ENVIRONMENTAL ASBESTOS AND INCIDENT MESOTHELIOMA: A CANCER REGISTRY-BASED CASE-CONTROL STUDY IN CALIFORNIA

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To explore the role of exposure to environmental asbestos on the risk of mesothelioma in California, 2908 incident mesothelioma cases 40 years old and over were obtained from California Cancer Registry from 1988 to 1997. Age- and sex-matched (frequency-matching) controls (n=2908) were selected by stratified random sampling from 28123 pancreatic cancer cases in the same time period. 95% of subjects were geocoded at house level and 5% at street or zipcode level. Exposure to environmental asbestos was estimated using the distance from subjects' homes at diagnosis to the nearest asbestos deposits in California. Exposure to occupational asbestos was derived by data on longest held occupation, available for 62% of subjects. Occupational asbestos exposure was determined by *a priori* classification and confirmed by their association with mesothelioma. High asbestos exposure occupations including shipyard. plumber, pipe and steam fitter, insulator, sheet metal worker, boilermaker, and plasterer (OR=10.3, 95%CI:2.2,14.6). Logistic regression analysis showed that there is a significant association between distance(km) to the nearest asbestos deposits and mesothelioma. The odds ratio of square root of distance is 0.97, 95%CI:0.96, 0.98) adjusted by age, sex and occupational exposure. These data support an association of environmental asbestos and mesothelioma but are limited by lack of environmental exposure validation and missing occupational data.

NCI: IR03CA81615-01
This abstract is funded by:

THE IMPACT OF AVIAN-ZOONOSES ON THE DEVELOPMENT OF PIGEON BREEDERS HYPERSENSITIVITY PNEUMONITIS

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Background: Factors determining clinical susceptibility to Hypersensitivity Pneumonitis(HP) after avian exposure remain unclear. Pro-inflammatory or adjuvant potential of avian-acquired infections to cause HP was examined. **Methods:** Volunteer pigeon breeders with and without symptomatic HP were selected. Blood samples were tested for antibody against avian infectious agents: bacterial endo- and exo-toxin (LPS and tetanus), viral and chlamydial antigens, feather-mites and lymphocyte responsiveness to avian TB. **Results:** Antibodies to routine respiratory viruses were increased and lymphocyte responses to TB were reduced in those with HP. Anti-chlamydial antibody was common among pigeon breeders but antibody activity to bacterial endotoxin and exotoxin was no different from normal. Feather mite-specific IgE activity was associated with symptoms of immediate hypersensitivity but not with HP. **Conclusions :** Pigeon breeders had extensive immunological evidence of avian acquired infection. The association of HP with multiple respiratory viral sensitisation is likely to reflect an anamnestic response rather than a specific pro-inflammatory effect of one particular virus. The reduced response to avian TB suggests than a putative adjuvant effect from this organism is unrelated to the onset or maintenance of HP. However, this reciprocal association may reflect immunological polarisation of responses. Despite extensive exposure to endotoxin-rich excreta in the pigeon loft environment, antibody titres to this and to tetanus were normal.

This abstract is funded by: British Pigeon Fanciers medical Research Trust

EFFECTS OF CIGARETTE SMOKING ON CLINICAL TESTS FOR HYPERSENSITIVITY PNEUMONITIS ASSOCIATED WITH METALWORKING.

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We have described results of the clinical approach, case finding, and evaluation of patients in the largest known outbreak of hypersensitivity pneumonitis (HP) in metalworkers (Hodgson et al, 2001). Here, we report findings from a chart review of the 61 patients from the outbreak, regarding the effects of smoking status on the results of clinical tests used to identify HP. The results suggest that a history of cigarette smoking exerts complex effects on these tests. Actively smoking patients with HP were less likely than non-smokers to develop dry crackles in the lungs, elevated ESRs, and restrictive spirometry patterns. Current and ex-smokers were more likely to have abnormal gallium scans and chest x-rays/CT scans than non-smokers. Smoking habits had little effect on corrected DLco (diffusion capacity) or alveolar-arterial oxygen gradients in patients with HP. It is thus possible that smoking may affect physical exam findings, spirometry, ESR and serologic changes associated hypersensitivity pneumonitis, so as to obscure the diagnosis, and thus may contribute to the generally reported finding that HP occurs more frequently in non-smokers than smokers. Additionally, our data also suggests that ex-smokers, with or without HP can have positive gallium scans, and ex-smokers with HP can have normalized ESRs, for at least several years after quitting cigarette smoking.

This abstract is funded by:

RESIDUAL ADDITIVES PLAY AN IMPORTANT ROLE IN THE CYTOTOXICITY AND INFLAMMATORY RESPONSES CAUSED BY POLYVINYL CHLORIDE (PVC) PARTICLES IN LUNG CELLS

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Occupational exposure to PVC dust has been linked to pulmonary disease. Our aim was to investigate, in vitro, the role of additives in the cytotoxicity and the release of inflammatory mediators caused by PVC particles in lung cells.

