
Inhalational mold toxicity: fact or fiction? a clinical review of 50 cases

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Background: Three well-accepted mechanisms of mold-induced disease exist: allergy, infection, and oral toxicosis. Epidemiologic studies suggest a fourth category described as a transient aeroirritation effect. Toxic mold syndrome or inhalational toxicity continues to cause public concern despite a lack of scientific evidence that supports its existence.

Objectives: To conduct a retrospective review of 50 cases of purported mold-induced toxic effects and identify unrecognized conditions that could explain presenting symptoms; to characterize a subgroup with a symptom complex suggestive of an aeroirritation-mediated mechanism and compare this group to other diagnostic categories, such as sick building syndrome and idiopathic chemical intolerance; and to discuss the evolution of toxic mold syndrome from a clinical perspective.

Methods: Eighty-two consecutive medical evaluations were analyzed of which 50 met inclusion criteria. These cases were critically reviewed and underwent data extraction of 23 variables, including demographic data, patient symptoms, laboratory, imaging, and pulmonary function test results, and an evaluation of medical diagnoses supported by medical record review, examination, and/or test results.

Results: Upper respiratory tract, lower respiratory tract, systemic, and neurocognitive symptoms were reported in 80%, 94%, 74%, and 84% of patients, respectively. Thirty patients had evidence of non-mold-related conditions that explained their presenting complaints. Two patients had evidence of allergy to mold allergens, whereas 1 patient exhibited mold-induced psychosis best described as toxic agoraphobia. Seventeen patients displayed a symptom complex that could be postulated to be caused by a transient mold-induced aeroirritation.

Conclusion: The clinical presentation of patients with perceived mold-induced toxic effects is characterized by a disparate constellation of symptoms. Close scrutiny revealed a number of preexisting diagnoses that could plausibly explain presenting symptoms. The pathogenesis of aeroirritation implies completely transient symptoms linked to exposures at the incriminated site. Toxic mold syndrome represents the furtive evolution of aeroirritation from a transient to permanent symptom complex in patients with a psychogenic predisposition. In this respect, the core symptoms of toxic mold syndrome and their gradual transition to chronic symptoms related to nonspecific environmental fragrances and irritants appear to mimic what has been observed with other pseudodiagnostic categories, such as sick building syndrome and idiopathic chemical intolerance.

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INTRODUCTION

Mold-induced toxic effects continue to engender public fear. Much of this concern stems from both distorted media coverage and the wide availability of the Internet. Thousands of mold-related Web sites exist, and one is only a few mouse clicks away from accessing a plethora of information ranging from purchasing mold cleaning kits to procuring the services of myriad consultants who offer legal, medical, and remediation expertise. The current climate of apprehension is also fueled by industrial hygienists, medical care providers, and an overzealous juristic community.¹

Clinical science has long accepted 3 mold-related mechanisms of human disease: immunologic sensitization, infectious disease, and mycotoxicosis via ingestion.^{2,3} Additionally, a number of epidemiologic studies have suggested a fourth category of symptoms, which can be best described as a transient aeroirritant symptom complex.^{4–6} Although still controversial and largely unproven, nonspecific aeroirritant symptoms are believed to

arise from aerosolized fungal constituents, such as volatile organic compounds, ergosterol, glucans, and possibly proteases.^{7–13} Lastly, some investigators have attempted to establish inhalational mold toxic effects as a viable mechanism of human disease^{14,15}; however, several critical reviews have not found any scientific support for such a claim.^{2,4,5,16–19}

The objective of this study was to describe the clinical characteristics of patients who present with presumed mold toxic effects. In doing so, we also identified previously unrecognized disease unrelated to mold exposure but that largely explained their presenting symptoms. Further, we segregated a subset of individuals with possible mold-related aeroirritant symptoms and compared this subgroup to previously identified diagnostic categories, such as sick building syndrome and idiopathic chemical intolerance. Finally, we propose a clinical paradigm in which to consider the surreptitious evolution of toxic mold syndrome.

