Mold and Mold Toxins: The Newest Toxic Tort

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When I first began reviewing toxic tort matters 25 years ago, I could not have dreamed of the progressive innovations as we moved from agent to agent. Early on, it was formaldehyde in the urea-formaldehyde foam insulation matters; then, it was low-level contaminants in drinking water; then, low-level chemicals in air causing first, "multiple chemical sensitivities" and now, allegedly, "toxic encephalopathy." Currently it has become "toxic mold," caus-
WHAT FUNGI CAN DO

Fungi exert their adverse effects primarily by acting as allergens and, to a lesser extent, as irritants. In sensitive individuals, levels found in the indoor setting, even some of the higher levels, produce primarily allergic rhinitis (hay fever) and may provoke an asthma attack in an asthmatic person. Very rarely can they cause a hypersensitivity pneumonitis (HSP) under these conditions. This disorder is more commonly associated with extremely heavily-exposed workers (e.g., mushroom workers) who may be exposed to spore counts of 100,000-1,000,000 spores/m³. However, HSP has arisen in indoor environments primarily due to bacterial or fungal contamination of water (e.g., as can be found in humidifiers). All of these allergic conditions are generally transient and depend upon ongoing exposure for ongoing symptoms. Allergies are extremely common and are not disabling conditions. Even hypersensitivity pneumonitis in the acute and subacute forms is a short-lived acute illness. Only in its severe, rare and chronic form, when it is associated with interstitial pulmonary fibrosis, can it become a permanent condition. Molds may also rarely cause infections in sensitive individuals. This has never been reported from molds contaminating homes or office buildings, but it is of concern in hospitals, where some patients are particularly vulnerable.

The second issue with molds, beside allergy or infection, is the least severe primary topic of this article: mold toxins. Here there exist marginal scientific data supporting health effects in homes or buildings; yet, fears, media coverage and claims are rising.

MYCOTOXINS

Mycotoxins are chemicals made by molds which can, under some circumstances, be injurious to animals upon ingestion, inhalation or dermal contact. The best known mycotoxins (until recent publicity about Stachybotrys) are the toxins from poisonous mushrooms.

Mycotoxins are large, complex molecules. They are, therefore, minimally, if at all, released into the air and, thus, are minimally accessible to occupants. There are thousands of mycotoxins and all of us are exposed to toxigenic molds every day both indoors and outdoors. At high doses mycotoxins can affect a number of metabolic processes. Mycotoxin consists of many diverse compounds produced by a wide variety of molds. A single mold species may produce several different mycotoxins; conversely, different mold genera may produce the same mycotoxin. Mycotoxin production for a given species is highly dependent on growth conditions, such as nutrient availability, temperature and humidity. In other words, the fact that a potentially toxicogenic mold is found does not mean it was producing any toxin. Moreover, when one says that a toxigenic mold was found in a home or office, that is no surprise and, in fact, is expected since hundreds of common, everyday, harmless molds are capable of producing thousands of mycotoxins. Dr. Rene Salazar attempted, in his Ph.D. dissertation work, to extract Aspergillus ochraceus toxin from contaminated ceiling tile and carpet, but was unable to do so. Also, Stachybotrys chartarum, the current focus of much attention, is highly sticky and may release neither spores nor toxins, under customary indoor situations. Thus, the mere presence, of a potentially toxigenic mold neither means that it was producing toxins, or that there was exposure in homes or offices. In that regard, restoration workers and flood control specialists are not known to have develop mycotoxins, despite extensive, unprotected exposure for many years. Since some of the manifestations of mycotoxins can be quite dramatic, i.e., coughing up blood, if they were so affected, surely reports would by now have been seen.

Examples follow of just a few mycotoxins, the molds that produce them and their role in human disease. For a more detailed discussion of the classes of molds potentially in indoor environments, see Burge 1999.

