

Diesel Exhaust and Solvents Are Risk Factors for Wheeze among Farmers in the Agricultural Health Study

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Farmers engage in a wide variety of activities including crop production, equipment repair, maintenance, and transportation. These activities result in exposure to diesel exhaust, solvents, welding fumes, and other respiratory irritants. Using the certified pesticide applicators enrolled in North Carolina, we evaluated the odds of wheeze on the farm. We used logistic regression and history of asthma or atopy to evaluate 20,898 farmers who provided complete tractors and driving trucks on the farm was associated with an elevated odds of wheeze (Odds Ratio (OR)diesel=1.29, 95% CI=1.15, 1.45; OR-painting=1.82, 95% CI=1.31, 2.41). A dose response relationship but not for driving gasoline tractors non-smokers had the highest odds of wheeze (OR=1.58, 95% CI=1.31, 1.91). Painting and use of solvents for wheeze in a duration dependent fashion. The odds of wheeze were highest for using solvents daily, either by painting (OR=1.82, 95% CI=0.89, 3.73), cleaning with gasoline (OR=1.43, 95% CI=0.85, 2.41), or cleaning with other solvents (OR=1.63, 95% CI=1.09, 2.43). These results add to the growing body of evidence of adverse effects of diesel exposure on the lung and suggest exposure to solvents may also be important.

This Abstract is Funded by: Intramural research funds of NIEHS and NCI

Cellular and Humoral Factors in a Subchronic Model of Toluene Diisocyanate-Induced (TDI) Asthma

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Occupational asthma (OA) is responsible for 10 percent of all cases of asthma, and, diisocyanates, a chemical class with wide application in industry, are the most common low molecular weight chemicals responsible for OA. TDI-induced asthma has been difficult to diagnose and control, in part, because the biological mechanisms responsible for the disease and the determinants of exposure have not been well defined. We hypothesize that TDI-induced asthma can occur through immunological and non-immunological mechanisms; the mechanisms responsible being dependent upon the exposure paradigm. We have developed a low level, subchronic inhalation model to reflect the most common exposure paradigm in the workplace. C57BL/6 mice were sensitized to TDI by inhalation (20ppb, 4hrs/day, 5 days/week) for 6 weeks, and challenged by inhalation 14 days later (20ppb, 1hr). Sensitized/challenged mice displayed significant inflammation in the upper and lower airways, characterized by lymphocytes, neutrophils and eosinophils accompanied by goblet cell metaplasia, epithelial damage, serum specific IgG antibodies and non-specific airway hyperresponsiveness (AHR) to methacholine challenge. Significant increases in IL-4, IL-5 and IFN γ mRNA were measured in the airways. Adoptive transfer experiments demonstrated that both T and B lymphocytes as well as IgG antibodies are important in the TDI-induced airway hyperreactivity. Taken together, these results suggest that in a subchronic model, with a dose reflective of the current permissible workplace exposure level, that sensitization to TDI can occur under these conditions and demonstrates the importance of both a cellular and humoral response in the manifestation of TDI-induced asthma.

This Abstract is Funded by: None

Comparison of Two Methods for Sampling Hexamethylene Diisocyanate Biuret Aerosol: A Chamber Study

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Hexamethylene diisocyanate (HDI) biuret aerosol exposure is an important cause of occupational asthma. Control in the workplace is hampered by lack of agreement on the best metric for quantifying exposure and a uniform analytical method. A new NIOSH method 5525 has recently been developed that uses the Institute of Occupational Medicine sampler, a single quartz filter and 1-(9-anthracenyl)methylpiperazine (MAP) as derivatizing agent. The purpose of this study was to compare this method with the established ISO-CHEK (ISO) cassette method in measuring HDI biuret aerosol. A closed exposure chamber was used to generate an HDI biuret (Desmodur N-100) aerosol with overall concentrations varied over an equivalent HDI monomer range of 4 to 70 ppb, as measured by the Autostep portable equipment. Twenty-seven side-by-side samples were taken from the chamber using both methods. Samples were analyzed by high performance liquid chromatography. For HDI monomer, MAP method found higher levels than ISO method [GM (GSD:ug/m³): 80.1(2.2) vs. 61.3(2.0), p<0.005, n=27]. For HDI biuret aerosol, MAP method found lower levels [75.4(2.7) vs. 99.0(3.3), p<0.05, n=25]. When exposure was expressed as total reactive isocyanate group (TRIG) mass, no difference was found between MAP and ISO methods [65.6(2.0) vs. 61.2(2.1), p>0.05, n=25]. MAP method was also found best correlated with ISO method for biuret aerosol (ISO=1.06MAP, R²=0.78). These results suggest that measurements of HDI aerosol by MAP and ISO methods were similar although the data were variable. The MAP method potentially provides an easier alternative for the measurement of HDI and HDI-based polyisocyanate aerosol.

