ASTHMA AND THE EFFECT OF IRRITANT CHEMICAL EXPOSURES ON LUNG FUNCTION. H.Glindmeyer, J.Lefante, R.Jones, L.Freyder, H.Weill. Tulane Medical School, Environmental Medicine, New Orleans, LA, USA.

As part of a larger chemical worker study, workers potentially exposed to irritant chemicals in user industries were evaluated to determine if history of exposure to irritant chemicals is associated with level (%Pred) or annual change (ml/yr) in FEV_1, and whether any association was influenced by susceptibility (history of asthma). 179 workers with a history of asthma (EverAsthma) were individually matched with 179 comparison workers by sex, age, race, smoking categories (Cur, Ex, and Nev), plant, and whether they indicated at interview that they had ever worked around irritant chemicals or gases. All workers had a minimum of 3 spirometric tests over 2 years (average, 5 tests over 5 years). Baseline values for FEV_1 were significantly lower among those with EverAsthma (yes = 93.9%Pred, no = 102.9%Pred); however, there was no overall difference in FEV_1 slope (yes = − 46.0ml/yr, no = − 48.8 ml/yr). For these workers, multiple regression of FEV_1 on smoking, EverAsthma and ever working around irritants indicated significant differences in FEV_1 level for smoking (vs Nev, Cur = − 8.6%Pred and Ex = − 4.0%Pred) and EverAsthma (yes = − 8.9%Pred), but there was no association with ever working around irritants. Of those with EverAsthma, 68 were currently on medication (ActiveAsthma) and 111 were not (NonActiveAsthma). Multiple regression for the ActiveAsthmatics and their comparison workers indicated that FEV_1 level was significantly associated with smoking (Cur = − 9.8%Pred), ActiveAsthma (yes = − 12.8%Pred) and ever working around irritants (yes = − 7.1%Pred). Ever working around irritants was not a significant determinant in NonActiveAsthmatics and their comparison workers, despite significant effects of smoking (Cur = − 6.9%Pred) and NonActiveAsthma (yes = − 6.5%Pred). To investigate the magnitude of the effect of working around irritants on the lung function of ActiveAsthmatics only, regression analyses were repeated separately on this group. FEV_1 level was significantly associated with ever working around irritants (yes = − 10.1%Pred), FEV_1 slope was not. When FEV_1 slope was regressed on potential explanatory variables, only age and smoking were significant in the entire population. Ever working around irritants was also not significant when analyses were confined to those with ActiveAsthma or NonActiveAsthma, and their respective comparison workers. The lack of an association between FEV_1 slope and working around irritants is possibly due to the limitation of the interview, which did not distinguish between past or current work with irritants. These results suggest that workers with active asthma may have an enhanced risk of adverse functional effects associated with irritant chemical exposures. (Supported by NIEHS Grant # 5 P42 E505946-02)

RESPIRATORY TRACT SYMPTOMS AFTER EXPOSURE TO A CHLORINE GAS LEAK SR Short, KB Kinsley, EL Petsonk, S Deitchman, JL Hankinson. Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Morgantown, WV.

Respiratory effects of toxic gas inhalation are related to the exposure concentration and duration, and the solubility of the gas. Inhalation of chlorine gas may result in upper and lower respiratory irritation, depending on the concentration inhaled. We investigated the development and persistence of respiratory symptoms in a group of firefighters who worked during a 70 ton chlorine gas leak in May 1991. Six months following the incident, a self-administered questionnaire was mailed to approximately 150 firefighters. It requested information on the occurrence and duration of upper and lower respiratory tract symptoms, the individual firefighter's location during the incident, the duration of exposure to the gas, and the timing and type of respiratory protection used (if any). Symptoms queried were cough, chest tightness, wheeze, tearing eyes, sore throat, headache, runny nose, and sneezing. Additionally, respondents were asked to describe symptoms not specifically listed in the questionnaire. Forty firefighters (approximately 27%) who were present during the chlorine leak responded, of whom 39 (98%) described inhaling the chlorine gas. Most, 28 (72%) had never smoked cigarettes regularly; and 2 (5%) were current cigarette smokers. Commonly reported symptoms included cough (79%), sore throat (71%), chest tightness (61%), headache (58%), tearing eyes (56%) and wheeze (49%). Gas exposure duration was estimated by 36 respondents, and ranged from a minimum of 2 minutes to a maximum of 14 hours, with a median of 3 hours exposure to the gas. Thirty-two (82%) related some use of respiratory protection during the incident, with 15 (46%) using it for less than 25% of the exposure time and 11 (33%) using it 75-100% of the exposure time. Response time prior to donning the respirator ranged from less than 1 minute, to 3.5 hours, with a median response time of 5 minutes. Two firefighters (5%) were still experiencing symptoms six months after the incident. One reported wheeze, and the other noted shortness of breath, hoarseness, and dizziness. No significant association was seen between the duration of a firefighter's symptoms and the duration of gas exposure, the time prior to donning the respirator, or the percentage of exposure time the respirator was used. Based on the available data, aside from location in the plume, no risk factors were identified for the persistence of respiratory tract symptoms in firefighters who were exposed to a chlorine gas leak.

