

# Role of microbial volatile compounds (mVOCs) in toxicity from molds-infested buildings: a case report

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## Abstract

Molds are ubiquitous, they grow optimally under high humidity, inadequate ventilation, and poor lighting, especially indoors. Components of molds (i.e.,  $\beta$ -glucans from the cell wall of spores and hyphal fragments) and toxic metabolites they produce (e.g., mycotoxins and microbial volatile organic compounds, mVOCs) are known to cause adverse health effects in humans. Indoors, components of molds easily reach unsafe levels. Most of the adverse health effects from mold exposure are routinely attributed to spores, hyphal fragments, and toxic mycotoxins while possible role of mVOCs is mostly overlooked. Here we report a case of 43-year old healthy African American male who was exposed mostly to mVOCs, emitted by molds inside the non-concrete walls and ceiling while living for ~3.5 months in a mold-infested apartment with overwhelming moldy smell. He worked from home; therefore, spent most of his time inside the apartment. The apartment was professionally cleaned and shampooed before he move-in and twice during the subject's brief stay in the apartment. Additionally, subject kept the apartment very clean by rigorous cleaning (vacuuming, dusting, brooming, wiping, and mopping – sometimes multiple times a day, especially vacuuming 2–3 times every day) after finding some molds and to get rid of the musty moldy smell. Consequently, very few mold spores were found in the air and dust of the apartment and negligible levels of mycotoxins in his urine. The subject started to suffer from rashes, ichthyosis, desquamation, dyspnea, fatigue, nocturnal awakening, headaches, dizziness, and syncope mostly from the exposure to mVOCs.

**Keywords:** Mold indoors, Mold toxicity, Microbial volatile organic compounds, mVOCs, mVOC risk assessment, Importance of mVOCs in mold toxicity

## Introduction

Molds are ubiquitous in the environment; they grow from microscopic spores of fungi under suitable conditions. Molds play an important role outdoors by decomposing dead organic matter (e.g., fallen leaves and dead trees), indoors, molds grow when spores land on moist/wet surfaces [1,2]. Indoors, molds are usually found in humid, damp/steamy, mostly in dark areas with poor ventilation (e.g., bathrooms, kitchens, cluttered storages, recently flooded areas, and basements) and easily reach to levels dangerous which can affect human health [1–4].

Components of molds (i.e.,  $\beta$ -glucans from the cell wall of spores and hyphal fragments) are known to cause/exacerbate allergies such as hay fever-type symptoms (sneezing, runny nose, red eyes), inflammation, skin rash, and chronic fatigue [2,3,5–13].  $\beta$ -glucans are natural polysaccharides and generally recognized as safe (GRAS) by the FDA for their use in food and supplements; however, fungal  $\beta$ -glucans are potent immunostimulators capable of causing adverse health effects by continuous overactivation of the immune system [14]. Molds cause hypersensitivity and immunomodulatory effects, especially in immunocompromised individuals [1,15–19].

Molds also produce secondary metabolites like mycotoxins and microbial volatile organic compounds (mVOCs) and are known to cause allergic reactions and other severe adverse health effects (e.g., headaches, dizziness, fatigues, difficulty concentrating, respiratory and skin issues) even at very low concentrations among humans [11,20,21]. Exposure to molds, mVOCs, and mycotoxins have been implicated in infants' deaths [1,22–26]. Mixtures of mVOCs are produced by all fungi with various composition and quantity depending on the matrix they grow [27–30]. Fungal mVOCs are mixtures of acids, alcohols, aldehydes, esters, ethers, ketones, terpenes, thiols and their derivatives which produce the distinctive moldy odor associated with damp indoor spaces. In addition to unpleasant odor, mVOCs are responsible for many adverse health effects at even very low (ppb) concentrations [11,20,31–35]. Some of the health effects of mVOCs include their impact on sensory organs (irritation of skin, eyes, nose, and throat), respiratory tract (allergies, asthma, bronchitis), central nervous system (headaches, dizziness, brain fog, fatigue, focusing issues, and mood changes); they also interfere with immune function, cellular health, and cause general malaise (nausea, lethargy) [11,20,31–35].

Almost all literature on the secondary metabolites of molds found indoors is dedicated to the toxicity of mycotoxins in humans and other vertebrates while possible role of mVOCs is mostly overlooked; literature on mVOCs is almost entirely dedicated to their aroma and flavor properties, as indicators of fungal growth, and/or as environmental signaling compounds (semiochemicals) [30]. Consequently, no effort is usually made to collect and/or analyze mVOCs inside mold-infested buildings for their possible adverse health effects to residents. Here, we report a case of relatively short-term (~3.5 months) exposure mainly to mVOCs and toxicity in a young healthy individual. This will help in developing consensus on the importance of collecting/analyzing indoor air from the mold-infested buildings for mVOCs, in addition to molds, components of molds, and mycotoxins.