Aspergillus

Aflatoxins are classic mycotoxins produced by Aspergillus flavus, A. niger and A. parasiticus. They are primarily associated with foods and are invariably in our diets at some low levels. Foods that can be contaminated include peanuts, pecans, pea, bread, cheese, rice, corn, oats, barley, grain, sorghum, wheat and cotton seed. Aflatoxins are also found in milk, eggs and live animals. Aflatoxins have been the subject of extensive research because they are potent liver toxins and are carcinogenic by ingestion. Fusarium, Stachybotrys Chartarum, Mononcilia Echinata and Others

Stachybotro toxocis was first reported in 1931 in Eastern Europe and Russia as a fatal hemorrhage disease of horses, with farm workers and those using straw for bedding reporting symptoms as well. The moldy straw, which contained S. chartarum and other fungi, killed horses and other farm animals and caused dermatitis, bloody rhinitis, cough and severe respiratory tract irritation in exposed people. Occupational stachybotro toxocis has been reported in farm workers, workers in contaminated oil plants and grain elevators, and in workers at facilities for reproducing moldy grain, processing malt grain, textile mills using plant fibers and binders in textiles factories. Symptoms included chest and upper respiratory symptoms, fever, dermatitis and leukopenia (in some cases). Recently, association has been reported for the presence of Stachybotrys in indoor environments with pulmonary hemosiderosis and hemorrhage in infants. These studies have since been criticized by the CDC (Center for Disease Control and Prevention, the sponsor of the research) and found to be deficient.
Inhalation studies of mycotoxins in animals were designed to measure acute effects at high exposure levels. These experimental exposures and concomitant effects do not represent exposures to mycotoxins at chronic, low exposure levels from molds in indoor settings. However, the data show decreasing toxicity with longer exposure for a given total dose, indicating that physiological mechanisms can mitigate the effect of exposure at low levels. These results point to a threshold for the effects of mycotoxins.

In an effort to model the effect of mycotoxins from inhalation of spores, Nikulin injected mice intranasally with S. chartarum spores. Mice were injected once with 10⁶ (1,000,000) spores or 4× 10⁷, a highly-toxic strain or 4× 10⁸, a slightly-toxic strain. The 72 strain contained saratrosatin. All mice receiving spores developed lung inflammation; however, there was a significant difference in the inflammation between the two strains. The changes in the 72 exposed mice were significantly milder than those produced by 72 and necrotic changes were seen only in the 72 exposed animals. For purposes of our claims issues, this illustrates two important issues: 1) even the various mycotoxins produced by Stachybotrys are vastly different in their degree of toxicity, and 2) required doses for any toxicity are high.

In another experiment, mice were injected intranasally with 10⁷ (1000) to 10³ (1,000,000) spores of less toxicity (72 and 200) and more toxicity (72) strains of S. chartarum. Lung inflammation was not detected in animals receiving 10⁸ of

**ANIMAL STUDIES**

Since the main route of human and animal exposure to mycotoxins is by ingestion, a few studies have been published examining the inhalation of mycotoxins in toxic-producing molds. Studies published by Cerecia et al. (1987, 1990) have been cited in support of the biological plausibility of mycotoxin-related illness from indoor exposure. Because their results indicate that mycotoxins are more toxic when exposure occurs by inhalation rather than ingestion. However, doses are still quite high and unlikely to be reproduced in homes or offices, even those with considerable contamination.

Levels That Produce Illness (Thresholds)

While threshold levels capable of producing illness have not been fully or formally defined, they are suggested, by studies, by principles of toxicologically and by the natural exposures shared by everyone.

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CASE REPORTS

Case reports cannot be used to determine causation for an environmental agent. They merely identify associations. A number of case reports are cited which purportedly show links between exposure to inhalation of mold and mycotoxin-induced illness in humans. Most involve high level occupational exposures. Only a few involve indoor air.