METHODS

Patient Population

Eighty-two patients with complaints of mold-induced illness were referred to one of the authors (E.J.B.) for evaluation.

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The focus of the evaluation was their contention that mold exposure in their home or workplace had precipitated ill health. Each was seen between 1999 and 2003 and underwent a comprehensive medical evaluation. A physician-patient relationship was not established in any of the cases. Referral sources were divided between insurance adjusters in the context of workers' compensation agencies from the states of Oregon and Washington or a defense attorney in the setting of civil litigation.

The lead author sequentially reviewed the case files from 82 cases and identified 50 cases for study inclusion. Criteria for inclusion required a comprehensive patient evaluation at Oregon Health and Science University (OHSU) that included a complete medical history, physical examination, core laboratory studies, imaging studies of the chest, sinus computed tomography (CT) imaging based on predominance of upper respiratory tract symptoms or clinical suspicion, and complete pulmonary function studies, including spirometry, lung volume studies, and diffusion capacity. Virtually all prior medical records were required along with the availability of indoor air quality studies of the site incriminated in the mold exposure. Thirty-two patients were excluded from the study for 1 or more reasons, including (1) evaluation at an off-campus site where laboratory studies, imaging, or pulmonary function studies could not be performed or were limited [7], (2) absence of core laboratory test results [7], (3) inability to obtain virtually all prior medical records [3], (4) refusal or inability to perform chest imaging studies [5], or (5) lack of indoor air quality studies of the putative exposure [10]. The 50 study patients were all seen at OHSU by a single evaluator and underwent all studies in the same laboratory, radiology department, and pulmonary function laboratory by the same respiratory technician.

Testing

Core laboratory studies included quantitation of serum IgG, IgA, and total serum IgE by established techniques. Serum specific IgE antibodies to mixed grass, mold, weed, and tree pollen and *Dermatophagoides pteronyssinus*, dog, and cat epithelium were assayed by a fluoroenzyme immunoassay using a UniCAP 100 instrument (Pharmacia Diagnostics AB, Uppsala, Sweden). Cockroach antigen was added to the aeroallergen panel in 2002. Serum specific IgE antibodies to other animals were ordered based on home pet exposures. Serum specific IgE and IgG antibodies were conducted against a core panel of 6 fungal allergens, including *Cladosporium herbarum*, *Aspergillus fumigatus*, *Aurobasidium pululans*, *Alternaria tenuis*, *Penicillium notatum*, and *Helminthosporium halodes*. Testing was expanded to include *Rhizopus nigricans*, *Fusarium oxysporum*, *Epicoccum purpurascens*, and *Botrytis cinerea* based on clinical suspicion. In 2002 additional fungal allergens were added to the panel, including *Chaetomium globosum* and *Stachybotrys atra*.

All invasive testing, such as phlebotomy and pulmonary function tests with bronchodilator or methacholine challenge

(MCC), was performed using widely accepted protocols with signed consent from the study patients.^{20,21} This study received institutional review board approval at OHSU.

Definitions

An individual was considered atopic if he or she had 1 or more positive IgE antibody test results to either an aeroallergen or mold allergen. To be considered positive, the assay had to be class 2 (0.7–3.5 kU_A/L) or greater. Sinusitis was defined as an air-fluid level in a sinus cavity and/or sinus opacification. Asthma was defined as a change in forced expiratory volume in 1 second of greater than 12% with a nebulized bronchodilator and/or a positive MCC result at or below a concentration of 16 mg/mL. An ratio of forced expiratory volume in 1 second to forced vital capacity of less than 70% was considered abnormal and indicative of obstructive lung disease. In reviewing indoor air quality reports, indoor mold levels were considered to be in an expected range if they fell between 40% and 80% of parallel outdoor levels with similar rank order of fungal species.

