HEALTH EFFECTS OF DIESEL EMISSIONS

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Abstract—We have reviewed the literature relating to the health effects of diesel emissions with particular reference to acute and chronic morbidity and to carcinogenicity. It is apparent that exposure to diesel fumes in sufficient concentrations may lead to eye and nasal irritation but there is no evidence of any permanent effect. A transient decline of ventilatory capacity has been noted following such exposures. There is also some evidence that the chronic inhalation of diesel fumes leads to the development of cough and sputum, that is chronic bronchitis, however, it is usually impossible to show a cause and effect relationship because of the concomitant and confounding exposures to mine dust and cigarette smoke.

Although there have been a number of papers suggesting that diesel fumes may act as an carcinogen, the weight of the evidence is against this hypothesis. Finally, the role of small particles, less than 10 μm, which are frequently present in diesel emissions requires further study since there is some limited evidence that they may be partly responsible for some of the exacerbations of asthma.

INTRODUCTION

The health effects of diesel emissions have received increasing attention over the past few years. A number of studies have been published, some of which purport to show that diesel fumes may induce a variety of conditions including lung cancer, asthma, bronchitis, and other respiratory ailments (Ball, 1984; Higgins, 1984; IARC, 1989; NIOSH, 1988). The design of many of these studies has been flawed and various confounding factors have not been taken into account. There is an urgent need for an objective appraisal of the hazards of diesel emissions, with particular emphasis on their epidemiological aspects. The ensuing review will deal with the following aspects: (i) history and background information, (ii) the effects of diesel fumes on morbidity, (iii) the effects of diesel fumes on mortality, with reference to carcinogenicity.

BACKGROUND

In 1892 Rudolph Diesel, a German engineer developed a new type of engine that differed from the standard gasoline engine which had been introduced 30 yr earlier. This became known as the diesel engine and was capable of spontaneous combustion of liquid fuel without requiring spark ignition. The first prototype exploded small coal dust particles rather than using liquid fuel. It was not until the 1920s that a suitably efficient diesel engine was developed. Shortly thereafter, because of the engines high reliability and because of its use of a less volatile and inflammable fuel, its popularity increased rapidly. The introduction of modern
transmissions, torque converters, rubber tires, and of diesel engines in motor vehicles, led to further improvements in performance. In the late 1950s the diesel engine became the conventional power unit used by U.S. railways and is now also extensively used in Europe. It is also used by the mining industry, in heavy construction machinery, buses, farm equipment, and heavy road vehicles.

While the diesel engine offers an efficient and reliable power source, it emits malodorous irritant fumes, and is generally noisier than its counterparts.

EXPOSURES

Diesel exhaust contains components of complete air and carbon combustion (nitrogen, water, and carbon dioxide), as well as the products of incomplete combustion (carbon monoxide, the oxides of nitrogen, various hydrocarbons, and partially oxidized hydrocarbons such as aldehydes, ketones, phenols, and various sulphur compounds; NIOSH, 1988). When compared with the gasoline engine, diesels produce far less carbon monoxide, but a greater amount of the oxides of nitrogen and aldehydes. The latter are the components of exhaust that can cause morbidity such as irritation of the upper respiratory tract.

Diesel engines also produce submicron particulates that lead to soiling and poor visibility. For the most part, these particles have been felt to pose a minimal health risk, but the presence of mutagens and carcinogens adsorbed on to particulates has generated concern about diesel exhaust and its potential for inducing lung cancer. More recently the possible effects of fine particles below 10 μm on respiratory morbidity and mortality, especially in subjects with established chest disease, has been broached (Department of Health, 1995; Maynard and Waller, 1996).

