Research: Mycotoxin Adducts on Human Serum Albumin: Biomarkers of Exposure to *Stachybotrys chartarum*

Iwona Yike,[1,3] Anne M. Distler,[2] Assem G. Ziady,[1] and Dorr G. Dearborn[1,3]

Departments of [1]Pediatrics and [2]Pharmacology, and [3]Mary Ann Swetland Center for Environmental Health, Case Western Reserve University, Cleveland, Ohio, USA

Abstract Objective:

Despite the growing body of evidence showing adverse health effects from inhalation exposure to the trichothecene-producing mold *Stachybotrys chartarum*, controversy remains. Currently, there are no reliable assays suitable for clinical diagnosis of exposure. We hypothesized that satratoxin G (SG) – albumin adducts may serve as biomarkers of exposure to this fungus.

Design:

We studied the formation of adducts of SG with serum albumin *in vitro* using Western blots and mass spectrometry (MS) and searched for similar adducts formed *in vivo* using human and animal serum.

Results:

Samples of purified human serum albumin that had been incubated with increasing concentrations of SG showed concentration- dependent albumin bands in Western blots developed with anti-SG antibodies. MS analysis found that as many as 10 toxin molecules can be bound *in vitro* to one albumin molecule. The sequencing of albumin-adduct tryptic peptides and the analysis of pronase/ aminopeptidase digests demonstrated that lysyl, cysteinyl, and histidyl residues are involved in the formation of these adducts. Serum samples from three patients with documented exposure to *S. chartarum* similarly revealed lysine–, cysteine–, and histidine–SG adducts after exhaustive digestion, affinity column enrichment, and MS analysis. These adducts were also found in the sera from rats exposed to the spores of *S. chartarum* in contrast to control human subjects and control animals.

Conclusions:

These data document the occurrence of SG–albumin adducts in both *in vitro* experiments and *in vivo* human and animal exposures to *S. chartarum*.

Relevance to clinical practice:

SG–amino acid adducts may serve as reliable dosimeter biomarkers for detection of exposure to *S. chartarum*.

POA REPORTER'S NOTEBOOK:

This research confirms research done at Texas Tech University's Health Sciences Center that found that trichothecene (mycotoxins from Stachybotrys or "Black Mold") were found in the blood sera of individuals exposed to Stachybotrys.

The Texas Tech study is available to POA members and is archived on POA's website.

Satratoxin G from the Black Mold Stachybotrys chartarum Evokes Olfactory Sensory Neuron Loss and Inflammation in the Murine Nose and Brain

by Zahidul Islam,1,2,3 Jack R. Harkema,1,4 and James J. Pestka1,2,3

1Center for Integrative Toxicology, 2Department of Microbiology and Molecular Genetics, 3Department of Food Science and Human Nutrition, and 4Department of Pathobiology and Diagnostic Investigation, Michigan State University, East Lansing, Michigan, USA

Abstract

Satratoxin G (SG) is a macrocyclic trichothecene mycotoxin produced by Stachybotrys chartarum, the "black mold" suggested to contribute etiologically to illnesses associated with water-damaged buildings. Using an intranasal instillation model in mice, we found that acute SG exposure specifically induced apoptosis of olfactory sensory neurons (OSNs) in the olfactory epithelium. Dose-response analysis revealed that the no-effect and lowest-effect levels at 24 hr postinstillation (PI) were 5 and 25 µg/kg body weight (bw) SG, respectively, with severity increasing with dose. Apoptosis of OSNs was identified using immunohistochemistry for caspase-3 expression, electron microscopy for ultrastructural cellular morphology, and real-time polymerase chain reaction for elevated expression of the proapoptotic genes Fas, FasL, p75NGFR, p53, Bax, caspase-3, and CAD. Time-course studies with a single instillation of SG (500 µg/kg bw) indicated that maximum atrophy of the olfactory epithelium occurred at 3 days PI. Exposure to lower doses (100 µg/kg bw) for 5 consecutive days resulted in similar atrophy and apoptosis, suggesting that in the short term, these effects are cumulative. SG also induced an acute, neutrophilic rhinitis as early as 24 hr PI. Elevated mRNA expression for the proinflammatory cytokines tumor necrosis factor-, interleukin-6 (IL-6) , and IL-1 and the chemokine macrophage-inflammatory protein-2 (MIP-2) were detected at 24 hr PI in both the ethmoid turbinates of the nasal airways and the adjacent olfactory bulb of the brain. Marked atrophy of the olfactory nerve and glomerular layers of the olfactory bulb was also detectable by 7 days PI along with mild neutrophilic encephalitis. These findings suggest that neurotoxicity and inflammation within the nose and brain are potential adverse health effects of exposure to satratoxins and Stachybotrys in the indoor air of water-damaged buildings. Key words: apoptosis, fungus, inflammation, inhalation, mycotoxin, neurotoxicity, olfactory sensory neuron, rhinitis, trichothecene. Environ Health Perspect 114:1099-1107 (2006) .

