Adverse Human Health Effects Associated with Molds in the Indoor Environment

In single-dose *in vivo* studies, *S. chartarum* spores have been administered intranasally to mice[31] or intratracheally to rats.[76,77] High doses (30 x 10^6 spores/kg and higher) produced pulmonary inflammation and hemorrhage in both species. A range of doses were administered in the rat studies and multiple, sensitive indices of effect were monitored, demonstrating a graded dose response with 3 x 10^6 spores/kg being a clear no-effect dose. Airborne *S. chartarum* spore concentrations that would deliver a comparable dose of spores can be estimated by assuming that all inhaled spores are retained and using standard default values for human subpopulations of particular interest[78] – very small infants,† school-age children,†† and adults.††† The no-effect dose in rats (3 x 10^6 spores/kg) corresponds to continuous 24-hour exposure to 2.1 x 10^6 spores/m^3 for infants, 6.6 x 10^6 spores/m^3 for a school-age child, or 15.3 x 10^6 spores/m^3 for an adult.

If the no-effect 3 x 10^6 spores/kg intratracheal bolus dose in rats is regarded as a **1-minute administration (3 x 10^6 spores/kg/min), achieving the same dose rate in humans (using the same default assumptions as previously)** would require airborne concentrations of 3.0 x 10^9 spores/m^3 for an infant, 9.5 x 10^9 spores/m^3 for a child, or 22.0 x 10^9 spores/m^3 for an adult.

In a repeat-dose study, mice were given intranasal treatments twice weekly for three weeks with "highly toxic" s. 72 S. chartarum spores at doses of 4.6 x 10^6 or 4.6 x 10^4 spores/kg (cumulative doses over three weeks of 2.8 x 10^7 or 2.8 x 10^5 spores/kg).[79] The higher dose caused severe inflammation with hemorrhage, while less severe inflammation, but no hemorrhage was seen at the lower dose of s. 72 spores. Using the same assumptions as previously (and again ignoring dose-rate implications), airborne S. chartarum spore concentrations that would deliver the non-hemorrhagic cumulative three-week dose of 2.8 x 10^5 spores/kg can be estimated as 9.4 x 10^3 spores/m^3 for infants, 29.3 x 10^3 spores/m^3 for a school-age child, and 68.0 x 10^3 spores/m^3 for adults (assuming exposure for 24 hours per day, 7 days per week, and 100% retention of spores).

The preceding calculations suggest lower bound estimates of airborne S. chartarum spore concentrations corresponding to essentially no-effect acute and subchronic exposures. Those concentrations are not infeasible, but they are improbable and inconsistent with reported spore concentrations. For example, in data from 9,619 indoor air samples from 1,717 buildings, when S. chartarum was detected in indoor air (6% of the buildings surveyed) the median airborne concentration was 12 CFU/m^3 (95% CI 12 to 118 CFU/m^3).[80]

Despite its well-known ability to produce mycotoxins under appropriate growth conditions, years of intensive study have failed to establish exposure to S. chartarum in home, school, or office environments as a cause of adverse human health effects. Levels of exposure in the indoor environment, **dose-response data in animals, and dose-rate considerations suggest that** delivery by the inhalation route of a toxic dose of mycotoxins in the indoor environment is **highly unlikely at best, even for the hypothetically most vulnerable subpopulations.**

ACOEM References To Dr. Carol Rao's Mechanistic Work, to which Bruce and Brian applied their extrapolations:

76. Rao CY, Brain JD, Burge HA. Reduction of pulmonary toxicity of Stachybotrys chartarum spores by methanol extraction of mycotoxins. Appl Environ Microbiol. 2000;66:2817-21.

77. Rao CY, Burge HA, Brain JD. The time course of responses to intratracheally instilled toxic Stachybotrys chartarum spores in rats. Mycopathologia. 2000;149:27-34.

(77). " We have demonstrated that a single, acute pulmonary exposure to a large quantity of Stachybotrys chartarum spores by intratracheal instillation causes severe injury detectable by bronchoalveolar lavage. The primary effect appears to be cytotoxicity and inflammation with hemorrhage. There is a measurable effect as early as 6 h after instillation, which may be attributable to mycotoxins in the fungal spores. The time course of responses supports early release of some toxins, with the most severe effects occurring between 6 and 24 h following exposure. By 72 h, recovery has begun, although macrophage concentrations remained elevated"

(76.) "We provide evidence that there is a dose-related association between an acute exposure to toxin-containing S. chartarum spores and measurable pulmonary responses. The consequences of low-level chronic exposure remain to be investigated, **as does the relevance of the rodent data to human exposure.**"