Human Health Effects of Airborne Mycotoxin Exposure in Fungi-Contaminated Indoor Environments

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In recent years, a great deal of interest has been generated regarding the study of toxigenic fungi and mycotoxins. Historically, mycotoxins have been a problem related to agricultural, food, poultry and cattle industries. However, many toxigenic fungi have been found to infest buildings with indoor environmental problems. Several recent cases have related toxigenic fungi and mycotoxins to building occupant health problems caused by contaminated indoor environments. For example:

- Courthouses in Florida were closed for extensive decontamination of toxigenic fungi at a cost that equaled the buildings' original construction cost (Yang 1).
- An old school building in Canada was so infested with toxigenic fungi that it had to be burned (Yang 1).
- Cases of pulmonary hemorrhage were reported in infants who were living in homes in the Cleveland area that were contaminated with toxigenic fungi (ACGIH *Bioaerosols* 24-26).

This article examines how mycotoxins are produced in the indoor environment and describes their potential health effects to humans with respect to exposure to indoor environmental sources.

TOXIGENIC FUNGI & MYCOTOXINS

To understand the health effects of mycotoxins, one needs a basic understanding of the biology of fungi and how mycotoxins are produced. Typically, fungi found in indoor environments consist of microscopic molds and yeasts. (Since yeasts do not produce mycotoxins, they are not discussed in this article.) Fungi are eukaryotic organisms composed of rigid-walled cells that contain a nucleus, other membrane organelles and mitochondria (Johanning). They are often categorized by their need for moisture. For example, hydrophylic fungi require extremely damp (close to saturation) conditions to proliferate, while Xerophilic fungi can grow in drier conditions.

Fungi colonize substrates in the form of long chains of cells called hyphae that range in size from 2 to 10 µm. These networks of hyphae are termed a mycelium. Most mycelial fungi produce airborne spores from the hyphae for reproduction. Most fungi found in indoor environments are saprotropic—they obtain the nutrients they need for metabolism from dead, moist organic materials or substrates such as wood, paper, paint, soft furnishings, potting soil, dust, skin scales and food (Johanning).

Fungi known to produce toxins (mycotoxins) are described as toxigenic fungi. These fungi are ubiquitous in the air and soil throughout the world; however, the most-common and well-documented species found in indoor environments include many species in the genera of Aspergillus, Penicillium and Cladosporium (Yang 2). Other toxigenic fungi often found in indoor environments include Alternaria, Trichoderma, Fusarium, Paecilomices, Stachybotrys, Chaetomium, Acremonium and Myrothecium (ACGIH *Guidelines* 3).

Fungi are known to produce several agents that can be toxic if exposure is sufficient. These toxic agents consist of 1) secondary products of fungal metabolism and 2) fungal structural components. The first category includes mycotoxins, antibiotics and volatile organic compounds; the second includes cellular membrane components such as ß-(1∏3)-D-glucans (ACGIH *Bioaerosols* 24). A 1990 World Health Organization publication establishes that more than 200 mycotoxins are produced by various toxigenic fungi.

Mycotoxins consist of relatively low molecular weight, nonvolatile compounds with diverse chemical structures ranging from the simple monolliformin to complex polypeptides with molecular

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weights over 2000 (ACGIH *Guidelines* 1) and include polyketides, terpenes and indoles (ACGIH *Bioaerosols* 24). With respect to indoor environmental exposures, the mycotoxins of primary concern are cytotoxins (i.e., aflatoxin) produced by Aspergillus flavus and Aspergillus parasiticus, and the trichothecene toxins produced by Stachybotrys chartarum, Mycrothecium verrucaria and others (Burge and Hoyer 402).

Mycotoxin production (types and amounts) depends on the fungal species, metabolism substrate, temperature, pH, presence of other organisms and related environmental factors. More than one fungal species or genus can produce the same mycotoxin compound. Additionally, a single fungal species can produce more than one mycotoxin. This is evidenced by the production of the mycotoxin sterigmatocystin by Aspergillus versicolor, Emericella nidulans and Cochliobolus; and production of the mycotoxins satratoxin F, G and H, roridin E and verrucarin J by Stachybotrys chartarum (ACGIH *Bioaerosols* 24). When mycotoxins are produced, they are typically identified in the fungal spores (mycelia) and in the growth substrates (wood, paper, etc.) in quantities dependent on the specific fungal species and strain.