The National Institute for Occupational Safety and Health (NIOSH) suggested that a potential carcinogenic hazard existed amongst those exposed to diesel exhaust emissions (NIOSH, 1988). The epidemiological evidence cited in support was fragile. In 1989 the International Agency for Research on Cancer (IARC) declared that diesel emissions were probably carcinogenic to humans (Group 2A carcinogen); a pronouncement that suggested there was sufficient evidence of carcinogenicity in experimental animals, but limited evidence of carcinogenicity in humans (IARC, 1989). IARC's use of the term 'limited' suggests some equivocation, and indicates that the available data do not exclude the possibility of chance, bias, or confounding factors being responsible for the positive associations.

NIOSH and IARC have relied almost entirely upon animal experimentation in giving credence to this theory that diesel exhaust is a human carcinogen. That animal experiments may provide a warning of possible carcinogenicity is not disputed, but the presumption that the induction of disease in animals can be equated with human disease is unjustifiable (Morgan, 1979). In the induction of cancer and other chronic diseases such as silicosis and asbestosis, the short life of the animal necessitates exposure to extreme concentrations in order to induce a response during the animal's life time. Such doses overwhelm the defence mechanisms of the animal, but do not remotely resemble the situation that occurs in the worker's occupational environment. Similarly, many animal species have an increased incidence of certain malignant tumors that do not occur in man. The assumption that animal experimentation is applicable to man depends on two highly dubious
presumptions, namely, that the animals' responses to high concentrations bear a relationship to estimated responses from low concentrations, and secondly, the inference that estimated responses to low concentrations in animals also pertains to low concentrations in humans. The leap from extreme exposures in animals to very small exposures in man suggests a dearth of scientific scepticism. The type of statistical analysis may also greatly influence the calculated extent of the risk. Many subscribe to the concept of a linear dose–response relationship. Such an hypothesis is convenient and simple, but not necessarily valid. Similarly, to infer that the line of identity must pass through the zero point is even less justifiable. In many instances, back extrapolation is contrived since it yields neatness and simplicity, but a failure to demonstrate a threshold does not mean that it does not exist. Moreover, a lack of a threshold is generally counter to the principles of biology.

MORBIDITY

Morbidity attributed to diesel exhaust exposure can be divided into acute and chronic effects. Morbidity is best assessed by the presence of respiratory symptoms, lung function and radiographic abnormalities. The administration of questionnaires indicates that high exposures may lead to acute symptoms, primarily affecting the conjunctivae and upper respiratory tract, that are nearly always reversible within a few days. Chronic symptoms such as cough, sputum production, and breathlessness are best determined from responses to the British Medical Research Council Respiratory Disease Questionnaire or its U.S. counterpart (Medical Research Council, Questionnaire on Respiratory Symptoms, 1966; Ferris, 1978).

Changes in ventilatory capacity over a shift may be used to evaluate the effects of the working environment on the lung. Sustained excessive decrements in lung function are a more reliable indicator of occupational illness, providing that confounding factors are excluded or taken into account. The most useful measures of ventilatory capacity are the forced vital capacity (FVC), the forced expiratory volume in one second (FEV₁) and the ratio of the FEV₁ to FVC (FEV₁/FVC).

The occurrence of acute symptoms has been studied in diesel garage workers (El Batawi and Noweir, 1964; Gamble et al., 1987) and in ferry stevedores, however, the latter were exposed to both gasoline and diesel engine exhaust (Purdham et al., 1987). In these studies, at least one or two workers experienced some eye irritation. In a U.S. bus garage, 8 out of 10 workers in the highly exposed group had eye irritation (NO₂ > 0.3 ppm and particulates > 0.3 mg/m³) (Gamble et al., 1987).

Battigelli (1965) measured the severity of eye irritation in volunteers exposed to different levels of diesel exhaust. Exposure for 10 min at a mean concentration of 2.8 ppm of NO₂ produced intolerable irritation in some subjects with the average irritation score being midway between some irritation (threshold) and ‘conspicuous but tolerable’ irritation. Reduction of the NO₂ level to 1.3 ppm was associated with an irritation score below the threshold, while peak irritation was rated as ‘conspicuous but tolerable’.

