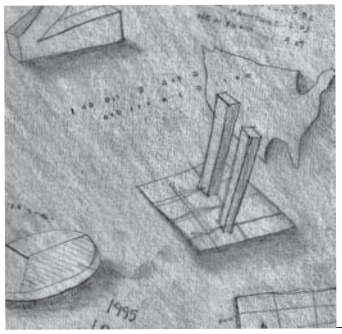

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Mold in Indoor Environments: A Critical Review of Research Studies

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Since exposure standards for molds or mycotoxins do not exist, it is useful to have broad knowledge of the potential for exposure and health effects associated with mold in the indoor environment. Headlines about "toxic molds" have elevated the level of concern and response for certain species of mold that are known to produce mycotoxins.

This article is based on a previous review of the toxic effects of molds associated with the production of mycotoxins, and the negative health effects due to mycotoxin exposure in the indoor environment. The more detailed review was first published in *Applied Occupational and Environmental Hygiene* in 2000 (volume 15, number 10).

What is Mold?

Molds belong to the broader category of Fungi. Fungi include molds, rusts, smuts, and mushrooms. Fungi do not need sunlight to grow, but only require a source of food and moisture. The paper backing of gypsum board moistened by a leaky pipe is an example of a food and moisture source in a building. Fungi reproduce typically by spores.

Health Effects

Table 1 shows the possible health effects associated with three broad groups of fungi/molds. These associations have been drawn from reports of toxicology studies, case reports, and epidemiological investigations.

The term "mycotoxin" is very general, and here is defined as a mold-produced secondary metabolite that is injurious when ingested, inhaled, or comes into contact with skin. Mycotoxins exert their effect on organisms in many ways, including interference with cellular respiration, interference with carbohydrate and lipid metabolism, and direct binding with DNA and RNA. In general, mycotoxins are complex and relatively large molecules, and thus are not volatile. Mycotoxins have been shown to occur in mycelia, spores, and the matrix in which mold grow.

Mycotoxins consist of many diverse compounds produced by a wide variety of molds. A single mold species may produce several different mycotoxins; and conversely, different molds may produce the same mycotoxin. Mycotoxin production for a given species is dependent on growth conditions, such as nutrient availability, temperature, and humidity.

Toxicology (Animal Inhalation) Studies

Animal studies on inhalation of mycotoxin and mold spores are used as models of human exposure and response. They provide a mechanism for comparing the toxicity of different compounds. A great deal of published research exists about mycotoxins in feed and foodstuffs. Since the main route of human and animal exposure to mycotoxins is by ingestion, the vast majority of animal research on toxicity has been done with ingestion studies. Few studies examine the inhalation of mycotoxins or toxin-producing molds.

Table 1

Group	Health Effect
Allergic:	sensitization and immune responses such as allergic rhinitis (hayfever), asthma or hypersensitivity pneumonitis
Infectious:	growth of the fungus in or on the body, as with aspergillosis or histoplasmosis
Toxic:	disruption of cellular function, as occurs with toxigenic effects including aflatoxin-induced cancer

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Studies of animals exposed to purified mycotoxins demonstrate the potency of these compounds, but the evidence that mycotoxins are more toxic via inhalation exposure is unclear. Studies of intratracheal instillation of mold spores indicate increased inflammatory response in the lung due to the presence of large numbers of toxic mold spores.

Inhalation studies of mycotoxins in animals were designed to measure acute effects at high exposure levels. These experimental exposure levels and the accompanying effects do not represent exposure to mycotoxins at chronic, low-exposure levels from molds in indoor settings. In addition, the applicability of these results to human exposure in indoor environments is limited due to the

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lack of comparability of the animal to human physiology, artificial exposure route, high exposure level, and the subjective grading of the response. However, the data do show decreasing toxicity with longer exposure for a given total dose, suggesting that physiological mechanisms can reduce the effect of exposure at low levels. These results suggest the existence of a threshold for the effects of mycotoxins.

Case Reports

Although case reports cannot be used to determine a causal link between environmental agent and a health outcome, they sometimes can be used to identify factors that need further investigation concerning their connection to symptoms or disease. Only a few reports exist regarding the possible effects of low to moderate mycotoxin exposures in indoor settings. Several additional case reports from agricultural settings describe the apparent effects of high exposure levels. From the studies examined for this review, a common finding was that symptoms ended upon removal from exposure, and did not reoccur when high-level exposures were avoided.

In two case reports, outbreaks are reported to be associated with S*tachybotrys*. Other case reports do not relate an association with a particular mold species. The health effects in these case reports may be associated with mycotoxins, toxins produce by bacteria (as opposed to molds), other bioaerosol constituents, or a combination of these components. The contribution of each component to cases of reported illness is still in need of further study.

Other historical case reports indicate that direct contact with *Stachybotrys* contaminated straw results in health effects. It is unlikely, though not impossible, that these extreme exposure conditions would occur due to surface mold growth in the indoor working or home environment. Exposures to airborne molds from surface contaminants is dependent on the degree of growth, how much it is disturbed, effectiveness of ventilation, and the required exposure pathway from the affected area to occupants.

In general, case reports indicate that exposures to high levels of airborne molds and/or bioaerosols were associated with acute clinical illness, likely due in part to mycotoxins. However, no single mold variety was consistently implicated in these cases.

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, the evidence is limited and generally insufficient to support this conclusion.

The evidence for health effects in indoor air from mycotoxins associated with *S. chartarum* was recently reviewed. In 1994, the issue of mycotoxins in indoor air received national media attention after the U.S. Centers for Disease Control and Prevention (CDC) reported association of *S. chartarum* in homes with infants diagnosed with infant idiopathic pulmonary hemorrhage and hemosiderosis (IPH). However, the CDC has recently published a summary of internal and external reviews of the investigation that conclude that the association between IPH and exposure to *S. chartarum* "was not proven."

Summary

Health-based exposure standards for molds and mycotoxins do not yet exist. While there is evidence of health effects in animals and humans after high levels of inhalation exposure or direct contact with mycotoxins, current published research does not provide compelling evidence that exposure at the levels expected in most mold-contaminated indoor environments is likely to result in measurable health effects (see the Table 2 summary).

While it is generally agreed that active mold growth indoors is unsanitary, the point at which mold contamination becomes a threat to health is currently unknown.

Whether mold such as *Stachybotrys* should be treated differently than other molds, when considering clean up or sampling and exposure issues, is also a controversial subject. Clean-up and repair of mold-contaminated buildings is often conducted using asbestos abatement-like methods and clearance sampling. These procedures are often triggered, and sometimes buildings are evacuated, because *Stachybotyrs* has been found in the building; the extent of contamination or exposure potential is not often considered prior to initiating abatement procedures. The information about health effects and exposure in the current scientific literature does not warrant the use of such conservative measures for mold remediation based on the presence of a particular species of mold. Instead, the available data indicate that evacuation and immediate clean-up is needed, regardless of the variety identified, if contamination in indoor environments is extensive.

Table 2. Summary of Studies

Types of Studies	Study Function	Limitations
Animal Inhalation	help create models of human exposure and response, provide a mechanism for comparing the toxicity	• lack of comparability of the animal to human physiology • artificial exposure route • unnaturally high exposure levels • subjective grading of the response of different compounds
Case Reports	help identify factors that need further investigations in human exposure	• cannot determine a causal relationship between exposure and response • few examine exposures in an indoor setting • most do not relate an association to a particular mold variety
Epidemiological Investigations	provide a more scientifically rigorous method for directly observing the effects of exposure	• too few epidemiological studies conducted • among studies conducted, the data are inadequate to support study claims