This Abstract is Funded by: NIOSH Grant R01H3457, NHLBI Grants 1P01-HL56389, R01HL62932

Specific Antibodies to Glutaraldehyde (GA) and Formaldehyde (F) and Medical Radiation Technologists (MRTs)

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Background: MRTs are exposed to sensitizers and irritants including GA and F. They may develop occupational asthma (OA) and work-related (WR) respiratory symptoms but the mechanism is not established. Methods: As part of a survey of respiratory problems in this profession, we investigated the prevalence of serum specific IgE and IgG antibody to GA-HSA and F-HSA conjugates by ELISA among 15 asymptomatic MRTs and 22 MRTs with possible OA, who had reported WR respiratory symptoms (based on Venables, 1993). Of these, 12 had asthma (methacholine PC20<8mg/ml) and 10 had WR symptoms but no asthma. All but one were females and all were nonsmokers. A positive antibody level was defined as absorbance \geq mean+3SD among 8 unexposed lab controls. Exposure challenge to GA with analysis of induced sputum was conducted in 2 MRTs with WR-changes in PC20. Results: The prevalence of positive specific IgE to GA-HSA increased from 1 (6.7%) among asymptomatic MRTs to 2 (20%) of those with symptoms but no asthma, to 3 (33%) of the asthmatics. Serum specific GA-HSA-IgG was observed in only 1 subject in each group; none had positive IgE or IgG antibody to F-HSA. Exposure challenge with GA (0.1 mg/M3) did not result in changes in spirometry or PC20; the first MRT who had a post-challenge increase in eosinophils in induced sputum from 0.25% to 3.25% was IgE positive, consistent with GA-induced eosinophilic bronchitis, while the other (0% eosinophils before and after challenge), was IgE negative. Conclusions: The increase in prevalence of GA-HSA IgE among those with asthma suggests that IgE-mediated responses may play a role in GA-related respiratory disease.

This Abstract is Funded by: Ontario Workplace Safety & Insurance Board

Sick-Building Symptoms in Medical Radiation Technologists Versus Physiotherapists

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Background: Medical radiation technologists (MRTs) have reported unexplained work-related symptoms which they attribute to chemical exposures. This study determines whether MRTs have an excess of a symptom complex consistent with sick building syndrome, and assesses associated factors. Methods: Questionnaires were sent to Ontario MRTs and as a control group, physiotherapists (PTs) as part of a larger study. SBS was defined as 3+ symptoms of: a) eye, b) nose, c) throat, irritant symptoms, or d) headache: (these symptoms worse at work, 15+ days in the past year) and/or e) abnormal fatigue. Results: 64% MRTs (1840) and 63% PTs (1714) responded. 231 MRTs and 295 PTs with physician-diagnosed asthma were excluded from analyses. Each SBS symptom was more frequent in MRTs (p<0.0001). SBS definition was met by 7.8% MRTs and 1.8% PTs (OR 4.8, CI 3.1-7.5). SBS in MRTs was associated with work-related asthma symptoms (e.g. wheeze, OR 4.0, CI 2.5-6.3), self-reporting of tasks reflecting increased work chemical exposures (e.g. cleaning a processor spill OR 2.7, CI 1.9-3.8) and factors reflecting greater workplace psychosocial stress (e.g. "burnout" OR 3.7, CI 2.4-5.9, unhelpful supervisor OR 2.5, CI 1.5-4.3). Findings were unchanged when adjusted for smoking, age group and gender. Conclusion: MRTs have an increased prevalence of symptoms consistent with SBS. These symptoms are associated with lower respiratory symptoms similar to asthma. Chemical exposures (self reported) and psychosocial stressors might be primary causative factors in this syndrome or could reflect increased perception by those with SBS.

This Abstract is Funded by: Ontario Workplace Safety and Insurance Board Research Funding

Occupational Shift towards a Th2 Dominant Status in the Mushroom Workers with Asthma-Like Illnesses

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To estimate the cause and immune basis of a mild asthma-like illness affecting workers in a mushroom factory cultivating *Hypsizygus Marumoreus* (Bunashimeji), we conducted cross-sectional and follow-up studies for 56 mushroom workers. Analysis of peripheral blood mononuclear cells (PBMC) revealed that percentages of monocytes, CD4+T, NK(CD3-/CD161+) and NKT(CD3+/CD161+) cells were significantly increased in the workers as compared with controls (p<0.001). Increases in Th2 type T cells, Th2/Th1 ratio and serum IL13 and decreased serum IFN- γ were detected (p<0.001), indicating a Th2-biased status of the workers. The follow-up study showed that monocytes and NK cells increased soon after employment while CD4+T, Th2 and NKT cells gradually increased as employment time lengthened. Serum precipitating antibody to the mushroom antigen could be detected at a later stage. Co-cultivation of PBMC with the mushroom extract induced much higher CD1b expression, and suppressed secretion of Th1 cytokines in culture supernatants as compared with controls (p<0.001). These results indicate that the mushroom antigen contains highly immunogenic substances which stimulate PBMC of the workers into a Th2-biased in vivo status. Asthma-like illness apparently induced by continuous exposure to the mushroom spores and some Th1 cytokines may play an important role.

This Abstract is Funded by: None



AMERICAN JOURNAL OF

Respiratory and Critical Care Medicine

Volume 167 • Number 7 • April 2003

Abstracts

2003
INTERNATIONAL
CONFERENCE

May 16–21, SEATTLE, WASHINGTON
AMERICAN THORACIC SOCIETY

This is a supplement of the American Journal of Respiratory and Critical Care Medicine

AN OFFICIAL JOURNAL OF THE AMERICAN THORACIC SOCIETY