When NO₂ was used as a surrogate measure of diesel exposure it was found that (Gamble et al., 1987), U.S. bus garage levels were lower (0.3–1 ppm) than those present in Battigelli’s subjects (Battigelli, 1965). Eye irritation was the prevalent symptom amongst bus garage workers exposed to high NO₂ and particulate matter.
Nose irritation, chest tightness and wheezing showed a weaker, but significant relationship to exposure.

Chronic effects have been evaluated in several groups of diesel exposed workers (El Batawi and Noweir, 1964; Gamble et al., 1987; Purdham et al., 1987). Those studied were mainly metal, nonmetal mineral, and coal miners (Attfield et al., 1982; Battigelli et al., 1964; Gamble et al., 1983; Gamble and Jones, 1983; Graham et al., 1984; Jorgensen and Svensson, 1970; Robertson et al., 1984). The prevalence of persistent cough in these workers ranged from 29 to 37% among smokers and from 8 to 16% in nonsmokers. The risk ratio (observed/expected) for diesel exposed workers for persistent cough was generally between 1.2 and 2.3. There was a consistent finding of increased risk for cough, and also an increase in the prevalence of sputum production. Breathlessness was present in 8–20% of the smoking diesel workers and 4–7% of the nonsmokers. A group of Canadian potash workers were found to have a prevalence rate of breathlessness for both smokers and nonsmokers of around 10% (Graham et al., 1984) In none of these studies was an exposure–response gradient apparent.

Somewhat surprisingly many of the cohorts had higher baseline FEV₁ values than the control groups (Ames et al., 1984; Attfield et al., 1982; El Batawi and Noweir, 1964; Gamble et al., 1987a; Jorgensen and Svensson, 1970; Purdham et al., 1987; Reger et al., 1982). Most studies showed no significant dust related reduction in the ventilatory capacity, but an exception occurred in diesel bus garage workers who showed a slight decrement in ventilatory capacity with longer tenure (Gamble et al., 1987a). In multiple regression models the effect of age and smoking may show a significant association with decreased ventilatory capacity, while exposure to diesel exhaust usually does not. Such an anomaly may exist even when a stratified analysis indicates that such an exposure effect exists, indicating that there may be a small effect of diesel exposure which may not be detected because of multicollinearity.

Recent epidemiological studies have demonstrated an association between respiratory disease and the inhalation of particles with a mass mean aerodynamic diameter (MMD) of less than 10 μm (PM₁₀). Of particular concern are ultrafine particles with a MMD of less than 0.05 μm. It has been shown that pollution due to PM₁₀ is associated with an increase in daily mortality and in hospital admission exacerbations of pre-existing asthma (Department of Health, 1995). In terms of mass, the particulate burden in such episodes is small and has until recently been felt to be unlikely to produce significant morbidity or mortality. Clouding the issue are confounding factors such as extremes of temperature.

Most airborne particulate pollution that is currently encountered in urban air originates from motor vehicles and in particular, from diesel combustion. The possibility that diesel emissions play a role in the excess respiratory mortality and morbidity needs to be borne in mind (Maynard and Waller, 1996). Nevertheless, asthma does not appear to be a problem in metal and coal mines where diesel engines are frequently used and where the concentrations of diesel fumes encountered underground tend to be significantly higher than those encountered in urban air. Much more investigative work needs to be carried out in regard to PM₁₀ pollution, and until reliable data are available it would be wise to err on the side of caution.
Changes in the FEV$_1$ over a work shift have been evaluated relative to NO$_2$ exposure in three studies of workers exposed to diesel exhaust (El Batawi and Noweir, 1964; Gamble et al., 1987; Purdham et al., 1987). The bus garage workers had no detectable reduction in the FEV$_1$. Reductions in the FEV$_1$ and the forced expiratory flow at 50% of FVC (FEF$_{50}$) have been noted in U.S. coal miners after exposure to diesel exhaust (Ames et al., 1982). The observed decrement was similar to that seen in coal miners who did not use diesel powered equipment. Salt miners showed a statistically significant association between concentrations of NO$_2$ and the FEV$_1$, but the effects only became of biological import at higher levels, that is 5 ppm of NO$_2$ produced a 70 ml fall in the FEV$_1$. Larger decrements occurred in cigarette smoking salt miners (Graham et al., 1984). Small reductions in FEV$_1$ have been noted in both ferry stevedores and their controls (Purdham et al., 1987). In none of these studies was it possible to detect a significant reduction in FEV$_1$ at NO$_2$ levels < 1 ppm. Similarly, no change in airways resistance was found among workers exposed for up to 1 h to diesel exhaust with NO$_2$ concentrations averaging 4.2 ppm and ranging up to 7 ppm, that is at concentrations that produced intolerable eye irritation (Battigelli, 1965).