In a review of stachybotrotoxicosis, Forssen compiled earlier information of human exposure to Stachybotrys that had been reported in the former Soviet Union during the 1940s. Most of the persons affected had handled contaminated animal feed, but some became ill after using contaminated straw for fuel or mattress stuffing. Symptoms included dermatitis, primarily on the scrotum and in the axillary region, and less often on the hands and other body areas. Other symptoms reported were bloody nose, cough, and complaints of throat pain, burning nasal passages and congestion in the chest. Some had elevated body temperature and some developed leukocytosis followed by leukopenia. Patients recovered rapidly after exposure cessation; however, upon subsequent exposure, the disease recurred with more serious sequelae.

In the often-cited 1986 report by Croft, a family reported cold and flu-like symptoms, sore throat, diarrhea, headache, fatigue, dermatitis, hair loss and general malaise. The self-reported complaints were thought by the author to be associated with massive growth of mold in the HVAC system and on the ceiling of one room. Although the air sample was not cultured, S. chartarum was identified from examination of spores and trichothecenes (mycotoxins) extracted from materials taken from the house. There were no objectively-measured disease outcomes and other possible causes for the reported symptoms were not ruled out, including the very likely potential of a viral infection. The persistence of such molds was also likely since the water infiltration and mold growth had been occurring for four or five years. This case, which has no scientific strength as proof of causation, is frequently cited in mold toxin claims.

As a whole, case reports show that clinically important health effects occur after exposure to conditions associated with high levels of bioceramics and, perhaps, with mold toxins. Historical reports indicate that direct contact with Stachybotrys-contaminated straw results in health effects. It is highly unlikely, however, that these extreme exposure conditions would occur due to surface mold growth in the indoor working or home environments. Exposure to airborne molds from surface contamination is dependent on the degree of colonization, the specific growth conditions (food for the mold), how much it is disturbed, the effectiveness of ventilation, and the exposure pathway from the affected area to the occupants.

Another important common finding among these reports is that symptoms ended upon removal from exposure. Such symptoms, moreover, did not recur when high level exposures were avoided. Chronic diseases, including brain damage, are not part of the clinical profile of even high dose mold toxin exposure.

EPIDEMIOLOGICAL INVESTIGATIONS

There are few epidemiological investigations of inhaled mycotoxins and disease in indoor air settings. Although some purport to show an association between inhaled mycotoxins and health effects, none has had sufficient data or experimental design to support this claim. The evidence for health effects in indoor air from mycotoxins associated with S. chartarum was recently reviewed and included the articles summarized here.

In 1998, Hodgson et al. reported the results of a study of occupants of a courthouse in Florida that had previously had extensive mold growth in its walls. They evaluated questionnaire results, lung function, blood and immunology test results among occupants of the courthouse and occupants from other, non-complaint buildings. Saratovasins G and H were isolated from ceiling tiles from the courthouse. Air samples revealed lower viable spore levels indoors compared to outdoors. Aspergillus versicolor and A. glaucus were found indoors, but not outdoors. Stachybotrys chartarum was found on air samples collected while books were being handled and was also found in bulk samples of water-damaged ceiling tiles.

Hodgson’s study group consisted of fourteen claimants, identified by the insurance carrier. They described symptoms consistent with work-related asthma in three cases (decreased FEV1 in one), interstitial lung disease (ILD) in one and rhinitis that improved over weekends in six.

There were two positive associations reported between courthouse occupation and outcome variables: 1) in the questionnaire survey, symptoms of a pulmonary disorder were reported more often among case building occupants; and, 2) statistically significant increased symptom reporting was found for courthouse occupants for individual symptoms and grouped symptom categories, except for...
wheezing. However, results from objective measures of health (lung function) (in this study, population did not support an association between exposure (building occupation) and health effects.

Selection and recall bias was likely to occur in this study because the building had been undergoing mold remediation and sampling prior to the study and some occupants were actively involved in litigation concerning mold in the building and claimed health effects. In addition, building occupants without symptom complaints would be less likely to participate, since subjects were acquired by posting a memorandum describing the purpose of the investigation. The authors concluded that a mycotoxin-induced effect was the most likely explanation for increased symptoms in the problem building. While this has become one of the stachybotrys-toxin cited "causation" papers, it did not begin to explain that. "Effects" were primarily symptoms in a biased sample and there was absolutely no substantiated toxin exposure in any of the patients/clients.