Analysis

The 50 study cases underwent data extraction of 25 variables: age, sex, ethnicity, referral source, symptoms, exposure site, exposure length, preexisting allergic rhinitis (AR) or asthma, family history, pet ownership, tobacco exposure, recreational drug use, physical examination abnormalities, IgG, IgA, and IgE levels, serum antibodies to aeroallergens and fungal allergens, chest or sinus imaging, spirometry, psychiatric diagnoses, environmental survey, and evaluation of established or plausible explanatory medical diagnosis supported by medical record review, examination, and/or diagnostic test results. Diagnoses were segregated into 2 subgroups: mold-related and non-mold-related medical conditions. Mold-related illness was further divided into immunologic, infectious, toxic effects by ingestion, transient aeroirritation, or psychological reaction.

Subjective complaints were subdivided into 4 categories: upper respiratory tract, lower respiratory tract, systemic, and neurocognitive. Upper respiratory tract involvement included 1 or more symptoms of the nose, eye, ear, sinus, or throat. Lower respiratory involvement included 1 or more symptoms of cough, wheeze, shortness of breath, or chest-related symptoms. Systemic involvement included 1 or more complaints related to skin, hair, fatigue, myalgia, arthralgias, glandular swelling, gastrointestinal (including dyspepsia and gastroesophageal reflux) or genitourinary tract problems, fever, chills, night sweats, or weight loss. Neurocognitive involvement was defined as 1 or more symptoms of dizziness, insomnia, headache, mood disorder, sensory deficits, tremor, memory loss, behavior change, vertigo, dyslexia, dysarthria, sleepwalking, lightheadedness, and irritability. In most cases, exposure onset was defined as the date the patient moved into the putative building, except in 2 cases where there was a specific water intrusion that predated symptom onset.

RESULTS

The demographic characteristics of the study group are given in Table 1. Five families in the study represented 15 individuals. The referral source was evenly divided between a variety of claims adjusters in a workers' compensation setting and 8 separate law firms.

There was no consistent set of complaints, because symptoms varied in both number and complexity. There was an average of more than 8 symptoms per patient. Eighty percent complained of at least 1 upper respiratory tract symptom, whereas 94% complained of lower respiratory tract symptoms. Seventy-four percent noted systemic symptoms and 84% had neurocognitive symptoms. Most individuals had symptoms in at least 3 of the 4 subgroups identified. The most common presenting symptoms were shortness of breath (76%), headache (74%), cough (72%), rhinitis or nasal congestion (52%), and fatigue (50%).

Sixty percent of the study group identified a first-degree relative with either AR or asthma, whereas 72% admitted a

personal history of preexisting AR or asthma (23 with AR, 24 with asthma, and 11 with both conditions). Of the 24 patients with a history of preexisting asthma, 33% had positive MCC results and 50% had negative MCC results. Four patients did not undergo MCC; 2 patients had low volumes that precluded MCC, and 2 patients refused to sign consent. Of the 23 patients with claims of preexisting AR, 61% had at least 1 IgE specific antibody to the aeroallergen or mold panel.

Twelve percent of patients had a previous history of recreational drug abuse that included marijuana, lysergic acid diethylamide (LSD), cocaine, or methamphetamines. The study group included 10 current smokers, 21 past smokers, and 19 never-smokers. Excluding children younger than 18 years, 71% of adults had a history of tobacco abuse. Sixty-one percent of patients with a complaint of cough were past or current smokers. Eighty-four percent of individuals had at least 1 pet (dog, cat, bird, or rabbit), and 14% of pet owners had developed IgE specific antibody to their pets.

Physical examination results were abnormal in 76% of patients. The most common findings were conjunctivitis and inferior turbinate congestion and/or erythema. Interestingly, of the 35 patients with documented conjunctivitis or nasal congestion, 43% had an elevated total IgE level or at least 1 serum IgE antibody to an aeroallergen or mold allergen. Twenty-six percent were active tobacco smokers.

Thirteen patients had an elevated total serum IgE level (greater than 180 IU/mL), and 85% of them had IgE specific antibody to at least 1 aeroallergen. Forty percent of individuals had at least 1 serum IgE antibody to the aeroallergen panel, whereas 12% had at least 1 antibody to the fungal allergen panel. Serum IgE specific antibodies to *S atra* were measured in 24 patients with 1 positive result (Table 2). Forty-two percent of the study group was considered atopic. Three patients had mild hypogammaglobulinemia and 2 had mild IgA deficiency. Only 1 of these 5 cases was clinically significant, with the affected person experiencing recurrent pulmonary infections and developing bronchiectasis as a result of IgA deficiency.