MYCOTOXIN GENERAL HEALTH EFFECTS

Several toxicological studies published within the last 30 years have examined the human health effects of mycotoxins. However, most of these studies have focused on contamination of animal feed and occupational exposures of agricultural grain handlers, not on indoor environmental substrates. These historical studies have established that cytotoxins cause cell disruption and interfere with cellular processes while trichothecenes impact the immune system and specific organs (ACGIH *Guidelines* 2).

Mycotoxin exposures have been linked to a variety of acute and chronic adverse health affects. Generally, these effects include acute symptoms such as pulmonary hemorrhage, dermatitis, recurring cold and flulike symptoms, burning/sore throat, headaches, excessive fatigue and diarrhea. Chronic effects include carcinogenicity, mutagenicity, teratogenicity, central nervous system effects, immune system damage, and specific effects of the heart, liver, kidneys and other organs (ACGIH *Guidelines* 2). Table 1 lists some common indoor toxigenic fungi, their associated mycotoxins and possible health effects.

TOXICOLOGICAL INFORMATION

As Table 1 indicates, mycotoxins are produced by various toxigenic fungi and are able to produce deleterious health effects. Doses of mycotoxins that cause toxic effects vary with each specific toxin, the animal species exposed, and the route and duration of exposure.

Toxicological data for some trichothecene toxins indicate rat ingestion LD_{50} values below 1.0 mg/kg (ACGIH *Guidelines* 2). However, the chronic effects from aflatoxin exposure may occur at dose concentrations as low as the microgram per kilogram range (ACGIH *Guidelines* 2). Inhalation exposures using mice, rats, swine and guinea pigs to T-2 toxin indicate a degree of toxicity 2 to >20 times more than intravenous dosages, which indicates that inhalation exposure may increase the potential for chronic health effects (ACGIH Guidelines 2).

TABLE 1 Mycotoxins & Potential Health Effects

FUNGUS	MYCOTOXIN	POSSIBLE HEALTH EFFECT
Acremonium spp.	Cephalosporin	antibiotic
Alternaria alternata	Tenuazoic acid	nephrotoxic, hepatotoxic, hemorrhagic
Aspergillus clavatus	Cytochalasin E, Patulin	cell division, protein synthesis inhibitor, nephrotoxic, carcinogenic
Aspergillus flavus, Aspergillus parasiticus, Aspergillus fumigatis	Aflatoxins Fumitremorgens Gliotoxin	mutagenic, carcinogenic, hepatotoxic, tremorgenic, cytotoxic
Aspergillus nidulans, Aspergillus versicolor	Sterigmatocystin	hepatotoxic, carcinogenic
Aspergillus ochraceus, Penicillium verrucosum, Penicillium viridicatum	Ochratoxin A	nephrotoxic, hepatotoxic, carcinogenic
Cladosporium spp.	Epicladosporic acid	immunosuppresive
Chladosporium cladosporiodes	Cladosporin, Emodin	antibiotic
Fusarium graminearum	Deoxynivalenol Zearalenone	emetic estrogenic
Fusarium monoliforme	Fumonisins	neurotoxic, hepatotoxic, nephrotoxic, carcinogenic
Fusarium poae, Fusarium sporotrichoides	T-2 toxin	hemmorrhagic, hepatotoxic, nephrotoxic, carcinogenic
Penicillium chrysogenum	Penicillin	antibiotic
Penicillium crustosum	Penitrem A, Roquefortine C	tremorgenic, neurotoxic
Penicillium expansum	Citrinin, Patulin, Roquefortine C	nephrotoxic, carcinogenic, protein synthesis inhibitor, neurotoxic
Penicillium griseofulvum, Penicillium viridicatum	Griseofulvin	tumorigenic, teratogenic, hepatotoxic
Stachybotrys chartarum	Satratoxins, Verrucarins, Roridins, Stachybocins	inflammatory agents, immunosuppressive, dermatitis, hemotoxic, hemorrhagic

Source: ACGIH. *Bioaerosols: Assessment and Control*. 1999.

