RETROSPECTIVE COHORT STUDY OF DIESEL EXHAUST EXPOSURE AND LUNG CANCER IN US RAILROAD WORKERS: MORTALITY UPDATE 1959-1996. E. Garshick, F Laden, TJ Smith, D Gagnon, SL Jackson, DW Dockery, FE Speizer. VA Boston Healthcare System; Channing Laboratory, Brigham and Women's Hospital; Harvard School of Public Health; Massachusetts Veterans Epidemiology and Research Center, Harvard Medical School, Boston, MA, USA.

RATIONALE: Studies of diesel exhaust exposure and lung cancer have been limited by a short duration of follow-up. Most US railroad diesel exhaust exposure started during the 1950's (95% diesel by 1959). Lung cancer mortality was previously assessed through 1976 in 55,407 US railroad workers aged 40-64 in 1959. Here we assess mortality through 1996. METHODS: The US Railroad Retirement Board (RRB) provided work history for 54,974 (99.2%) workers. Mortality was assessed using RRB, Social Security, and Health Care Financing Administration sources. Cause of death was obtained from death certificates and the National Death Index. Proportional hazard methods were used to assess mortality. Job code in 1959 was used as an exposure index since railroad jobs are stable. RESULTS: There were 43,600 deaths overall; 4,277 from lung cancer. Adjusting for age, workers aged 40-44 in a diesel exhaust exposed job in 1959 (workers with greatest duration of exposure) had an elevated relative risk (RR; 95%CI) of lung cancer mortality of 1.36 (1.19-1.55). Workers aged 45-49, 50-54, 55-59 also had an elevated RR (1.23, 1.22, 1.32, respectively), whereas the RR in the oldest workers (60-64) was not elevated. Workers on operating trains had the greatest RR. CONCLUSIONS: Workers aged 40-59 in diesel exhaust exposed jobs in 1959 had an increased risk of dying of lung cancer. Although the age group with the longest exposures after 1959 had an elevated risk, risk was also elevated in other workers. Occupational exposures to diesel exhaust and other inhaled particles in the 1940's to 1960's may be contributors to lung cancer mortality in this cohort.

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ENVIRONMENTAL ASBESTOS AND MESOTHELIOMA IN CALIFORNIA

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All 2949 incident mesothelioma cases with census tract information during the period 1988-1997 were obtained from the Calif. Cancer Registry. The digital map of ultramafic rocks in Calif. that are the principal source of asbestos in the environment was obtained from the Calif. Dept. of Conservation, Div. of Mines and Geology. Exact residential addresses at diagnosis for 2737 (93%) of cases were available and were matched to a unique intersection. 204(7%) of cases only had PO Box matched to a 5-digit zip vicinity. Mesothelioma cases were geocoded on the Calif. state map and assigned to census tracts. Mesothelioma cases were reported from 2061/5859 (35%) of census tracts. Ten-year census tract-specific incidences of mesothelioma ranged from 0 to $660/10^5$. Many cases were located in cities near the West Coast or along rivers in Calif., most likely reflecting occupational asbestos exposure. Ten-year age-adjusted mesothelioma incidences within asbestos deposits and their buffers (1 to 10 km around asbestos deposits with an interval of 1 km) were evaluated. The incidences in 4- to 8-km buffers were, 15.5(P=0.08), 17.6(P<0.01), 17.6(P<0.01), 16.7(P=0.03), 18.9(P<0.01)/10^5 respectively, significantly higher than the incidence ($12.7/10^5$) in Calif. while the incidences in asbestos deposits and 10-km buffers were lower. There was no evidence of a dose-response between mesothelioma incidences and the distances from asbestos deposits and their buffers. Similar results were showed when coastal counties with a higher incidence were excluded. Occupational exposure to asbestos is a dominant determinant for occurrence of mesothelioma. The relation between environmental asbestos and mesothelioma must be assessed based on more detailed information such as histories of occupational exposure and residence, population change and residence history of asbestos workers.

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Malignant pleural mesothelioma: epidemiologic study from 1996 to 1999 in the Province of La Spezia.

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Introduction: Malignant Pleural Mesothelioma (MPM) is a rare pleural tumor, frequently associated to asbestos exposure. **Aim of the study**: to evaluate the incidence of MPMs in the Province of La Spezia in a period of time (January 96-December 99) and focus on the percentage of MPMs occuring in subjects with occupational exposure to asbestos. **Methods**: MPMs were collected by Register Malignant Mesothelioma (REMM) in Liguria Discrict. The data regarding the environmental, occupational or domestic exposure to asbestos were achieved by means of a specific questionnaire from REMM. **Results**: From January 96 to December 99, 97 MPMs were found: 88 males and 9 females (mean age: 71 years, range 43-91 yrs), with the incidence rate by 24 per 100000 in males. The most part of MPM (67%) was found and followed by Department of Pneumology in La Spezia. 92% of all subjects showed an exposure to asbestos (85% occupational exposure). The more frequent occupational exposure was represented by shipyards (51%), sea transport (15%) and finally building trade (10%). **Conclusions**: High rate of MPMs with significant prevalence in the males occurs in the Province of La Spezia. The incidence rate by REMM is higher than that by world register. The highest percentage of MPMs associated to occupational exposure to asbestos in the Province of La Spezia occurs in an urban area where for many years several industrial activities have widely used asbestos, in particularly shipyards showing an important role both because of the exposure intensity and the number of subjects involved in different occupational duties.

