Aflatoxin exposure in the allergic lung: agriculture-related health pilot project

Alec Espeland, Scott A. Hoselton, Jane M. Schuh, and **Sumit Ghosh,**
Veterinary and Microbiological Sciences, North Dakota State University, Fargo, ND 58105, USA

ISSUE/PURPOSE

Asthma is an inflammatory disorder which is characterized by airway dysfunction and infiltration of inflammatory cells driven in large part by the activation of Th2 lymphocytes. Airway wall remodeling is an irreversible outcome of asthma that is observed in many, if not all cases of allergic asthma. The chronicity of asthma is evident in the number of adults who have the disease, nearly 32 million in the U.S. Agricultural operators/Occupational workers are continuously exposed to a complex mix of chemical, biological, and particulate insults and are at risk for developing chronic inflammatory lung diseases.

APPROACH

When corn is stressed and the outer layer of the kernel (pericarp) is damaged, it allows a place for mold and bacteria to grow, increasing the concentration of endotoxin and other mycotoxins that might be in the product. The *objective* of this proposal was to determine the extent to which secondary exposures to aflatoxin **(a mycotoxin)** can impact the development and maintenance of allergic fungal asthma. The following specific aims tested our *central hypothesis* that the initiation and maintenance of airway inflammation and airway remodeling in fungal allergic asthma is exacerbated by exposure to aflatoxin, a biological irritant that is found in the grain.

Specific Aim 1: We determined the extent to which aflatoxin exposure exacerbated fungal asthma induced by sensitization and challenge with* Aspergillus fumigatus *to recapitulate agriculture-related occupational exposure. Our working hypothesis was that exposure to aflatoxin will result in an increase in the allergic immune response as assessed by airway hyperresponsiveness, pulmonary inflammation, Th2 cytokines, IgE/IgG1/IgA Ab levels and chronic remodeling.

Specific Aim 2: We determined the extent to which aflatoxin exposure exacerbated Th2 polarization of dendritic cells (DCs) in fungal asthma. Using *in vivo* and *ex vivo* strategies, we tested our working hypothesis that aflatoxins interfere with DC maturation that enables the maintenance of a Th2 phenotype.

RESULTS

We compared disease progression after aflatoxin exposure in sensitized and challenged C57BL/6 mice that were exposed to repeated fungal exposures. We found that overall pulmonary inflammation and goblet cell metaplasia is significantly increased after aflatoxin exposure in allergic animals. Similarly, the Th2-type cytokines, (IL-4 and IL-13), were significantly increased after aflatoxin exposure. IgE, which is considered as the hallmark of allergic asthma was also significantly elevated at high doses of aflatoxin exposure. Taken together, these findings demonstrate that aflatoxin exposure exacerbates the allergic immune response in a murine asthma model.

THE BOTTOMLINE

The findings of this study which demonstrate that aflatoxin exposure exacerbates the allergic immune response will allow farmers and ranchers to make evidence-based health and safety decisions for their animals, families, and communities. The interpretation of the results from this study provides evidence-based information to reduce the direct and indirect costs associated with agricultural exposures and pulmonary dysfunction, potentially helping to offset a nearly $20-billion annual price tag and limiting the financial burden of asthma. The financial benefits that are projected as a result of this research include increased productivity with a reduction in missed work days, decreased medication expenses for the treatment of chronic asthma, and a reduced number of doctor's visits/hospitalizations for the complications of asthma.

Funding source: This study was funded by a pilot grant from Upper Midwest Agricultural Safety and Health Center (P002283011 to **Sumit Ghosh**).