### Case History

A healthy 43-year old African American male lived in a mold-infested apartment for ~3.5 months. Physical examination of the subject was unremarkable with normal heart rhythm, no ischemia, BP of 123/80 mm Hg, pulse of 76, non-fasting blood glucose of 125–140 mg/dL, slightly overweight with BMI of 26.11, higher total cholesterol and lower HDL levels, and negative for COVID.

Apartment had a strong mold-like musty odor at the time of inspection, prior to his move-in, that was linked by the management to the residual cleaning agents left in the carpet after cleaning and assured to dissipate within 24 h. The odor returned within one week of subject's moving into the apartment. Later, molds were discovered at several places including under the peeling new paint in the bathroom. Due to odor and molds, subject started to clean (vacuuming, dusting, brooming, wiping, and moping) the apartment rigorously (daily and sometimes multiple times a day, especially vacuuming 2–3 times every day). Soon after the move-in, subject started to suffer from rashes, ichthyosis, desquamation, dyspnea, fatigue, nocturnal awakening, headaches, and dizziness.

Within one month of living in the apartment, subject started getting dry and scaly feet with red bumps and rashes on skin. Within two months, subject started experiencing headaches. By third month, breathing issues along with dermatitis (skin inflammation, often accompanied by redness, itching, and rashes) of the face, started. By the fourth month, subject's symptoms worsen as he started to experience headache, chest pain, lightheadedness, and syncope (fainting, temporary loss of consciousness and the ability to stand). One of the dizziness spells led to syncope resulting in falling in the bathtub and injuring one of his knees and rushed to an emergency. Subject moved out of the mold-infested apartment after ~3.5 months to a non-mold-infested residence, mold-related toxicity symptoms, i.e., headache, chest pain, lightheadedness, and syncope, started to decrease after moving to the non-mold-infested residence.

### Levels of Molds in the Samples (Air and Dust) Collected from Inside the Apartment

As a result of several professional cleaning/shampooing and extensive daily cleaning regimen, very few molds were detected in the air and dust collected from inside the apartment. Very low levels (16, 23, 27, and 4 molds/g dust) of only four mold species (*Aspergillus fumigatus*, *Stachybotrys chartarum*, *Cladosporium caldosporides* L., and *Cladosporium herbarum*, respectively) were detected out of 36, mostly toxic, mold species the collected dust from inside the apartment was analyzed for fungal specific DNA, through PCR amplification (Table 1). The collected air from inside the apartment contained only two genera of molds, one in the living room and bathroom (*Cladosporium*, 20 spores/m<sup>3</sup> each) and one in the living room (*Myxomycetes*, 20 spores/m<sup>3</sup>), data not shown.

**Table 1.** Types of fungi detected through DNA/PCR sequencing in the dust Sample collected from inside the apartment.

Types of Fungus Detected	Pathogenic (Y/N)	Spores/mg Dust
1. <i>Aspergillus Flavus</i>	N	ND
2. <i>Aspergillus fumigatus</i>	Y	16
3. <i>Aspergillus niger</i>	Y	ND
4. <i>Aspergillus ochraceus</i>	Y	ND
5. <i>Aspergillus penicillioides</i>	Y	ND
6. <i>Aspergillus restrictus</i>	Y	ND
7. <i>Aspergillus sclerotiorum</i>	Y	ND
8. <i>Aspergillus sydowii</i>	Y	ND
9. <i>Aspergillus unguis</i>	Y	ND
10. <i>Aspergillus versicolor</i>	Y	ND

Types of Fungus Detected	Pathogenic (Y/N)	Spores/mg Dust
11. <i>Eurotium (A.) amstelodami</i>	Y	ND
12. <i>Aureobasidium pullans</i>	Y	ND
13. <i>Chaetomium globosum</i>	Y	ND
14. <i>Cladosporium sphaerospermum</i>	Y	ND
15. <i>Paecilomyces variotii</i>	Y	ND
16. <i>Penicillium brevicompactum</i>	Y	ND
17. <i>Penicillium corylophilum</i>	Y	ND
18. <i>Penicillium crustosum (group 2)</i>	Y	ND
19. <i>Penicillium purpurogenum</i>	N	ND
20. <i>Penicillium spinulosum</i>	N	ND
21. <i>Penicillium variabile</i>	Y	ND
22. <i>Scopulariopsis brevicaulis</i>	Y	ND
23. <i>Scopulariopsis chartarum</i>	Y	ND
24. <i>Stachybotrys chartarum</i>	Y	23
25. <i>Trichoderma viride</i>	Y	ND
26. <i>Wallemia sebi</i>	Y	ND
27. <i>Acremonium strictum</i>	Y	ND
28. <i>Alternaria Alternata</i>	Y	ND
29. <i>Aspergillus ustus</i>	Y	ND
30. <i>Cladosporium caldosporides I.</i>	Y	27
31. <i>Cladosporium caldosporides II.</i>	Y	ND
32. <i>Cladosporium herbarum</i>	Y	4
33. <i>Epicoccum nigrum</i>	Y	ND
34. <i>Mucor-Rhizopus Group</i>	Y	ND
35. <i>Penicillium Chrysogenum</i>	Y	ND
36. <i>Rhizopus stolonifer</i>	Y	ND