Thirty-two patients underwent chest CT scans, whereas 18 had plain films of the chest. Two scans had changes suggestive of hypersensitivity pneumonitis, 3 had changes indicative of emphysema, and 3 revealed evidence of mild cylindrical bronchiectasis. Etiology of bronchiectasis was unknown in 1 patient, due to IgA deficiency in another patient, and due to past pneumonitides in another patient. All plain chest films were normal. Sinus CT scans were performed in 26 individuals, and 6 had evidence of sinusitis. Complete pulmonary function testing revealed 2 patients who met the criteria for chronic obstructive pulmonary disease. Forty-three individuals underwent MCC, which revealed 11 patients with mild to moderate bronchial hyperreactivity. Diffusion capacity was abnormal in 26% of individuals after correction for alveolar volume. Sixty-nine percent of those with abnormal diffusion were current or past smokers or had a history of recreational drug abuse.

Table 1. Demographic Characteristics of a Population With Perceived Mold-Induced Illness (N = 50)

Characteristic	Finding
Sex, No. (%)	
Male	14 (28)
Female	36 (72)
Ethnicity, No. (%)	
White	48 (96)
African American	2 (4)
Age of symptom onset, mean (range), y	34.08 (5–68)
Exposure duration before symptoms, mean (range), mo	21.66 (0–156)
Exposure duration after symptoms, mean (range), mo	39.12 (2–144)
Total exposure duration, mean (range), mo	60.78 (7–288)
Mold exposure site, No. (%)	
Home	17 (34)
School	7 (14)
Workplace or office	26 (52)
Evidence of water intrusion, No. (%) [*]	46 (92)
History, No. (%)	
Asthma	24 (48)
Allergic rhinitis	23 (46)
Asthma and allergic rhinitis	11 (22)
Family history of allergic rhinitis or asthma	30 (60)
Social history, No. (%)	
Active tobacco exposure	31 (62)
Recreational drug use	6 (12)
Pet ownership	42 (84)
Referral source, No. (%)	
Workers' compensation	25 (50)
Defense attorney	25 (50)

* Water intrusion defined as either visible water leak or evidence of indoor water leak, such as watermarks, pooling, water damage, or mold growth.

Table 2. Results of Serum Antibody Studies in a Population With Perceived Mold-Induced Illness

Positive antibodies	No. (%) of patients			
	Total*	Asthma†	Allergic rhinitis‡	Atopy§
Elevated total IgE level	13/50 (26)	4/11 (36)	9/19 (47)	11/21 (52)
Aeroallergen IgE	20/50 (40)	5/11 (45)	14/19 (74)	20/21 (95)
Mold IgE	6/50 (12)	2/11 (18)	5/19 (26)	6/21 (29)
Aeroallergen and mold IgE	5/50 (10)	2/11 (18)	5/19 (26)	5/21 (24)
<i>Stachybotrys</i> IgE	1/24 (4)	1/8 (13)	1/6 (17)	1/9 (11)

* Total represents all 50 patients not the total of the other 3 columns.

† Asthmatic patients are those with positive methacholine challenge or bronchodilator challenge results.

‡ Allergic rhinitis is based on diagnosis by examiner.

§ Atopy is defined as having 1 or more positive specific IgE antibodies.

Indoor air quality testing revealed 23 studies with elevated airborne fungal levels; 19 were within expected levels when compared with outdoor measurements with no differences in rank order of species. Eight studies did not measure airborne mold propagules (ie, relied on bulk sampling or tape lifts) or were performed after complainants had vacated the premises. The 23 surveys that measured elevated indoor mold levels represent 10 different buildings (7 offices and 3 homes) and account for 59% of patients diagnosed as having aeroirritation. None of these properties was considered to be a newly constructed “tight” building. Of the 14 buildings, representing 26 work-related exposures, most were described as “older buildings” with evidence of water leaks. Only 2 structures were referred to as “tight” buildings, relying on recirculated air with no outside air entry.

