusion, this case report highlights the possible importance of systemic and intranasal antifungal treatment in patients exposed to damp or moisture-damaged buildings with persistent symptoms despite removal from the exposure. Future studies are needed to offer insight into effective treatment interventions, such as the role of antifungal therapy in the mold- and mycotoxin-exposed patient.

A proposed area of interventional study is to test mold remediators. Nanoparticle-sized mycotoxins can pass through P100 respirators, meaning that mold remediators represent a unique group of unfortunate willing recruits for mycotoxin exposure. Results of interventions could be compared to matched controls of other mold remediators exposed to the same building environment. Studies like this and more are needed to appreciate the full scope of the problem and possible treatment interventions for moisture-damaged building exposure.

CONFLICTS OF INTEREST

The author declares no conflict of interest.

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