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Address correspondence to J.J. Pestka, 234 G.M. Trout Building, Michigan State University, East Lansing, MI 48824 USA. Telephone: (517) 353-1709. Fax: (517) 353-8963. E-mail: pestka@msu.edu

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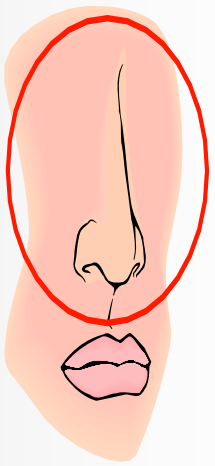

The Nose

Indoor Exposure to Molds and Allergic Sensitization

Beate Jacob,1,2 Beate Ritz,3 Ulrike Gehring,1,2 Andrea Koch,4 Wolfgang Bischof,4 H. E. Wichmann,1,2 and Joachim Heinrich1 for the INGA-Study Group

1GSF-Institute of Epidemiology, Munich, Germany; 2Institute of Medical Data Management, Biometrics, and Epidemiology, Ludwig-Maximilians-University of Munich, Munich, Germany; 3Center for Occupational and Environmental Health, UCLA School of Public Health, Los Angeles, California, USA; 4Department of Indoor Climatology, University of Jena, Erfurt, Germany

ABSTRACT:

Evidence that indoor dampness and mold growth are associated with respiratory health has been accumulating, but few studies have been able to examine health risks in relation to measured levels of indoor mold exposure. In particular, little is known about the contribution of indoor molds to the development of allergic sensitization. As a part of an ongoing study examining the effects of ambient air pollutants on respiratory health and atopic diseases in German school children, we examined the relation between viable mold levels indoors and allergic sensitization in 272 children. We examined whether allergic sensitization in children is associated with higher fungal spore count in settled house dust sampled from living room floors. Adjusting for age, sex, parental education, region of residency, and parental history of atopy, we found that mold spore counts for *Cladosporium* and *Aspergillus* were associated with an increased risk of allergic sensitization.

Sensitized children exposed to high levels of mold spores (> 90th percentile) were more likely to suffer from symptoms of rhinoconjunctivitis. We conclude that elevated indoor concentrations of molds in wintertime might play a role in increasing the risk of developing atopic symptoms and allergic sensitization not only to molds but also to other common, inhaled allergens. These effects were strongest in the group of children who had lived in the same home since birth.

http://ehpnet1.niehs.nih.gov/docs/2002/110p647-653jacob/ abstract.html

Address correspondence to B. Jacob, GSF-Institute of Epidemiology, Ingolstädter Landstr. 1 D-85758 Neuherberg, Germany. Telephone: +49-89-3187-4150. Fax: +49-89-3187-3380. E-mail:

beate.jacob@t-online.de

The Inga-Study Group: GSF--National Research Center for Environment and Health, Neuherberg, Institute of Epidemiology (H.E. Wichmann, J. Heinrich, P. Schneider, J. Cyrys, I. Groß, G. Wölke, G. Silbernagl, U. Gehring, B. Jacob, A. Houzer) , Institute of Ecological Chemistry (I. Gebefügi, G. Lörinci, J. Schnelle) ; Friedrich Schiller University--Jena Institute of Occupational, Social and Environmental Medicine (W. Bischof, A. Koch, J. Witthauer, K.J. Heilemann) , Institute of Clinical Immunology (L. Jäger, B. Fahlbusch, G. Schlenvoigt) ; Großhansdorf Hospital--Hamburg Center for Pneumology and Thoracic Surgery (H. Magnussen, K. Richter, R. Jörres) ; University of Utrecht--Division of Environmental and Occupational Health (B. Brunekreef, J. Douwes, G. Doekes) .