INHALATION HEALTH EFFECTS

Since mycotoxins are relatively nonvolatile, inhalation exposure is mostly limited to the inhalation of airborne fungal particulates (usually spores) or fungi-contaminated substrates that contain concentrations of mycotoxins. Inhalation of these particulates can result in the transportation of mycotoxins to the alveoli. Once in the alveoli, trichothecenes could interfere with immune responses while other mycotoxins have been shown to interfere with foreign particle clearance by the macrophage response (ACGIH *Guidelines* 2). These effects have the potential to initiate bacterial infections (ACGIH *Guidelines* 2) and invasive Aspergillosis (ACGIH *Bioaerosols* 24-25).

Human inhalation exposure to mycotoxins, as indicated by agricultural and manufacturing exposures, have also been linked to various health conditions.

•*Organic toxic dust syndrome (OTDS).* This manifests in the form of flulike symptoms and is similar to hypersensitivity pneumoconiosis. The condition results from the inhalation of organic dusts that contain a mixture of endotoxins, glucans, antigens and mycotoxins. OTDS has been termed a pulmonary mycotoxicosis; however the actual role of mycotoxins has not been proven (ACGIH *Bioaerosols* 24-26).

•*Aflatoxin.* Aflatoxin has been linked to various cancers in agricultural and food processing applications and interstitial pneumonitis in textile workers (ACGIH *Bioaerosols* 24-26).

•*Miscellaneous.* Fungal spore exposure associated with Stachybotrys chartarum, Trichoderma spp. and Acremonium spp. has been documented to cause skin inflammation and scaling on women working in a large-scale horticultural setting. Also, a case of dementia and tremors has been linked to exposure to a tremorgenic myco-

toxin associated with Aspergillus fumigatus during silo unloading. Finally, reports of farm worker toxicosis have been associated with exposure to aerosols from straw containing Stachybotrys chartarum (ACGIH *Bioaerosols* 24-26).

Specific health effects associated with indoor environment (e.g., offices, schools, hospitals and homes) inhalation exposures have not been well-documented. As noted, most epidemiological and toxicology data available are derived from animal ingestion studies and case studies of occupational inhalation exposures among agricultural workers. However, following is one of the few well-documented cases of human mycotoxicosis resulting from indoor air exposure in a home heavily infested with Stachybotrys atra (chartarum).

> *Water damage had occurred in a house over a period of several years. Extensive growth of the black sooty-appearing S. atra was evident on the ceiling of an upstairs bedroom and in the air ducts. Numerous S. atra spores were collected from room air samples, and a series of highly toxic trichothecene mycotoxins were isolated from both the ceiling material and the debris found in the air ducts (Croft, et al). The complaints reported by occupants (ranging from headaches, sore throats, flu symptoms, diarrhea and hair loss to fatigue, dermatitis and general malaise) are consistent with chronic trichothecene intoxication. The symptoms disappeared after the home was thoroughly cleaned (ACGIH* Guidelines *2).*

As noted, one recent study examined infants who had suffered pulmonary hemorrage while living in homes contaminated with Stachybotrys chartarum and other fungi. However, the actual role of fungi and any mycotoxin produced has not been positively identified. Other case studies of fungal infestation and links to mycotoxin exposure have been documented; however, no definitive relationship between fungal spore mycotoxins and health symptoms has been established. In addition, to date, no significant evidence links indoor environmental inhalation exposure to mycotoxins with cancer.

CONCLUSION

It is apparent that there is a significant lack of meaningful data relative to the human health effects of airborne exposure to mycotoxins. While a great deal of data are available from animal ingestion studies and epidemiological studies of agricultural and industrial workers, even these data do not appear to demonstrate a definitive link between inhalation exposure of mycotoxins and disease.