QUALITY OF SMOKING INFORMATION FOR OCCUPATIONAL CANCER EPIDEMIOLOGY IN MEDICAL RECORDS IN A HOSPITAL IN ONTARIO

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Objective: To determine the proportion of records in lung and colon cancer patients with information on: smoking status (current/ex/never), lifetime dose, tobacco type.

Rationale: Data on smoking are important for nested case control studies of occupational respiratory diseases, especially cancer. Studies to date have surveyed subjects or proxy respondents, but there are disadvantages which include recall biases and imprecision, and the potential to elicit distress through proxy respondents. Information gathered during hospitalization may be less subject to recall errors and therefore provide better quality. However, a literature review did not reveal the accuracy or completeness of hospital data.

Methods: From the Princess Margaret Hospital Cancer Registry data base, 15 patients with lung cancer and 15 with colon cancer were randomly selected from each 5 years interval from 1965-94. We examined the records for data on smoking habits; dose was determined from the data including age started/stopped, duration, and daily amount. Gender and age were also noted.

Results: 180 charts were analyzed: 108 male, 72 female; mean age 62.3 years. For lung cancer, the proportion of charts with data on smoking status, dose and type were 95.5% 91.4%, 97.5%, respectively. For colon cancer these proportions were 62.2%, 51.8%, and 53.6%. For both cancer types, completeness improved in more recent records.

Conclusion: Smoking data appear to be adequately completed for lung cancer records; for one other cancer site, e.g. colon cancer, the data are less complete probably because treating physicians put a greater emphasis on getting smoking information from patients with respiratory diseases.

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P53 mRNA EXPRESSION AND MUTATIONS IN P53 GENE IN MICE WITH SILICOSIS.

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Although epidemiological study reported that the onset of silicosis conferred a significant increase in the risk of subsequent lung cancer. The role of silicosis as either a necessary or incidental condition in silica associated lung cancer is not fully elucidated. The aim of this project is to study the modulation of p53 tumor suppresser gene as the greatest risk factor for lung cancer in mice with silicosis.

Five weeks old Male C57 BL/6N mice, received a single intratracheal injection of 5 micron crystalline silica at a dose of 2 mg/mouse. At 3.5, 7.5 and 14.5 M after treatment, mice were sacrificed. Expression of p53 mRNA and mutation of p53 gene in the lung tissue studied by RT-PCR and SSCP analysis methods respectively.

Localized silicotic lesions were found in all of mice injected with silica, but not tumor lesion was found in the lung. Expression of p53 mRNA did not change at 3.5 and 7.5 M, but it decreased significantly at 14.5 M compared with corresponding control mice. Expression of p21 mRNA in the lung was not different between normal and silicotic mice at 14.5 M. There was no mutation of p53 gene in mice with silicosis compared with control mice at 14.5 M.

These data indicate that diminution of host resistance associated with down regulation of p53 rather than its mutation is relevant to the relationship between silicosis and lung cancer in aging mice.

*: p<0.05 vs 14M Normal group

Expression of p53 and p21 mRNA in the lung

	Control mice		Silicotic mice	
	3.5M(n=5)	14.5M(n=5)	3.5M (n=5)	14.5M(n=5)
p53	1.34±0.3	1.21±0.18	1.11±0.29	0.81±0.10*
p21	0.89±0.34	1.26±0.17	0.94±0.34	1.04±0.10
p53/p21	1.68±0.56	0.96±0.02	1.22±0.17	0.78±0.09

PARTICLE OVERLOAD ASSOCIATED EFFECTS OF CARBON BLACK IN THE MOUSE LUNG.

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Inhaled carbon black (CB) particles induce overload-associated lung tumors in rats at high inhaled concentrations, but not in mice or hamsters. The key to this specificity in response may lie in species-dependent progression of lung inflammation via the activity of pro- and anti-inflammatory mediators. In order to investigate particle dose-related lung inflammation and its persistence, female $B_6C_3F_1$ mice were exposed to CB (1, 7, 50 mg/m^3) for 13 weeks; groups of mice were euthanized at intervals during and after exposure. There was a dose-related increase in lung CB burden during the exposure phase and the particles were more persistently retained in the lung after exposure in the 7 and 50 mg/m^3 groups than in the low dose group. The total cell number in lavage fluid increased in mice exposed to 7 and 50 mg/m^3 CB; the magnitude of this increase was greater 3 months after exposure as compared to the end of exposure. At the end of the exposure, the percentage of neutrophils (PMNs) in lavage fluid was similar in the 7 and 50 mg/m^3 groups; after 3 months of recovery, the percentage was slightly lower in the high-dose group. The absolute number of PMNs, however, was 2-3x higher in the high-dose group at both time points. Biochemical indices of inflammation were also increased in the mid- and high-dose groups, but were higher at the end of exposure than after 3 months of recovery. This study indicates that no adverse effects were observed in mice exposed to 1 mg/m^3 CB. Furthermore, the results indicate that high concentrations of inhaled particles lead to persistent inflammation and are consistent with observations from similarly-exposed rats.

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ABSTRACTS

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