Three surveys tested for volatile organic compounds, the results of which were unremarkable. None of the surveys measured for mycotoxin, ergosterol, glucans, or proteases. Similarly, none of the surveys addressed other confounding allergens or substances at the putative site (eg, house dust mite, animal dander, cockroach, or endotoxin).

Thirty individuals had evidence of a non-mold-related illness that could explain most, if not all, of their mold-related complaints (Table 3). Many of the neurocognitive and systemic complaints, such as headache and poor memory, could easily be attributed to sinusitis, allergic rhinoconjunctivitis, or obstructive sleep apnea. Sixty-four percent of individuals had evidence of a previously diagnosed mood disorder, including depression, generalized anxiety, and adjustment disorders. One individual had evidence of fear-induced somatic symptoms and was diagnosed as having toxic agoraphobia. He displayed an obsessive preoccupation with “toxin” exposure. This individual objected to the office in which the evaluation was to be performed, requested an alternate examination site, and sprayed the table and walls with a “bromide” antifungal spray on entering the room.

Seventeen individuals had a symptom complex that could best be characterized as a mild, transient annoyance or irritational syndrome.²² They complained of symptoms that were temporally related to exposure to mold without confirmatory objective evidence to relate it to mold (glucans, volatile

organic compounds, or proteases) as opposed to endotoxin, other indoor pollutants, or relative humidity in the structure. There were no objective biomarkers that permitted certain linkage to a causative agent. In fact, only 3 of these patients exhibited fungal sensitization, and none correlated with elevated indoor levels in the putative site. There was no evidence of permanent impairment related to this symptom complex.

Of the 12% of patients with IgE antibodies to mold antigens, 2 had evidence of mold-related allergy linked to the putative site. One individual had allergic asthma and another had a fungal mycetoma. In the former case, objective evidence existed of serum specific IgE antibodies to fungal allergens represented in the worksite. Although one could never be certain that the initial sensitization occurred at the worksite, evidence clearly showed that the worksite had elevated airborne mold propagules to which the subject had a bona fide sensitivity and temporally related symptoms. In the case of fungal sinusitis, a mycetoma was removed at surgery. Unfortunately, it was not sent for culture, and we cannot be certain whether it was composed of a species found in the putative site. Although 2 patients had CT scans of the chest consistent with hypersensitivity pneumonitis, they failed to meet any of the clinical, physiologic, or immunologic criteria of this condition.

DISCUSSION

Toxic mold syndrome continues to be a symptom complex that presents as a purported cause of permanent impairment and disability, despite the lack of credible scientific evidence establishing a cause-and-effect relationship. Unlike the accepted mold-related illnesses, this symptom complex is not associated with a specific set of symptoms that can be linked to mold by a known pathophysiologic mechanism. Our study indicates that this presentation is characterized by a widely disparate constellation of symptoms summarily linked to the presence of mold without a defined pathogenesis. Individual complaints were heterogeneous and involved almost every body organ. In our view, no case definition is possible for so-called toxic mold syndrome. In fact, when the entire history and objective evidence were scrutinized, a number of

Table 3. Major Subgroups of Established and Plausible Disorders Present in a Population With Perceived Mold-Induced Illness

