CANCER RISK FROM DIESEL EXHAUST: EVIDENCE FROM DIESEL-EXPOSED WORKERS

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The assessment of the health risks from exposure to diesel exhaust has relied on toxicological studies, and on epidemiological studies of health effects in workers exposed to diesel exhaust. Although a variety of health effects have been investigated, the focus of most research and risk assessments has been on cancer, with a particular emphasis on lung cancer. Toxicology studies have found evidence of increased lung cancer in rats at high levels of exposure, most likely due to a biological mechanism related to the inability of the rat lung to clear high doses of particles. This leaves open the question of whether humans, exposed at lower levels, might still be subject to increased risk based on a different, perhaps genotoxic, mechanism related to the chemicals adsorbed on diesel particulate matter.

In 1995, the Health Effects Institute published *Diesel Exhaust: A Critical Analysis of Emissions, Exposure, and Health Effects,* which summarized and analyzed the toxicologic and epidemiologic research on diesel exhaust. In January, 1996, HEI sponsored, along with the California Environmental Protection Agency, U.S. EPA, World Health Organization, and National Institute of Occupational Safety and Health, a public workshop on the use of diesel epidemiologic data in risk assessment. The following summarizes the results of the HEI review, and places it in the context of the workshop's discussions, and of recent developments on the use of epidemiology studies of diesel exhaust in risk assessment.

OCCUPATIONAL STUDIES

To date, over thirty epidemiological studies have investigated the relative risk of lung and other cancers among railroad workers, truckers, dock workers, and others. These studies have focused exclusively on male workers exposed to diesel emissions after 1950, when these industries widely converted to diesel engines. Two types of studies have been conducted: (1) studies of occupational cohorts exposed to relatively high concentrations of diesel emissions, and (2) studies that used interviews or questionnaires to identify individuals from the general population who had received occupational exposures to diesel exhaust. The occupational cohorts studied most extensively include railroad, dock, trucking industry, and bus garage workers. Underground miners are also exposed to diesel exhaust; however, they have not historically been targeted for epidemiologic studies of diesel emissions because they are often exposed to other pollutants such as radon, asbestos, dust, and metals. (A long-delayed study of miners is just now beginning to get underway). No data are available on the effects of diesel exposure on women, children, or individuals with cardiovascular or respiratory disease.

The results of the occupational cohort and case-control studies of diesel exhaust, especially those published in the last fifteen years, are generally consistent in showing a weak association between exposure to diesel exhaust and lung cancer. They suggest that prolonged exposure to diesel exhaust over many years is associated with a 1.2 to 1.5 times increase in the relative risk of lung cancer incidence or mortality in workers. Figures 1 and 2 summarize the relative risks and confidence intervals for railroad workers and truckers respectively. In all studies, the incidence rate for lung cancer was higher in workers classified as "exposed to diesel exhaust" than in workers classified as "unexposed." However, as illustrated in Figures 1 and 2, the increase in the relative risk of lung cancer was generally small, and many of the

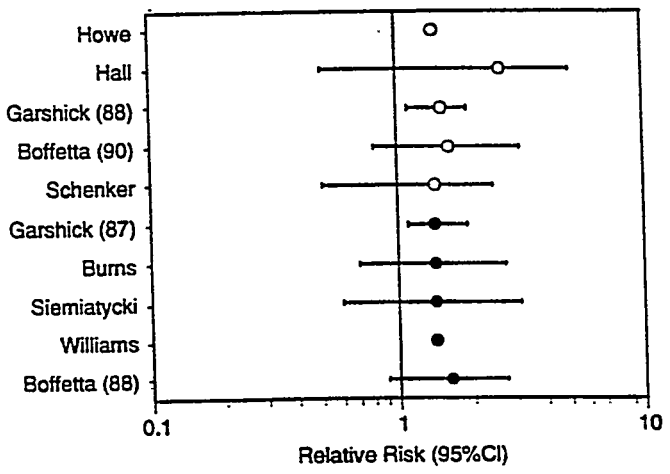

Figure 1. Lung cancer and exposure to diesel exhaust in railroad workers. ● = RR adjusted for cigarette smoking; ○ = RR not adjusted for cigarette smoking. For the two studies by Howe and Williams, CIs were not reported and could not be calculated.