CHLORINE GASSING EPISODES AND OBSTRUCTIVE PULMONARY DISEASE AMONG CHEMICAL PULP MILL WORKERS. P.K. Henneberger, ScD, MPH, Division of Respiratory Disease Studies, NIOSH, 944 Chestnut Ridge Road, Morgantown, WV 26505, U.S.A.

Workers in chemical pulping processes are normally exposed to relatively low levels of irritant gases like chlorine. Occasionally, accidental releases of gases cause the exposure levels to be very high for brief periods of time. In a study of older workers from a pulp and paper production facility in Berlin, New Hampshire, chronic decreases in the forced expiratory volume in one second (FEV1) and the ratio of the FEV1 to forced vital capacity (FVC) were associated with these episodic, high-level exposures to irritant gases. Since most of the subjects were older and had worked when ambient exposure levels were higher, it was unclear whether the findings could be generalized to younger employees. Therefore, a cross-sectional study of current workers from the same plant was initiated. The subjects were selected from employees who were first hired after a major cleanup of the factory in the early 1960's. Three-hundred white male subjects from the pulp and paper production facility were tested in 1992. Each participant completed both a pulmonary function test and a questionnaire. The mean age was 40.4 years and the mean tenure with the company was 18.5 years. A total of 105 of the 300 subjects (or 35%) reported experiencing at least one episode of high exposure to chlorine or chlorine dioxide while working at the pulp and paper company. Controlling for both cigarette smoking and years of pulp mill work, the gassed subjects were over six times more likely to have obstructive pulmonary disease than were the non-gassed subjects ($p<.05$). Despite the improvements in background levels of irritant gases, high-exposure episodes continue to occur and are still associated with decreased pulmonary function. Hence, additional controls are needed to minimize the number of gassing events in this and other chemical pulp mills.

THE INFLAMMATORY RESPONSE TO GRAIN DUST IS DEPENDENT ON ENDOTOXIN RESPONSIVENESS. P.J. JAGIELO, P.S. THORNE, K.L. FREES, S.A. BLEUER, D.A. SCHWARTZ. Departments of Internal Medicine and Preventive Medicine and Environmental Health, The University of Iowa College of Medicine, Iowa City, Iowa

To identify the role of endotoxin in grain dust-induced airway inflammation, we performed two experiments using an animal model of grain dust-induced airway inflammation. In the first experiment, we compared the inflammatory response in endotoxin sensitive (C3H/HeBFEJ) and resistant (C3H/HeJ) mice exposed to inhaled endotoxin (LPS), corn dust extract (CDE), and filter sterilized corn dust extract (SCDE). Mice were exposed for 4 hours in groups of 12 (6 resistant and 6 sensitive strains) to one of the following nebulized solutions: E. coli (0111:B4) LPS, CDE (0.1% w/v), SCDE (0.1% w/v), or sterile saline . Dose-response relationships for endotoxin concentrations between 0.1 $\mu g/m^3$ and 10.0 $\mu g/m^3$ were performed in the LPS, CDE, and SCDE exposed mice. Following the exposure, bronchoalveolar lavage (BAL) was performed for cell counts and lavage fluid analysis. Endotoxin sensitive mice demonstrated significantly higher concentrations of total cells, neutrophils, and BAL fluid TNFα in response to LPS, CDE, and SCDE in comparison to resistant mice ($p<0.001$). In fact, the inflammatory response was at least two orders of magnitude greater in the sensitive mice than in the endotoxin resistant mice at the high dose. Moreover, clear dose-response relationships between the endotoxin concentration and the inflamatory response were demonstrated among endotoxin sensitive mice. In a second experiment, we investigated whether endotoxin tolerance would alter the inflammatory response to inhaled LPS and SCDE in sensitive mice. Endotoxin sensitive mice were injected intraperitoneally on days 1-4 with increasing doses of LPS (100μg/kg, 500μg/kg, 1000μg/kg, 5000μg/kg) to induce tolerance, or were injected with sterile saline. On day 5, eighteen mice (nine from each group) were exposed to nebulized LPS (44$\mu g/m^3$) and twenty mice (ten from each group) to SCDE (endotoxin concentration 3.4$\mu g/m^3$) for 4 hours. BAL was performed following exposure. Sensitive mice preexposed to endotoxin demonstrated a significantly reduced concentration of total cells, neutrophils, and TNFα as compared to controls ($p<0.01$) for both inhaled LPS and SCDE. In fact, each of the measures of inflammation were reduced by at least 50% in comparison to those measured in control mice. These results demonstrate that responsiveness to endotoxin is critical to the development of grain dust-induced inflammation in the lower respiratory tract. These results support our hypothesis that endotoxin may be the principle mediator of the acute inflammatory response to inhaled grain dust.

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ABSTRACTS

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