We compared two types of emulsion PVC particles (E3 and E8) to their "additive-free" counterparts (W3 and W8). A positive control (crystalline SiO_2, MIN-U-SIL) and the pure additives, sodium lauryl sulfate (A3) and sodium alkylbenzenesulfonate (A8), were tested concurrently. Cytotoxicity (MTT test after 24h) was assessed in the A549 cell line, primary cultures of rat alveolar macrophages and type II pneumocytes. Hemolytic potential was assessed after 2h incubation with human erythrocytes. Production of IL-8 and IL-6 by A549 cells was measured by ELISA at 4, 16, 24 and 48h after exposure.

Cytotoxicity and hemolytic activity of the washed particles were abolished or markedly decreased compared to their non-washed forms. In A549 cells, E3 and E8 (2.5 mg/ml) caused a 3-fold increase in IL-8 release and a more than 10-fold increase in IL-6 release, whereas W3 and W8 did not elicit any significant response at similar concentrations. Compared to MIN-U-SIL (0.1, 0.5 and 2.5 mg/ml), the response to E3 and E8 occurred later and was slightly lower (IL-8) or much more pronounced (IL-6). A3 and A8 exhibited similar responses as E3 and E8, at concentrations corresponding to those present in the particles.

In conclusion, the cytotoxicity and inflammatory potential of some PVC particles appear to be mostly due to their residual additives.

This abstract is funded by: APME (Association of Plastics Manufacturers Europe)

TUMOR NECROSIS FACTOR ALFA GENE EXPRESSION IN HUMAN MONOCYTIC THP-1 CELLS EXPOSED TO PIGEON DROPPING EXTRACTS.

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Bird fanciers lung (BFL) is an immunologically induced granulomatous lung disease caused by inhalation of bird-related antigens. These antigens include immunoglobulins, such as IgA and degraded IgA, and intestinal mucin present in bird droppings. Tumor necrosis factor-α (TNF-α) is an inflammatory cytokine produced mainly by monocytic cells and macrophages, and has many regulatory functions in inflammation. In the present study, human monocytic cells (THP-1) were cultured and exposed to pigeon dropping extracts (PDE). We performed realtime polymerase chain reaction (PCR) analysis to quantify the TNF-α m-RNA expression, and measured the concentration of TNF-α in the culture media by ELISA. PDE-exposed cells showed an enhanced expression of TNF-α m-RNA associated with an increase of TNF-α production. Then we examined the involvement of NFκB in the up-regulation of TNF-α. NFκB was activated in THP-1 cells after exposure to PDE. We conclude that PDE directly stimulate human monocytic cells to produce TNF-α, which maybe important in the development of BFL.

FILM QUALITY IN CHEST X-RAY SCREENING FOR PNEUMOCONIOSIS.

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Chest X-ray (CXR) screening can identify workers affected by job exposures, and can help guide preventive interventions. We investigated film quality, a key element in effective screening, for CXRs received from October 1, 2000, to September 30, 2001, under the U.S. National Coal Workers' X-ray Surveillance Program (CWXSP). The study included 7,018 CXRs from 88 NIOSH-approved facilities, and 14,731 independent readings of these CXRs, based on the 1980 ILO Classification System, by 92 NIOSH-certified readers (25 'A' and 67 'B'). During each reading, film quality was graded 1 - Good (n=11,102, 75.4%), 2 - Acceptable (n=2601, 17.7%), 3 - Poor (n= 922, 6.3%), and 4 - Unacceptable (106, 0.7%). Frequently recorded film defects included underexposure (27%), improper positioning (19%), and overexposure (17%). For the same CXRs, 'B' readers tended to grade film quality more severely than 'A' readers. Only 13 films (0.2%) were considered unreadable (i.e. Grade 4 by 2 readers), but 950 films (13.5%) were considered of Lower Quality (i.e. Grade 3 or 4 noted by ≥ 1 reader). Among 11 facilities submitting at least 100 CXRs, Lower Quality films were significantly (P<0.0001) more frequent for two facilities and less frequent for three. Overall, quality for mobile X-ray vans was similar to fixed facilities, but particular fixed and mobile facilities were much more likely to submit films with specific defects. Certain quality defects appeared to influence the final pneumoconiosis classifications. These results suggest that occupational CXR screening programs that do not already do so may benefit from efforts to monitor and improve film quality.

This abstract is funded by: Funded by NIOSH

AMERICAN JOURNAL OF

Respiratory and Critical Care Medicine

ISSN 1073-449X

SUPPLEMENT

April 2002 Volume 165 Number 8

AMERICAN THORACIC SOCIETY

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