THE EXPRESSION OF INTEGRIN αVβ6 IN A HETEROTOPIC TRACHEAL MODEL OF ALLOGRAFT REJECTION

A. Dosanjh, T. Ikonen and H. Alho. Scripps Research Institute,Stanford University, CA and University of Helsinki, Finland

Obliterative bronchiolitis (OB) is the major cause of morbidity and mortality after lung transplantation. One initiating event in the development of obliteration of the airway lumen is epithelial injury. In isografts, there is initial ischemic injury and denudation of the epithelium with eventual re-epithelialization and patency of the airway lumen. Allografts in contrast, do not recover epithelium and the airway lumen becomes obliterated. We hypothesized that since integrin αVβ6 is expressed in healing epithelium, that integrin αVβ6 would be expressed in isografts, but not in allografts. **Methods:**Using a rat tracheal allograft rejection model as a source of 4-5 micron tissue sections, we compared integrin staining in allografts vs. isografts from six animals at post-transplant days 3,7 and 10. The sections were analyzed by immunohistochemistry after incubation with a specific monoclonal antibody E7P6 against integrin αVβ6, by methods previously described *(ref: Wang et al, AJRCMB, 15, 664-672,1996)*. Negative control slides were processed identically except that primary antibody was omitted. A positive control of normal rat lung tissue was used.**Results:**The sections from the healing re-epithelializing isografts showed intense staining using the antibody recognizing integrin αVβ6, compared to the allografts studied. Day 3 isografts and allografts demonstrated low level staining, whereas by day 10 the epithelial expression of αVβ6 in the isografts was strong and that in allografts was weak. Baseline expression of αVβ6 was observed in the positive controls.**Conclusions**: Integrin αVβ6 is readily detectable in healing isografts. Integrin αVβ6 may be crucial in the maintenance of a viable epithelial cell layer which is related to preventing obliteration of the airway in OB.This abstract was funded by: Novartis

SEVERE REFLUX IS ASSOCIATED WITH REDUCED GAS TRANSFER

Linda M Schachter [1], John Dixon[2], Paul O'Brien[2], Robert J Pierce[1]
[1]Department of Respiratory Medicine, Austin & Repatriation Medical Centre, [2]Department of Surgery, Monash Medical Centre, Victoria, Australia

To assess whether severe gastro oesophageal reflux (GER) is associated with changes in lung function including gas transfer. Methods: 147 patients with severe obesity (BMI range 31.7 – 70 kg/m^2) presenting for obesity surgery were sequentially recruited preoperatively from a surgical weight loss clinic. A history of frequency and severity of symptoms of GER, investigations and medications for GER were obtained. A history of lung disease, sleep disordered breathing and smoking history was also obtained. Lung function testing was performed using a Vmax system including spirometry, lung volumes and gas transfer. Results: After adjusting for age, gender, BMI and smoking history, patients with severe GER had a reduced gas transfer as measured by DLCO 21.1 (18.9, 23.2) than those with no GER 26.3 (24.4, 28.2) p=0.001. DLCO/VA was also reduced in the group with severe GER 4.6(4.3,4.9) compared to the group with no GER 5.3 (5.1, 5.5) p=0.001. There was no significant difference in other measures of lung function including airway obstruction, restriction or gas trapping. Conclusion: Severe GER was associated with a reduction in gas transfer. This may be due to microaspiration or ventilation perfusion mismatch. More focus must be placed on GER as a potential cause for lung disease or a potential exacerbating factor in pre-existing lung disease.

Department of Respiratory Med, Austin & Repatriation Medical Centre

This abstract is funded by:

GENETIC POLYMORPHISM OF *XRCC1* AND LUNG CANCER RISK AMONG AFRICAN-AMERICANS AND CAUCASIANS

Gloria L. David-Beabes and Stephanie J. London

Epidemiology Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709, USA

RATIONALE: Reduced DNA repair capacity has been suggested as a risk factor for lung cancer. XRCC1 plays an important role in base excision repair and in rejoining DNA strand breaks. Two relatively common polymorphisms of the *XRCC1* gene that induce amino acid changes in codon 194 (exon 6) and codon 399 (exon 10) have been described. METHODS: We examined the relation between these two polymorphisms and susceptibility to lung cancer among 331 incident cases and 690 population controls of African-American and Caucasian ethnicity in Los Angeles County, California using a multiplex PCR-RFLP technique. RESULTS: African-Americans carrying at least one variant allele for codon 194 were at statistically significantly decreased risk of lung cancer (OR, 0.40; 95% CI, 0.19-0.87). No comparable association was seen among Caucasians. For the codon 399 polymorphism, we found a decreased risk of lung cancer, although not statistically significant, among subjects homozygous for the variant allele. CONCLUSION: These results suggest that genetic variation of *XRCC1* may partially underlie interindividual variability in the susceptibility to environmental lung carcinogens.