Disorder subgroup	No. (%) of patients
Infection disease	
Sinusitis	27 (54)
Otitis media	11 (22)
Pharyngitis	7 (14)
Bronchitis or bronchiolitis	17 (34)
Mononucleosis	2 (4)
Pneumonia	8 (16)
Allergic disorders	
Allergic rhinitis	19 (38)
Bronchial asthma	11 (22)
Nonallergic disorders affecting respiration	
Rhinitis	4 (8)
Eustachian tube dysfunction	3 (6)
Vocal cord dysfunction	5 (10)
Acid reflux or dyspepsia	11 (22)
Chronic obstructive pulmonary disease	4 (8)
Bronchiectasis	3 (6)
Obstructive sleep apnea	6 (12)
Metabolic, toxin, or musculoskeletal conditions	
Thyroid dysfunction	4 (8)
Diabetes mellitus	1 (2)
Recreational drug abuse	6 (12)
Tobacco abuse	31 (62)
Musculoskeletal disorders	4 (8)
Obesity	20 (40)
Central nervous system disorders	
Migraine	9 (18)
Head injury	3 (6)
Learning disorder	1 (2)
Psychiatric disorders	
Generalized anxiety disorder	15 (30)
Panic disorder	7 (14)
Adjustment disorder	6 (12)
Depressive disorder	23 (46)
Mycotoxin agoraphobia	1 (2)

well-established and plausible diagnoses emerged that explained many, if not all, the complaints (Table 3).

Often individuals had a preexisting allergic diathesis with symptoms that predated the putative exposure. Approximately 14% of study patients exhibited evidence of allergies to their own pets but attributed their symptoms to mold exposure. Sixty-one percent of individuals who complained of shortness of breath and/or cough had past or ongoing tobacco exposure. Interestingly, these people were more concerned about the possibility of adverse health effects from mold exposure than the known adverse health effects from the thousands of chemicals inhaled every time a cigarette is smoked. Still other patients had evidence of active sinus disease. Forty percent of the population had antibodies to at least one common aeroallergen, which could easily be linked to their respiratory symptoms.

Twelve percent of study patients were sensitized to at least 1 fungal allergen that could arguably cause symptoms of

asthma or AR. In this regard, it must be remembered that presence of immunologic sensitivity does not necessarily mean an individual will become symptomatic on a given exposure. This depends entirely on the degree of immunologic sensitivity and the concentration of the allergen encountered. Barnes et al²³ found IgG and IgE specific antibody to *S atra* in 49.2% and 9.4% of asymptomatic Red Cross donors, respectively. More importantly, if the mold species in the home were found at expected levels (ie, 40%–80% of parallel outdoor levels), there would be no possible way to attribute symptoms to a putative home or worksite, since there was an equal or better opportunity of encountering the same exposure in the outdoors.

The fact that a mold is present is not evidence of exposure. Growth of toxigenic fungi indoors does not necessarily indicate the presence of mycotoxins unless they are actually measured.²⁴ Although all patients linked their symptoms to mycotoxins, not one site survey measured mycotoxins. Therefore, assertions that mycotoxins caused health effects were entirely speculative. Furthermore, the environmental testing usually focused only on mold and did not test for other common allergens or irritants. Atopic patients especially could be reacting to one of many indoor allergens. Portnoy et al²⁵ recently described the ideal approach to sampling for indoor fungi. We can categorically state that none of the indoor air quality studies reviewed in these 50 cases met even the minimal expectations outlined by these investigators.

Testing was never conducted in other nonputative buildings to which the patient was exposed. In attempting to determine any relationship between indoor mold exposure and health effects, it is likely that significant exposure occurs outdoors and away from the putative location and would include automobiles, barns, and schools. Ignoring alternate sources would likely confound any perceived causality. In fact, a number of patients had evidence of fungal sensitization that did not correlate with species found in the incriminated location. Alternative sites of exposure may contain high levels of aeroallergens, including molds, that could account for sensitization and symptoms. This is especially true in rural areas of the Pacific Northwest. It must be remembered that mold is ubiquitous and can be found in practically all buildings. This is the fundamental challenge in attempting to establish sensitization or indoor mold-related disease to exposure from one specific location, even in the presence of high-quality environmental surveys. Guidance on remedial measures and patient care of suspected inhalational mold toxic effects are beyond the scope of this article but are similar to recommendations for sick building syndrome.²⁶

