

COMPARISON OF METHACHOLINE PROTOCOLS IN THREE OCCUPATIONAL STUDIES

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Rationale: Methacholine challenge testing has become a common tool for detecting nonspecific bronchial hyper-responsiveness. We examined the impact of differences in field and analysis protocols on the degree of measured airway responsiveness in our three recent studies of working populations exposed to respiratory hazards; apprentices exposed to metalworking fluids, boilermaker construction workers exposed to combustion particulate, and auto body shop workers exposed to hexamethylene diisocyanate.

Methods: All three protocols used the tidal breathing method. Slopes were based on concentration rather than cumulative dose of methacholine and anchored by the saline FEV1. The protocols differed in the number of dose levels, the maximum concentration administered (64, 25, and 10 mg/ml) and in the maximum time elapsed before the FEV1 measurement after each dose (up to 3, 2, and 1 minutes). Slopes were recalculated after standardizing the protocol across studies by truncating the data at a similar final concentration and waiting the same length of time before measuring FEV1.

Results: There were no significant differences in methacholine slopes or the prevalence of responsiveness ($PC_{20} < 8$ mg/ml) between auto body shop workers exposed to isocyanates and apprentice machinists exposed to metalworking fluids, -14.2 and -19.0, respectively. The boilermakers exposed to combustion particulate were more responsive. When the protocol in the auto body shop study was truncated at 10 mg/ml (the highest dose in the boilermakers' protocol) the mean response slope did not change significantly.

Conclusions: Low dose protocols may be adequate for assessing airway responsiveness in working populations. The findings have practical implications for the cost of conducting field studies of occupational and environmental respiratory hazards.

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INCIDENCE AND HOST DETERMINANTS OF OCCUPATIONAL ASTHMA IN APPRENTICES EXPOSED TO LABORATORY ANIMALS.

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Introduction: Laboratory animal (LA) workers are frequently affected with allergic sensitization and occupational asthma (OA). The role of pre-exposure host factors, in particular airway responsiveness, on the incidence of OA has not been satisfactorily studied. **Methods:** A prospective cohort study of 417 apprentices in animal-health technology was conducted to investigate the incidence and determinants of OA. A questionnaire, and skin-prick tests with common and work-specific allergens were administered on entry and at follow-up visits (up to three) from 8 to 44 months after starting apprenticeship; responsiveness to inhaled methacholine was assessed at baseline and at follow-up in apprentices who developed a new specific skin sensitization and in controls (1:2). Pre-exposure host characteristics and the school attended were compared between cases and all cohort subjects not meeting the criteria for OA. **Results:** Twenty-eight apprentices satisfied the definition for OA, i.e., onset of immediate skin reactivity to > 1 occupational inhalant and a ≥ 3.2 -fold decrease in PC_{20} . The incidence of OA was 2.7% (28/1043 person-years). Baseline immediate skin reactivity to pets (RR 4.1, 95% CI=1.6-10.2), bronchial responsiveness ($PC_{20} \leq 32$ versus $PC_{20} > 32$ mg/ml) (RR=2.5, 95% CI=1.0-5.8), and FEV1 (RR 1.06, 95% CI=1.02-1.1) were associated with an increased risk of OA. **Conclusions:** 1) apprentices in animal-health show a high incidence of OA; 2) pre-exposure airway calibre and responsiveness as well as sensitization to pets are associated with an increased risk..

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SYMPTOM ONSET IN THE FIRST TWO YEARS OF EMPLOYMENT AT A WOOD PRODUCTS PLANT: SOME OBSERVATIONS RELEVANT TO OCCUPATIONAL MEDICAL SCREENING. Wang ML, Petsonk EL. National Institute for Occupational Safety and Health, Division of Respiratory Disease Studies, Morgantown, WV

Medical monitoring during work with sensitizers has been recommended, to facilitate early detection of health effects at a point when prompt control of long term health consequences. A two-year prospective study among workers at a newly established wood products quid mixture of methylene diphenyl diisocyanate (MDI) s. An initial health survey was completed by 214 participated in semiannual follow-up health surveys, and