Johanning compared self-reported symptoms and blood and immunological tests in 53 cases from a "problem" building (a building with moisture problems and visible mold growth) with 21 controls from a "non-complaint" building (a building without known problems)." These were true controls is unlikely since that would imply no mold exposure, an impossibility. This study appears to include results for 43 infection or exudating (immune tests) reported previously by Johanning, et al.," thus, only the most recent article is discussed here. Results of air samples showed that levels of airborne viable spores were similar on all levels of the building and these, in turn, were similar to outdoor concentrations. Several mycotoxins, including Saratxox H, were found in bulk building material. That exposure to mycotoxins occurred in this building was not shown and the authors themselves admitted that there was no relationship between IgE antibodies to S. chartarum and the reported symptoms. This finding mitigates against an exposure-dependence relationship for S. chartarum and reported symptoms.

Two statistically positive results emerged. First, some of the immune tests were in the "exposed" group. However, these differences, although statistically significant, were minute and clinically irrelevant. Also, many of the tests were esoteric and of no common use or value.

The authors conclude that their results suggested an immune competency dysfunction associated with prolonged and intense toxicogenic mold exposure. However, they did not demonstrate exposure, they failed to note that the differences were meaningless and they considered no other causes (of which there are hundreds) for slight differences in these immune parameters.

They also studied reported symptoms and reported excesses of infections. Clinical evaluation or reviews of records to confirm these perceptions were not performed. In a situation in which a perceived hazard exists (in this case, the mold) and the patients were in litigation, symptoms are routinely over-reported and must be objectively confirmed before reported symptoms can be considered to represent reliably the incidence of illness or disease. The level of mold exposure was assigned based upon the presence and amount of mold contamination reported. Also in this study, the "central nervous system" (CNS) complaints were not statistically different from the controls. This belies one of these authors' current testimony in claims that S. chartarum causes toxic encephalopathy.

Finally, the notion that mycotoxins cause toxic encephalopathy comes largely from a non-peer reviewed presentation which was published in a book. There, Dr. Wayne Gordon, a neuropsychologist, evaluated 20 patients who, it was claimed (he had no independent knowledge), were exposed to mycotoxins. He then claims that he was able to detect subtle differences between them and a control group (presumably, but not proven, unexposed to mycotoxins) on certain neurophysiological tests. He noted, that "While other neurotoxins may have been present, the details were not provided." Based on review of this material (sic, the testing), one would be led to believe that the group was unimpaired, however, with closer examination using the above criteria (sic, which he devised after the fact) impairment becomes evident. It is largely this non-peer reviewed, non-scientific writing which has become the basis for the claim that mycotoxins cause brain damage.

SUMMARY

Despite considerable amounts of litigation and hundreds of millions of dollars in damage demands, molds in the indoor environment are primarily minor allergens at most under exposure circumstances found even in heavily mold-contaminated buildings and homes. Molds or their toxins have not been shown to cause brain damage, cancer or a generalized set of symptoms recently dubbed "fungal syndrome" by one author. Key points include:

- Molds are everywhere, indoors and outdoors.
- Most molds produce mycotoxins, even those commonly found indoors and outdoors.
- Stachybotrys is sticky, fastidious, and unlikely to release large numbers of spores or mycotoxins. Up to 30 percent of homes have some Stachybotrys growth.
- Molds in homes or office buildings are neither known, nor likely, to cause brain damage, cancer, birth defects or other serious illnesses.
- Mold levels outdoors may reach 100,000 cfu/m^3, particularly on a windy day and particularly, near wooded areas.
- Indoor levels and genera are extremely variable from depending on such factors as geographical location and time of year.

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