The possible nonmalignant effects of diesel emissions can be classified as follows:

(i) An increased prevalence of cough, phlegm, and dyspnea has been observed. However, diesel fumes cannot be incriminated as either a direct or indirect cause because of marked confounding by general mine dust and other exposures, including cigarette smoke. Moreover, for the most part no exposure–response relationship is evident.

(ii) The FEV$_1$ and FEF$_{50}$ of diesel exposed populations show a significant reduction over a shift in environments when NO$_2$ levels approach or exceed 5 ppm, but pulmonary function changes at NO$_2$ levels below 5 ppm are rarely detectable.

(iii) The baseline FEV$_1$ is more often higher than predicted in diesel exposed populations, probably as a consequence of an 'healthy worker effect'. Otherwise, no consistent relationship between lung function and exposure is evident.

(iv) The prevalence of pneumoconiosis amongst diesel exposed populations is generally less than 1%, and is best explained by other occupational exposures (for example coal mining, foundry work, etc.).

(v) Acute irritant symptoms occur amongst workers exposed to diesel emissions. These can sometimes be present when levels of individual contaminants in the exhaust are within the threshold limit value (TLV).

(vi) Possible exacerbations of asthma and on respiratory morbidity originating from the inhalation of PM$_{10}$ particles from diesel fumes.

In regard to nonmalignant outcomes, Glenn et al. (1983) provided a summary regarding diesel emissions at the International Pneumoconiosis Conference in Bochum, Germany:

On balance, neither consistent nor obvious trends implicating diesel exhaust in the mining atmosphere were revealed as being deleterious to respiratory health. Increased symptoms have been reported, but these may well be associated more with inhalation of mineral dust than with diesel fumes.
MORTALITY

The investigation of the role of diesel emissions in the induction of cancer, and in particular, lung tumors, has been confined to those employed in transportation, operators of heavy construction equipment, railroad workers, and miners exposed to diesel emissions. Although the review that follows is not exhaustive, the inclusion of results from other studies would not influence our conclusions.

Raffle (1957) and Waller (1980) studied the incidence of lung cancer between 1950 and 1974 in male employees aged 45–64 yr who worked for the London Transit Authority (LTA). They assumed that mechanics and engineering staff working in bus garages had the greatest exposures to diesel exhaust and might be expected to have a higher incidence of lung cancer than the general population and other employees of the LTA. Lung cancer cases amongst LTA staff relative to those expected from the Greater London population were calculated by job category and related exposures. The annual lung cancer rate for the exposed LTA workers was 159 per 100,000, which is significantly lower than 202 per 100,000 in Greater London. All SMR’s by job category were well below expectations, and moreover, no consistent relationship existed between the presumed level of exposure and respiratory cancer. Information on the smoking status of the workers and follow-up of workers who had left the LTA was not available. Harris (1981) re-analyzed these data using a relative risk model and showed that although some risk estimates were greater than unity, they were not significant.

In another British study, Rushton et al. (1983) evaluated the mortality of maintenance workers in London bus garages and at Chiswick Works who had been employed for at least 1 yr between 1967 and 1975. There were 705 deaths from all causes. Observed deaths from lung cancer closely resembled national death rates (SMR = 101). Elevated mortality, however, was found for several malignancies, for example bladder cancer, but these were based on small numbers. The study was unable to identify risks, but the group studied was limited and the follow-up short.

