Effect of Work Cessation on Lung Function in Exposed Swine Farmers: Results of a Fourteen-Year Follow-Up

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Pulmonary function studies were conducted on 302 male swine workers in 1990-91(Cycle 1) (mean age ± SD 37.2 ± 11.7 years), (mean exposure years ± SD 12.23 ± 7.44), of whom 217 were studied in 1994-95 (Cycle 2)(age 41.97 ± 11.65 years), (exposure years 16.20 ± 7.46) and 163 in 2003-04 (Cycle3) (age 50.54 ± 10.72 years) (exposure years 22.51 ± 9.08). Variables obtained were forced vital capacity (FVC), forced expired volume in one second (FEV1), ratio of FEV1/FVC, and maximum mid-expiratory flow rate (FEF25-75). Only 20 farmers stopped working in the swine barns between Cycle 1 and Cycle 2, but 68% of farmers (111) quit hog farming between Cycle 2 and 3 (quitters). Among 111 farmers destined to be quitters in Cycle 3 as compared to those destined to be survivors in Cycle 3, values when tested at Cycle 2 for FEV1/FVC ratio (76.0 ± 7.0% vs. 79.0 ± 6.1%, $p < 0.01$), and FEF25-75 (3.58 ± 1.25 L/s vs. 4.08 ± 1.99 L/s, $p < 0.05$), were lower. In addition, among those destined to be quitters and those destined to be survivors, annual losses between Cycle 1 and 2 for FEV1 (-69.22 ± 17.27 mL/yr vs. –59.62 ± 21.02 mL/yr; $p < 0.05$) and FEF25-75 (-160.87 ± 30.15 mL/s/yr vs. –117.82 ± 35.43 mL/s/yr; $p < 0.05$) were greater. Similarly, between Cycles 2 and 3, mean annual losses were greater for quitters than for survivors for FEV1 (-44.26 ± 9.37 mL/yr vs. –42.21 ± 6.69 mL/yr, $p < 0.05$). These findings raise the possibility that these workers who stayed in the industry, as supposed to those who left, represent the healthy worker phenomenon.

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Occupational Exposure to Organic Dust of Non-Naïve Non Exposed Volunteers Induces Symptoms of Endotoxin Tolerance

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Work with occupational levels of organic dust is associated with a chronic inflammatory response that must somehow be controlled. TNF is a central mediator of the inflammatory cascade. Endotoxin tolerance has previously been described in vitro or in animal studies as a mechanism that modifies the threshold at which the response sets in. We investigated whether work exposure to occupational levels of organic dust in swine confinement buildings induces endotoxin tolerance through TNF. We exposed sixteen non-naïve persons in a swine confinement building with low to moderate representative levels of organic dust and characterized their acute immune response. Under a work-like three hour exposure conditions non-naïve volunteers developed an inflammatory response documented by an increase in BAL IL-6 from 3,08 pg/ml to 6,11 pg/ml and visual indices of bronchial inflammation. Similarly, serum IL-6 increased with a peak at 3 hours after exposure. TNF-a was not detected in BAL, but serum TNF-a was reduced from 3,7 pg/ml at baseline to less than 2 pg/ml within three hours after exposure, and remained repressed until 2 weeks after exposure. This is a cardinal marker for immune hyporesponsiveness, which was supported by other markers; reduction of HLA DR expression on alveolar macrophages and CD14 expression on blood monocytes. We report findings that are consistent with long lasting endotoxin tolerance, and perhaps immune hyporesponsiveness, and that are induced by a brief exposure to organic dust in the low range of occupational levels.

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Silica Exposure Induces Arginase I Expression in Rat Lung

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RATIONALE: Induction of arginase (ARG) in some inflammatory lung diseases (e.g. asthma) suggests that it may play a role in bronchoconstriction, fibrosis and airway remodeling by reducing substrate for NO synthesis and enhancing metabolism of arginine to proline and polyamines. Our objectives were to ascertain whether ARG induction is also a feature of silicosis and, if so, to identify the cells expressing type I ARG (ARG I) in rat lung following silica exposure. **METHODS:** Sprague-Dawley rats received vehicle or 0.1, 1.0 or 5.0 mg silica/100 g body weight by intratracheal instillation. After 24h, bronchoalveolar lavage (BAL) was performed and markers of pulmonary inflammation, damage and alveolar macrophage (AM) activation were examined. ARG expression was examined by real-time PCR and activity assay. ARG I and iNOS were analyzed by immunohistochemistry. **RESULTS:** Markers of pulmonary inflammation, damage and AM activation and NO production were significantly increased at all silica doses tested. Silica caused 2- and 3-fold increases in ARG activity at 1 and 5 mg/100 g doses, respectively. ARG I, but not type II ARG, mRNA increased in a similar pattern. In control lungs, ARG I immunoreactivity was observed in AM only. In silica-treated lungs, ARG I immunoreactivity was observed in alveolar type II epithelial cells and in clustered AM, while iNOS expression was seen in AMs and PMNs. Coexpression of ARG I and iNOS was seen only in some AM. ARG activity in AM isolated by BAL also increased significantly after silica treatment. **CONCLUSIONS:** The pattern of ARG I induction is similar to that seen in other models of acute lung disease, suggesting that increases in ARG I may play a common role in the pathology of some lung diseases. Studies to evaluate the impact of inhibiting ARG activity in lung disease are warranted.