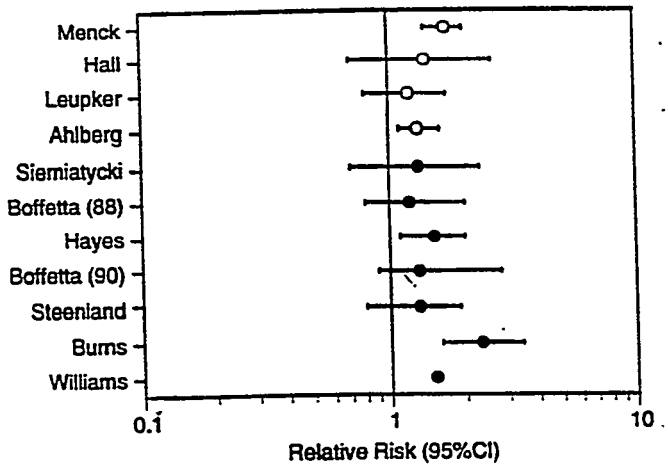

Figure 2. Lung cancer and exposure to diesel exhaust in truck drivers. ● = RR adjusted for cigarette smoking; ○ = RR not adjusted for cigarette smoking. For the study by Williams, CIs were not reported and could not be calculated. For the Steenland study, the data were gathered from union reports of long-haul truckers; for the Boffetta (1988) study, the data were self-reported by diesel truck drivers; and for the Siemiatycki study, they were self-reported by heavy-duty truck drivers (personal communication).

measurements were imprecise; thus the results of most of the studies were not statistically significant. However, the results of the studies with larger populations were statistically significant, which increases confidence in interpreting the positive lung cancer data in occupational cohorts. Moreover, in some of the studies, the largest relative risks were seen in the categories expected to have the greatest cumulative exposure to diesel exhaust (Garshick et al. 1987,1988; Gustavsson, et al. 1990; Steenland et al. 1992, Emmelin et al. 1993). The general population studies also indicate small elevations in lung cancer rates among workers in similar occupational groups such as truckers, railroad workers , mechanics, and dock workers; however, these estimates are based on small numbers of exposed subjects.

In addition to lung cancer, some epidemiologic studies suggest that an elevated risk of bladder cancer may be linked to diesel exhaust exposure in occupational settings. The evidence for bladder cancer, however, is not as consistent as that for lung cancer.

LIMITATIONS

The epidemiologic studies of diesel exhaust have been criticized on two fronts. First, many of the studies did not control for possible confounding factors which might also be linked to elevated lung cancer, such as cigarette smoking, environmental tobacco smoke, nondiesel particulate matter, diet, socioeconomic factors, or exposures to other air pollutants. Controlling for such factors is a common methodologic challenge for epidemiologists. Cigarette smoking is particularly important because it is the dominant cause of lung cancer, and failure to control for its effects can seriously compromise any epidemiologic study of lung cancer risks. An analysis by Cohen and Higgins (Health Effects Institute, 1995) indicates that controlling for smoking, which reduces the risks in some studies, could not fully explain the associations between exposure to diesel exhaust and lung cancer. Also, when Cohen and Higgins estimated the impact of hypothetical differences in cigarette smoking prevalence on the lung cancer rates observed in two studies of emissions that did not control for smoking, their estimate supports the idea that cigarette smoking cannot fully explain the observed increases in lung cancer in railroad workers (Garshick, et al. 1987) or

bus garage workers (Gustavsson et al. 1990).

Only a few epidemiological studies considered other potential confounders such as asbestos exposure, environmental tobacco smoke, diet, and socioeconomic factors. No study has addressed possible confounding due to exposure to nondiesel particles, which are possibly important in light of recent animal studies that demonstrate that, at high concentrations, many poorly soluble particles cause lung tumors in rats.

The second criticism of the epidemiologic studies of diesel exhaust is that none included measurements of any constituent of diesel emissions during the time the study population was actually exposed. Instead, exposure classification was based on self-reported work histories or company records and on the investigator's or the industrial hygienists' opinions about whether the reported job or occupation entailed exposure to diesel exhaust. Although these approaches are probably sensitive to diesel exhaust exposure (i.e. they tend to identify most truly exposed subjects), they are not specific (i.e., they tend to classify some unexposed subjects as exposed). Misclassification of exposures can cause spurious increases or decreases in estimates of effects depending on whether the misclassification differs between subjects with and without disease.