ND: Not Detected, remained below the lowest limit of quantification (LLQ) even after PCR amplification.

Pathogenic, documented in the scientific literature to be disease causing to humans.

### Levels of Mycotoxins in the Urine of the Subject

Consequently, only negligible levels, barely above the threshold of toxicity, of two mycotoxins were detected in the urine of the subject (Table 2). Urine was analyzed for 11 known mycotoxins produced by the molds commonly found inside the mold-infested buildings. The level of Ochratoxin A (OTA), produced by species of *Aspergillus*, *Eurotium*, *Fusarium* and *Penicillium*, in urine of the subject was 8.63 ng/g creatinine, only 1.13 ng/g higher than the toxicity threshold of 7.5 ng/g creatinine. Similarly, the level of Gliotoxin, produced by *Aspergillus*, *Eurotium*, *Neosartorya*, *Trichoderma*, and some species of *Penicillium*, *Acremonium* and *Alternaria*, in the urine of the subject was 217.97 ng/g creatinine, only ~18 ng/g higher than the toxicity threshold of 200 ng/g creatinine (Table 2).

The fact that very low levels of molds were detected in the air and dust samples collected from inside the apartment along with levels of two mycotoxins detected in urine that remained barely above the threshold of toxicity, adverse health effects observed by the subject could not correlate with the components of molds (i.e.,  $\beta$ -glucans

from the cell wall of spores and hyphal fragments, mycotoxins). Detection of extremely low levels of molds, their components, and mycotoxins is consistent with removal of all visible molds promptly, three professional cleaning/shampooing of the apartment within the short period (~3.5 months) of occupancy and keeping very rigorous cleaning regimen.

Presence of the persistent strong moldy odor, even after several professional cleaning/shampooing and rigorous daily cleaning regimen, was likely from the active growth of molds in hidden areas like inside the walls, ceiling, and insulation materials therein. Mixtures of mVOCs are produced by all fungi with various composition and quantity depending on the matrix they are growing on [27–30]. In addition to unpleasant odor, mVOCs cause many adverse health effects even at very low (ppb) concentrations [11,20,31–35]. Some of the health effects of mVOCs include irritation of skin, eyes, nose, throat, allergies, asthma, bronchitis, headaches, dizziness, brain fog, fatigue, concentration, mood. They also interfere with immune function, cellular health, and cause general malaise (nausea, lethargy) [11,20,31–35]. Therefore, adverse health effects observed by the

**Table 2.** Mycotoxins detected in the urine of the subject.

Type of Mycotoxin	Level (Normal*) (ng/g creatinine)
Aflatoxin-M1	ND
Ochratoxin A	8.63 (<7.5)
Gliotoxin	217.97 (<200)
Sterigmatocystin	ND
Mycophenolic Acid	ND
Roridin E	ND
Verrucaric Acid	ND
Enniatin B	ND
Zearalenone	ND
Chaetoglobosin A	ND
Citrinin (Dihydrocitrinone DHC)	ND

\*Threshold values above which toxicity is expected.

ND: Not Determined, remained below the LLQ.

subject while residing at the mold-infested apartment, i.e., rashes, ichthyosis, desquamation, dyspnea, fatigue, nocturnal awakening, headaches, dizziness, and syncope, are likely from the exposure to mVOCs (alcohols, ketones, aldehydes, terpenes, esters, and sulfur-containing compounds) a mixture of which is produced by all molds [27–30].

This case report underscores the importance of mVOCs when assessing adverse health effects of residents living in mold-infested buildings. These findings will hopefully help in developing consensus on the importance of collecting/analyzing indoor air from inside the mold-infested buildings for mVOCs, in addition to molds, components of molds, and mycotoxins.

### Statements and Declarations

Shakil A Saghir and Jeremiah Bancroft work for a mold testing company and at times are hired as expert witness by the plaintiffs or defenders.

Rais A Ansari has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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