144 completed an occupational history. Associations between exposures and the development of specific symptoms were investigated using univariate and multivariate logistic regression analysis methods. For nocturnal dyspnea, chest tightness (TC), and attacks of dyspnea with wheeze (ATK), onset during the first 2 years was associated ($p < 0.01$) with job activities involving liquid MDI but not current tobacco smoking, while cough onset was correlated ($p < 0.01$) with smoking and dusty job activities. New phlegm production was increased with either a dusty job or work with liquid MDI. Among employees working with liquid MDI, onset of ATK & TC tended to occur earlier in employment than other symptoms. Work-related spirometry changes ($\Delta FEV_1 > 10\%$) were more prevalent among those with symptom onset ($p < 0.01$). The data suggest that responses to certain questionnaire items may have potential utility in occupational medical screening programs, as early indicators of sensitizing exposures.

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THE INCIDENCE OF RESPIRATORY SYMPTOMS AND ASTHMA BY OCCUPATIONAL AIRBORNE EXPOSURE IN A COMMUNITY SAMPLE

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INTRODUCTION: Few longitudinal community studies have examined the incidence of asthma and respiratory symptoms by work-related exposures. **METHODS:** We examined the incidence of morning cough, chronic cough, phlegm cough, dyspnea grade 2, wheezing, and asthma in an eleven years cohort study ($n=2819$, age 15-70) from the general population in Norway. **RESULTS:** The prevalence of lifetime exposure to dust or gas was 27.7%, and for asbestos 4.8%, at baseline. For asthma and all symptoms except dyspnea, the incidence of asthma and symptoms was higher among those occupationally exposed. All the odds ratios (OR) for the incidence of respiratory symptoms and asthma by dust and gas exposure were significant, varying between 1.3 (1.0-1.8) for morning cough and 1.8 (1.4-2.4) for phlegm cough, after adjusting for gender, age, smoking habits, and pack-years. The corresponding OR by asbestos exposure reached significance for morning cough [1.8 (1.1-3.0)] and phlegm cough [1.9 (1.2-3.0)]. **CONCLUSION:** Both specific and unspecific occupational airborne exposures were independent predictors of the incidence of respiratory symptoms and asthma in a general population.

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OXIDATIVE STRESS IN CHLORINE EXPOSED A/J MICE J.G. Martin, H.R. Campbell, H. Iijima, K. Maghni, J.L. Malo, D. Gautrin, and D.H. Eidelman. Meakins-Christie Laboratories, McGill University Health Centre and Sacre Coeur Hospital Research Centre, Montréal, Québec, Canada.

Acute chlorine (Cl_2) exposure is a cause of occupational asthma. Cl_2 has been shown to evoke a neutrophilic inflammation and airway remodeling in the rat. Neutrophils are capable of producing several reactive oxygen and nitrogen species. Of particular interest is NO_2 that reacts with HOCl to form 3-nitrotyrosine (3NT) and 3-chlorotyrosine, markers of inflammation-mediated protein modification and tissue injury. In this study, we examined effects of Cl_2 exposure on oxidative and nitrosative stress in A/J mice. Mice (25 g) were exposed to 0, 100 or 800 ppm Cl_2 for 5 min and monitored for 24 h. Animals were then sacrificed and bronchoalveolar lavage (BAL), immuno-histochemistry and Western analysis were performed. In the 800 ppm group, there was epithelial desquamation and immuno-histochemical staining showed neutrophils that were strongly positive for 3NT and inducible nitric oxide synthase (iNOS). At 100 ppm, there was less epithelial damage and cells stained positively for iNOS. Western blotting and densitometry showed that iNOS expression was increased by 205% at 100 ppm, 85% at 800 ppm when compared to 0 ppm. In lung tissue, oxidation of component proteins rich in carbonyl groups was examined by Western blotting for DNPH (2,4-dinitrophenylhydrazine-hydrazone). Levels of oxidized proteins of molecular weights 51, 57, 62, and 70 kDa increased in a dose-dependent manner with Cl_2 concentration. These findings suggest that Cl_2 exposure causes oxidative and nitrosative stress in association with leading to airway epithelial damage.

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This special supplement of the *American Journal of Respiratory and Critical Care Medicine* contains abstracts of the scientific papers to be presented at the 2001 International Conference. The abstracts appear in order of presentation, from Sunday, May 20 through Wednesday, May 23 and are identified by session code numbers. To assist in planning a personal schedule at the Conference, the time and place of each presentation is also provided.