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Lung-Retained Fiber in Pets Confirms Environmental Exposure to Naturally-Occurring Asbestos in Western El Dorado County, California

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RATIONALE: Tremolite-actinolite asbestos has been identified in locations in the western portion of El Dorado county in the Sierra Nevada area of California. This area is under considerable pressure for real estate development. There has been concern about exposure to residents and to children attending schools there, with air and soil measurements and limited remediation by state and federal agencies and individual hygiene companies over the last several years. Previous animal testing found this fiber to have high mesothelioma risk. Analysis of animal lungs for retained mineral fiber has proven useful in exposure assessment in other locations worldwide. **METHODS:** We obtained both lungs from four animals at the time of death through veterinarians. Of these, one cat had not lived in the area; one had, but remained indoors, and two dogs had lived in the area for different periods. Analysis of lung fiber burden was by analytical electron microscopy with identification of fiber types by EDS, using Scanning EM in the SUNY LAB and Transmission EM in the McGill Lab. **RESULTS:** The following results were obtained:

LUNG FIBER CONCENTRATION IN EL DORADO COUNTY PETS

ANIMAL	EXPOSURE	SUNY LAB >5μm length	McGill LAB >5μm length	SUNY LAB >10μm length	McGill LAB >10μm length
Cat 1	none	0	0	0	0
Cat 2	9 years, indoors	86,000	157,000	86,000	157,000
Dog 1	> 2 years	1,250,000	566,500	192,000	412,000
Dog 2	> 8 years	9,162,000	928,000	2,030,600	928,000

All results in fibers of Tremolite/ Actinolite / gram dry lung.

CONCLUSIONS. Animals studied show long-fiber tremolite-actinolite asbestos in great excess, proportional to exposure.

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Comparison of 3 Methods for Assigning Exposure Metrics for Evaluating Occupation Effect upon COPD

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Spirometry and work descriptive data from the Lung Health Study, a multi-site early intervention (smoking cessation/bronchodilator) clinical trial, were analyzed to assess the influence of occupational exposures upon the lung function at the baseline examination in 3025 male smokers with early COPD. Methods: Subjects were assigned to 55 workgroups using a computerized lexical analysis system for interpretation. Exposure was summarized by three methods: SR: Individual self reported response to questions about dust and fume at the worksite; GAR: Group Average Response- proportion of subjects in each workgroup reporting the exposure; and JEM: Job Exposure Matrix-ratings assigned by a panel of four experts to each workgroup. The health outcome variable was spirometry measurements at basecline pre and post bronchodilator administration. The predictor variables included occupational exposure, smoking intensity, and airway responsiveness by methacholine challenge testing. Results: After adjustment for smoking intensity and airway responsiveness, there was statistically significant negative association between FEV1 % predicted and exposure when exposure was determined by the JEM and by JEM and GAR weighted by years in the job, but not by SR (e.g., a 1 point increase in fume exposure by JEM [scale 1-10] was associated with a 0.219 % predicted reduction in mean FEV1 post bronchodilator) Conclusions: Occupational exposures, particularly fume exposure, are associated with reduction of lung function in males with early COPD. The new method of computerized lexical analysis to assign individuals into workgroups is an effective epidemiologic tool. Exposure described on a group basis appears to be more effective than using individual self-stated exposures.

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Health Outcomes of Patients Presenting with Symptoms Related to Non-Industrial Indoor Work Environments

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RATIONALE: Increased risk of nonspecific symptoms and asthma has been associated with non-industrial indoor work environments, with much focus on causative factors. Little is known about the longer-term health and socioeconomic outcomes of patients with building-related symptoms. **METHODS:** We performed a retrospective longitudinal study of patients who presented with symptoms related to a non-industrial work environment to characterize health and socioeconomic outcomes. **RESULTS:** 130 patients seen at Yale or University of Connecticut Occupational Health Clinics between 1997 and 2002 completed a telephone survey to assess current symptoms and health, home and work modifications, and job status a mean of 3.6 years after initial evaluation. The most common presenting symptoms were respiratory and irritant (>90% patients) and neurologic (60% patients). Over 75% patients reported onset of symptoms following a specific office renovation or move. 57% had current asthma, 73% of whom were diagnosed after the trigerring event. About 70% reported their overall health had improved at follow-up, although over 70% had persistent symptoms that interfered with activities. Of note, it often took several years for symptoms to resolve (mean 4.1 yrs), and substantial modifications to lifestyle, work and home environments were made in about 80%. Asthmatics had a higher prevalence of respiratory symptoms and lower prevalence of nonspecific symtpoms, and were more likely to make modifications in their home and work environments. **CONCLUSIONS:** Patients with building-related symptoms have symptoms and modified life styles which can persist long after the initial office event.

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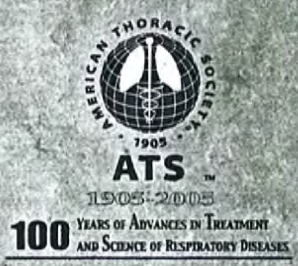

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