This abstract is funded by: National Institute of Environmental Health Sciences

A case control study of lung cancer among European rock/slag wool production workers

Kjaerheim K[1,2], Boffetta P[1], Andersen A[2], Chang-Claude J[3], Cherrie J[4], Hansen J[5], Olsen J[5], Plato N[6], Saracci R[1] & Westerholm P[7]

Rationale To investigate the risk of lung cancer associated with exposure to man-made mineral fibres (MMVF) while controlling for other occupational exposures and tobacco smoking.

Methods Workers in seven production plants in Denmark, Norway, Sweden, and Germany were included. Information was obtained for 133 cases and 513 matched controls. Occupational exposure was assessed based on the interview data combined with information from expert panels set up in each factory. Analysis was done using conditional logistic regression models.

Results For cumulative exposure to MMVF assessed with a 15-year lag, the smoking adjusted odds ratios (ORs) in the second to fourth quartile of exposure were 1.25 (95% confidence interval (CI) 0.66-2.34), 1.02 (CI 0.54-1.93), and 0.67 (CI 0.35-1.27). Similar results were obtained when only workers employed for more than one year were included, with other indicators of MMVF exposure, and with control for coexposures.

Conclusions The study provided no evidence of a carcinogenic effect of MMVF on the lung under exposure circumstances as exprienced in the production industry during the last four decades.

[1] International Agency for Research on Cancer, France, [2] Cancer Registry of Norway, Norway, [3] German Cancer Research Center, Germany, [4] Institute of Occupational Medicine, Scotland, [5] Danish Cancer Society, Denmark, [6] Department of Occupational Health, Karolinska Hospital, Sweden, [7] National institute for Working Life, Sweden

This abstract is funded by: The Joint European Medical Research Board (in part)

HISTORICAL ESTIMATION OF DIESEL EXHAUST EXPOSURE IN A COHORT STUDY OF RAILROAD WORKERS AND LUNG CANCER.

F. Laden, A Eschenroeder, TJ Smith, D Gagnon, SL Jackson, DW Dockery, FE Speizer. E Garshick. Channing Laboratory, Brigham & Women's Hospital, Harvard Medical School; Harvard School of Public Health; VA Boston Healthcare System, Boston MA, USA.

Rationale: Although 95% of the locomotives in service in the US railroad industry were diesel by 1959, individual railroads transitioned from steam to diesel at different rates from 1945 to 1959. We hypothesize that accounting for these differences when modeling exposure will help characterize lung cancer risk attributable to diesel exhaust exposure in a cohort of 55,407 workers employed during this period and followed through 1996. Methods: We estimated the percent of diesel locomotives for each for the 95 largest railroads (93% of the cohort) using roster information and manufacturing data, and accounted for locomotive model using EPA emission factors and builder data. The railroad-specific diesel locomotive fraction for a given year was calculated, representing the probability of exposure in a specific year. Cumulative exposure (pre-1959) was defined for engineers/firemen and conductors/ brakemen as the sum of the diesel fraction from 1945 to 1959. Results: The median diesel fraction was 8% in 1945 and 72% in 1952, the midpoint of the transition period. Rates of change from 25 to 75% diesel ranged from 1 to 12 years. The median adjusted cumulative exposure was 9.6 years (interquartile range 8.6-10.3). In analyses comparing each quartile of exposure with unexposed, the relative risks (RR) for the first three quartiles were all approximately 1.30, similar to the RR when exposure was modeled as a dichotomous variable (1.34). The RR for the fourth quartile was 1.43 (CI:1.30-1.59). Conclusion: There was little variation in cumulative probability of pre-1959 exposure to diesel exhaust. Therefore, adjustment for railroad-specific rates of dieselization had little effect on lung cancer associations.

This abstract is funded by: NCI R01 CA 79725-01A1 and NIOSH R01 CCR115818-02

AMERICAN JOURNAL OF

Respiratory and Critical Care Medicine

ISSN 1073–449X

SUPPLEMENT

April 2001 Volume 163 Number 5, Part 2

AMERICAN THORACIC SOCIETY

ABSTRACTS

2001 International Conference

May 18–23, 2001 • San Francisco, California

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.