Another complicating factor is that the diesel exhaust to which the populations were actually exposed were never fully characterized. This information gap cannot be filled by using later characterizations of diesel exhaust because the characteristics of emissions depend greatly on factors such as the type of engine, how it is operated ; and the specific fuel used. For example, diesel fuel for locomotives has a higher content of aromatic hydrocarbons than the diesel fuel used in truck engines (Sawyer and Johnson, in Health Effects Institute, 1995). Therefore, the PAH content of locomotive exhaust is probably higher than that of exhaust from trucks and other diesel engines that use diesel fuels - a factor that needs to be considered if data obtained in railroad worker studies are extrapolated to the general population. Furthermore, both the particulate and the PAH content of diesel emissions have decreased dramatically over the last two decades. Therefore, large uncertainties are associated with applying emissions or exposure data from one type of engine during a specific time period to risk assessments for other populations and time periods. These uncertainties limit the use of the epidemiologic data for quantitative risk assessments.

HEI CONCLUSIONS

Based on its review of the epidemiologic and exposure data, HEI drew the following conclusions about the epidemiologic data:

- The epidemiologic data show that long-term exposure to diesel exhaust in a variety of occupations is associated with small increases (in the 1.2 - 1.5-fold range) in the relative risk of lung cancer occurrence, or mortality, or both. The epidemiologic studies are consistent in showing weak associations between exposure to diesel exhaust and lung cancer, but vary in the strength of the statistical association; only a few studies showed relative risks that were statistically significant.

- The absence of exposure measurements in the study populations is the main methodologic problem limiting interpretation of the epidemiologic data and its use in quantitative risk assessments. None of the published studies measured actual levels of exposure to diesel exhaust or characterized the actual emissions from the exposure source.

- The issue of confounding is difficult to assess. Cigarette smoke is a major potential confounder in lung cancer studies. Most studies that controlled for cigarette smoking found that the association of lung cancer with exposure to diesel

exhaust persisted after such controls were applied, although in some cases the risks were lower. Only a few epidemiologic studies considered other potential confounders such as nondiesel particles, environmental tobacco smoke, asbestos exposure,, diet, and socioeconomic factors. At present there is insufficient evidence to conclude whether confounding by these factors influenced the results.

- The above conclusions are based on studies of male workers. None of the epidemiologic studies conducted to date examined the risk of diesel exhaust exposure for women or potentially susceptible populations such as infants, children, or people with health disorders.

WORKER STUDIES AND RISK ASSESSMENT

A variety of State, Federal, and international agencies have considered the question of whether the epidemiologic evidence on diesel exhaust is adequate to support quantitative risk assessment and determinations of whether or not diesel exhaust is a human carcinogen. A summary of those reviews is presented below:

- In 1989, the *International Agency for Research on Cancer* reviewed the data, and concluded that there is "limited human evidence" for carcinogenicity in humans of diesel exhaust. (IARC, 1989)

- In 1994, The *U.S. Environmental Protection Agency*, in its draft risk assessment for diesel, concluded that there was limited evidence for carcinogenicity in humans and that, given conflicting dose/response analyses of the Garshick study, the data was insufficient for quantitative risk assessment (EPA,1994)

- In 1996, the *World Health Organization* concluded that the "results of the available epidemiological studies were considered inadequate for a quantitative estimate of human risk." (IPCS, 1996)

- In 1997, the *California Environmental Protection Agency*, in its draft identification of diesel exhaust as a Toxic Air Contaminant, concluded that a "causal association of diesel exhaust exposure and lung cancer" was "a reasonable and likely explanation for the increased rates of lung cancer observed in the epidemiological studies," and found the data adequate to make a quantitative estimate of cancer risk. (CALEPA, 1997)

SUMMARY

To date, over thirty studies have investigated the relative risk of lung and other cancers among railroad workers, truckers, dock workers, and others. These studies suggest that the risk of lung cancer among workers classified as having been exposed to diesel exhaust is approximately 1.2 to 1.5 times the risk in those workers classified as unexposed. Although the data appear consistent, the association is weakened because the reported effects were small, and the absence of concurrent exposure information limits the interpretation of the epidemiologic studies and the use of these data for quantitative estimates of cancer risk. However, the association of increased lung cancer at levels of exposure which appear to be below those to which animals have been exposed (i.e. 100 μ/m^3 vs. 2,000μ/m^3) suggests that a biological mechanism based on the chemicals carried by diesel exhaust particles cannot be excluded.

In reviewing this data, risk assessment agencies have generally not found that the epidemiologic data are adequate to produce a quantitative estimate of cancer risk for humans exposed to diesel exhaust in ambient settings. The one exception to this is the DRAFT risk assessment produced by the California Environmental Protection Agency, which is currently undergoing public and scientific review.

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