Seventeen individuals were found to have a nonspecific, transient aeroirritant symptom complex. We are not able to definitively link this symptom complex to mold exposures in the incriminated workplace or home. No objective manner exists by which we can eliminate other indoor pollutants, allergens, or building-related conditions as possible contributors to these nonspecific complaints. It is possible, though unproven, that this nonspecific symptom complex could be

caused by an irritant effect related to the exposure to mold-related proteases, ergosterol, glucans, or volatile organic compounds or possibly a combination of all 4 factors. The only manner in which this could be proven would be to demonstrate elevated levels of these mold constituents in the putative site and to eliminate sources other than mold, since 2 of the 4 constituents can be produced by alternate sources. This would be further reinforced by demonstrating the absence of other allergens, indoor pollutants, or endotoxin that could also contribute to such a syndrome. Hence, the challenge would be considerable.

In the absence of rigorous environmental testing, a diagnosis of aeroirritation can, by definition, only explain transient symptoms and not chronic symptoms or permanent injury for which many patients were seeking compensation. We propose that this subpopulation of individuals initially may have had transient building-related aeroirritation. Often there appeared to be a gradual evolution of temporally related symptoms to the development of a broader chronic symptom complex that involved a variety of nonspecific fragrances, perfumes, or fumes. Ultimately, the symptom complex shifted from one with a plausible pathogenetic mechanism to one better described as a pseudodiagnosis without scientific credibility (ie, environmental intolerance). In fact, the core symptoms of this aeroirritant symptom complex are similar to those of sick building syndrome and idiopathic chemical intolerance (ie, mucous membrane irritation, headache, fatigue, and cognitive impairment)²⁷⁻³¹ (Fig 1). The fundamental premise of toxicology, the dose-duration-response relationship, does not apply here. Clearly, this symptom complex

does not meet the criteria set by Hill³² to evaluate a cause-and-effect association.

Psychogenic and social factors may play a role in this subtle evolution of symptoms. The suggestion of living or working in a "toxic" environment can arouse significant concern about long-term health or self-perceived loss of it. Strong belief systems that link symptoms to poor air quality can become deeply entrenched and lead to somatization and symptom permanence outside the putative building.³³ Once this transition is established, these patients take comfort in being labeled as having toxic mold syndrome, which justifies their chronic complaints. The number of study patients with preexisting psychiatric diagnoses lends credibility to the premise that psychogenic factors may play a role in symptom evolution. Mood disorders may influence coping mechanisms and promote linkage of self-perceived loss of health to environmental toxins and increase the likelihood of symptom transformation from transient to permanent. In summary, toxic mold syndrome may represent the surreptitious evolution of aeroirritation from a transient process to a chronic one in certain patients with a psychogenic predisposition.

Our study has some limitations. The physical examination, laboratory testing, imaging, and spirometry were performed at the time of the medical evaluation, which could have been months to even years after exposure to the putative building had ended. However, each of these individuals was complaining of ongoing symptoms and disability or seeking compensation for permanent injury. Thus, it is reasonable to expect abnormalities to be present at the time of case review.

Psychiatric conditions noted in the medical record were often diagnosed in the absence of psychometric testing. Unfortunately, unlike bona fide medical conditions that can be supported by objective data, psychiatric diagnoses were based on prior treating physicians' clinical judgments alone in most cases and cannot be substantiated in hindsight. This is a significant limitation that unfortunately cannot be avoided in a retrospective review.

Stachybotrys testing was not routinely available and not added to the UniCAP profile until 2002. Thus, it was not performed consistently in all patients. Nonetheless, only 2 patients had evidence of elevated indoor levels of *Stachybotrys* on the environmental survey that suggested significant exposure and both underwent *Stachybotrys* IgE studies. It would have been desirable to perform skin puncture tests to allergens on all patients. For a variety of reasons, however, including risk prevention and time-related issues, this was not done.

Ideally, the study would have benefited by having 1 well-respected industrial hygienist conduct all 50 surveys. This would have led to a standardized approach and more clinically meaningful results. Unfortunately, this was not feasible, because environmental studies were already executed before case reviews. Additionally, the surveys reviewed herein are the same ones used to make the case for mold toxic effects in the first place.

