Risks Associated with Exposure to *Stachybotrys* and Other Fungi Mycotoxins

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The media and public continue to be concerned about health risks resulting from exposure to mycotoxins produced by *Stachybotrys* and other fungi present in indoor air. Mycotoxins are by-products of the natural life-cycle of all fungi. Their production is dependent on complex interactions among numerous factors including nutrition availability, moisture, temperature, and competition from other microorganisms.(1) The characteristics, type, and quantity of mycotoxins produced by any species of fungi varies widely. Thus, as I have stated in previous communications, the mere presence of a toxigenic mold detected in indoor air does not mean that mycotoxins also are present. Of particular importance is the quantity that might be present. Several investigators have attempted to shed some light on this issue.

A review of the literature indicates that acute and long-term chronic effects are more commonly associated with extremely high inhalation concentrations.(2) The term organic dust toxic syndrome (ODTS) has been used in referring to respiratory problems such as pulmonary mycotoxicosis, grain fever, farmer's lung, mill fever, and inhalation fever.(3) Exposures documented for ODTS are described as extremely thick airborne dust or fog.(4) Total microbial concentrations related to these diseases are reported ranging from one hundred thousand (10^5) to one billion spores (10^9) per cubic meter (m^3). Such concentrations are rarely, if ever, observed in the indoor ambient air of residential or commercial buildings.

The majority of animal *in vivo* data on toxicity of mycotoxins are limited to studies of mice, rats and guinea pigs, in which lethal concentrations are identified. In these studies, the doses are administered to a test animal in ways that are not equivalent to human inhalation exposures.(5, 6) Also, there is variability observed in animal sensitivity with rats being most sensitive. Even testing the more sensitive rat with a *Fusarium* trichothecene (T-2), no mortality occurred at a single administration of 1.0 mg/m^3. Data about the quantity of T-2 recovered in a single spore are not available. However, it has been reported that per spore concentrations of satratoxin H in *Stachybotrys* spores is estimated at 0.0004 ng/spore.(7) Using this value, Hardin, Saxin and Kelman, in a recent, excellent review, have estimated that 10 billion spores would be required to reach 1.0 mg of this toxin in a cubic meter of air.(8)

Similar requirements for high spore counts in ambient air have been reported by others investigating the potential for airborne mycotoxins from other fungal species.(9) Fischer et al. estimated that to obtain 1 ng of an *Aspergillus* mycotoxin would required an airborne density of 10^7 cfu/m^3. To place these estimates in a more human context it is useful to review Burge's risk model.(10) In this model, the potential accumulation of

mold toxin in the lung could be estimated based on indoor ambient air spore counts. Making assumptions about spore content and human inhalation frequency and duration, results of this model suggest that it would require 1,100 days of an individual inhaling 100 spores/m^3 to accumulate 1 ng of a toxin in the lung.

In animal dose-response data associating pulmonary inflammation and hemorrhage with exposure to *Stachybotrus chartarum*, a no-effect dose of 3 million spores/kg body weight has been identified.(8) Airborne concentrations representing human doses comparable to this no-effect dose have been estimated recently by Hardin et al.(8) Their calculations were based on an assumption that all of the airborne spores would be retained in the human lung and on the application of standard risk assessment default values. Thus, the animal no-effect dose is comparable "to a continuous 24-hour exposure to 2.1 x 10^6 spores/m^3 for infants, 6.6 x 10^6 spores/m^3 for school-aged children, and 15.3 x 10^6 spores/m^3 for an adult."(8)

Hardin et al. emphasize that these no-effect estimates represent an over-estimate of risk because they have assumed that the toxic effect would be the same despite a major difference in route of exposure between animals and humans. Cumulative doses experienced over time-periods more typical of human exposures would be less acutely toxic than the large single doses administered to test animals. These larger doses could overwhelm inherent, internal protective measures. When Hardin et al. made the assumption that the animal no-effect dose represented a 1 minute administration, the estimates for a human comparable dose become 3.0 x 10^9 spores/m^3 for infants, 9.5 x 10^9 spores/m^3 for school-aged children, and 22.0 x 10^9 spores/m^3 for adults.

Finally, using data from a repeat-dose study in which a concentration of 2.8 x 10^5 *Stachybotrys* spores/kg produced severe pulmonary inflammation, but no hemorrhaging, Hardin et al. estimated human equivalent doses.(8) Applying the same assumptions, the estimated airborne concentration required to "deliver the non-hemorrhagic cumulative three-week dose of 2.8 x 10^5 *Stachybotrys* spores/kg" is 9400 spores/m^3 for infants, 29,000 spores/m^3 for school-aged children, and 68,000 spores/m^3 for adults. I agree with the authors assessment that these levels are improbable for residential and commercial indoor ambient air and inconsistent with reported airborne concentrations.

Several problems need to be resolved before we can begin gathering evidence of an association between inhalation exposure to mycotoxins and adverse health outcomes. One problem is the fact that there is insufficient evidence with which one can evaluate the relevance of mycotoxins produced in a laboratory culture setting as predictors of those that might be present in indoor ambient air. Data supporting comparability are extremely limited. A recent study has revealed that when comparing strains of mycotoxins present in pure cultures and extracted from spores, there is only a 60 percent match.(9) Some fungal species have more consistent mycotoxin production than others. For example, *Aspergillus fumagatus, Penicillium polonicum* and *Penicillium crustosum* exhibit consistent results between pure culture and spore extracts.(9) *Aspergillus niger* and *Paecilomyces variotii* reveal inconsistent results. There is

currently no research on differences that might exist with *Stachybotrys* species, today's popular mold concern. However, these data make it clear that one cannot assume that mycotoxins detected in laboratory cultures would be the same as those potentially present in spores or on particulates in ambient air, simply because a particular mold has been detected. We currently have no reliable analytical methods with which ambient air samples can be evaluated for the presence of mycotoxins.

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