Extrapolation of the animal toxicology data proves difficult due to several factors:

- Dose variations and ingestion route of exposure of the mycotoxin to animal species create a great deal of uncertainty when attempting to transfer to human indoor environmental exposures.
- Experimental animals used and their various sensitivities to particular toxins introduce problems when attempting to extrapolate to human health effects.
- Use of animal data to predict human risk involves the drawing of many assumptions such as 1) humans will react to a toxin in a similar manner as the test animal and 2) the natural human exposure scenario is identical to the test animals' laboratory exposure.

Use of epidemiological study data of human occupational exposures to predict health risks associated with indoor environmental exposures also proves problematic for many of the same reasons, specifically in terms of dose, route of exposure and environmental variables. Based on these uncertainties, there does not appear to be sufficient, definitive information to predict human health exposure effects when dealing with inhalation of mycotoxins in a typical, nonindustrial indoor environment. Thus, further study is needed.

This lack of definitive information creates the need to eliminate or reduce the potential for exposure. This can only be achieved via the proactive control of mold growth. As noted, mold growth requires an adequate substrate (food source), suitable temperature conditions and moisture. Controlling one—or all—of these parameters will help prevent mold growth. To do so, a facility should establish an effective preventive maintenance program that includes:

- systematic facility inspections that focus on typical moisture sources such as roofs, piping systems, HVAC systems, condensation sources and humidification systems;
- timely repair or elimination of identified water leaks or other unwanted sources of water;
- routine HVAC maintenance that includes filter change-outs, humidity control adjustments, airflow adjustments and cleaning;
- routine inspections to look for visible evidence of mold growth/water damage;
- adequate cleaning of mold growth/water-damaged nonporous materials with suitable cleaning agents such as a 10-percent bleach solution and/or the removal of potentially contaminated porous materials such as carpeting, drywall, furniture and ceiling tiles.

These simple tips can also help a facility control mold growth:

- Repair plumbing and other building leaks as soon as possible.
- Watch for condensation sources and fix them. To achieve this, 1) increase the surface temperature by insulating or increasing air flow or 2) reduce indoor humidity levels by repairing leaks, increasing ventilation or dehumidification.
- Maintain HVAC drip pans, piping systems and other components in a clean, unobstructed condition.
- Vent moisture-generating appliances and processes directly to the outside.
- Maintain indoor relative humidity levels in the range of 30 to 50 percent.
- Clean and dry wet/damp spots as soon as possible.
- Keep foundations as dry as possible through proper drainage and sloping. ■

REFERENCES

American Conference of Governmental Industrial Hygienists (ACGIH). *Bioaerosols Assessment and Control.* Cincinnati: ACGIH, 1999.

ACGIH. *Guidelines for the Assessment of Bioaerosols in the Indoor Environment*. Cincinnati: ACGIH, 1989.

American Industrial Hygiene Assn. (AIHA). *Biosafety Reference Manual.* 2nd ed. Fairfax, VA: AIHA Publications, 1995.

Burge, H. and M.E. Hoyer, ed. *The Occupational Environment: Its Evaluation and Control.* Chapter 19, "Indoor Air Quality." 1997.

Croft, W.A., et al. "Airborne Outbreak of Trichothecene Toxicosis." *Atmospheric Environment.* 20(1986): 549-552.

EPA. "Mold Remediation in Schools and Commercial Buildings." Washington, DC: EPA, 2001.

Johanning, E. "Hazardous Molds in Homes and Offices: Stachybotrys atra and Others." The EnvirosVillage Library website, November 1999.

Wald, P.H. and G.M. Stave. *Physical and Biological Hazards of the Workplace.* New York: Van Nostrand Reinhold, 1994.

Williams, P. and J.L. Burson, eds. *Industrial Toxicology Safety and Health Applications in the Workplace.* New York: Van Nostrand Reinhold, 1985.

Yang, C.S. "Toxic Effects of Some Common Indoor Fungi." *Enviros: The Healthy Building Newsletter.* Sept. 1994.

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