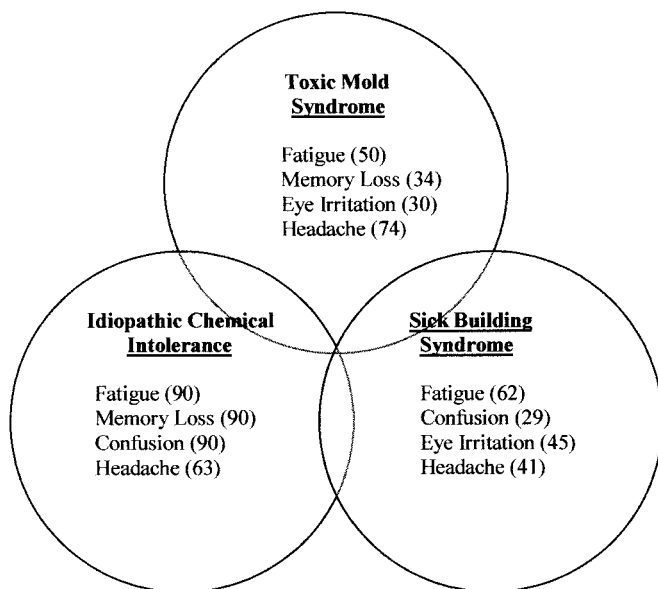


Figure 1. Three controversial disorders with overlapping symptoms. Numbers in parentheses represent the percentages of patients with that symptom. Data adapted from Buchwald and Garrity³⁰ and Li et al.³¹

All history obtained through personal interview and questionnaire is subject to recall bias, although this can be mitigated to some degree by a careful review of medical records. Belief about one's state of health and its presumed cause significantly affects recall.³⁴ Furthermore, many patients may consciously or subconsciously inflate the number of their symptoms or temporal relation to the problem building to make a more compelling case of disability or injury, since all these patients have potential secondary gain issues.

Finally, the acquisition of our study population is subject to referral bias. It is true that the sequence of referrals that leads patients from primary to tertiary centers raises the proportion of more severe or unusual cases. However, none of the study individuals was referred to our study physician (E.J.B.) by his or her primary care physician. Our examiner performed a case review only after the documented assertion that symptoms were related to toxic mold exposure and indemnification was desired. Thus, these individuals may represent the typical patient who visits their physician seeking affirmation of their preconceived conviction.

Our study also suffers from selection bias and may not be applicable to individuals with similar complaints who do not seek disability compensation or litigation. However, if objective evidence of inhalational mold toxic effects is lacking in individuals who are convinced that their health has been permanently affected, then the probability of objective disease in those who do not pursue compensation would likely be equal to or less than that of our study population.

CONCLUSION

Despite the lack of credible evidence, claims of mold toxic effects are common and poorly understood. We retrospectively characterized 50 patients with suspected mold-induced illness and found that in all cases some or all symptoms could be attributed to either noncontroversial mold-related disease or other medical conditions. No patients had objective findings in the absence of explanatory conditions. In the end, each case of presumed mold-related illness has to be taken on a case-by-case basis to evaluate the likelihood that symptoms are mold related and not myriad other likely disorders. When evaluating a patient with self-perceived mold-induced illness, it is important to approach the patient objectively and recognize all preexisting disorders that could produce similar symptoms. One must entertain a differential diagnostic process that considers all disorders that can mimic presenting symptoms.

Many proponents of mold-induced illness argue that currently we do not have the tools to identify the pathogenesis and that future medical science will validate it as a bona fide disease. Although this might be true, currently toxic mold syndrome does not satisfy what Burge calls the aerobiological pathway leading to inhalational exposure.³⁵ Toxic mold syndrome represents the furtive transition from one ill-defined, unvalidated, and unsubstantiated symptom complex to another, with greater potential for economic reward. In our view, it is medically and socially irresponsible to monetarily acknowledge a symptom complex

that lacks scientific credibility. In this respect, it is preferable to view toxic mold syndrome as a societal phenomenon rather than a disease process.

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