Wong et al. (1985) studied heavy equipment operators and observed an overall SMR of 81 for deaths from all causes; a figure that was significantly lower than expected. The SMR for lung cancer was 99, with risk increasing with the interval between first exposure and death, and was significantly increased for retirees. No association between diesel exhaust exposure levels and lung cancer was evident and in fact the SMR for lung cancer was lower in those workers with the higher exposures.

Hall and Wynder (1984) conducted a case–control study of lung cancer in subjects exposed to diesel exhaust. They observed a strong association of lung cancer with cigarette smoking and a two-fold increase in lung cancer for those exposed to diesel exhaust. When allowance was made for smoking, the excess lung cancer first attributed to diesel exposure disappeared. Kaplan (1959) studied the cause of death in railroad workers and found no association between exposures to diesel exhaust and lung cancer deaths. The work tenure of this cohort was brief, thus it is questionable if sufficient latency existed for the induction of lung cancer. A large group of male pensioners of the Canadian National Railroad Company was studied by Howe et al. (1983). They observed highly significant exposure–response relationships for lung cancer in individuals employed in occupations involving
exposure to diesel exhaust and coal dust. The relative risks of those possibly exposed or probably exposed to diesel exhaust were 1.20 and 1.35 respectively. Nearly identical values were observed for those with coal dust exposures. The roles of confounding factors such as asbestos exposure and cigarette smoking were not considered, and no quantitative data on duration or level of exposure were available. The authors maintained that cigarette smoking could not totally explain the increased risk, but their arguments are specious in view of the group's increased mortality from emphysema.

Schenker et al. (1984) noted an overall SMR of 87 for railroad workers compared to the U.S. national rates. The SMR for lung cancer was 82, however, the authors also calculated the SMRs for respiratory cancer in railroad workers with and without exposure to diesel exhaust. Although the relative risk for respiratory cancer was 142 in those exposed, it failed to reach statistical significance. Odds ratios were calculated using a proportional hazards model and the results were somewhat consistent with that shown with the SMR, but again the relative risk was not statistically significant. Thus, the low and high risk of lung cancer for diesel exposure was 1.50 and 2.77 respectively. While these data are suggestive of a diesel exposure effect, they did not take cigarette smoking into account, and furthermore, no estimates of diesel exhaust exposure were available. The extremely wide disparity in lung cancer risk using external and internal controls remains unexplained.

Waxweiler et al. (1973) studied potash workers and found no significant difference in mortality between miners exposed to diesel fumes and those not. The number studied was small, and the duration of exposure was relatively short.

Garshick and colleagues have evaluated the mortality experience of railroad workers (Garshick et al., 1987, 1988). In their first paper (1987), over 15,000 deaths occurred amongst 650,000 railroad workers between 1981 and 1982. Death certificates were obtained for 87% of these deaths, of which 1256 were from lung cancer. These deaths were compared with two sets of decedent referents randomly chosen from all deaths other than cancer, suicides, accidents, or unknown causes. Smoking habits were obtained for cases and controls by mail or by telephone conversations with the next of kin. Occupational histories were determined from yearly job reports available to the Railroad Retirement Board. Specific exposures by job were assessed for men from several railroads. Particulate exposures ranged from 9 to 76 µg/m³ for clerks and station agents (considered to be unexposed), from 83 to 168 µg/m³ for all diesel exposed groups, and from 87 to 322 µg/m³ for shop workers. The industrial hygiene estimates were derived from other parallel work (Woskie et al., 1988). The results were presented in a dichotomous fashion for men aged under and over 65 yr. A clear and consistent effect of cigarette smoking on lung cancer was seen in each age group. A weak effect of diesel exposure was present only in younger men, but was not apparent in older workers. It was suggested that the anomaly was due to the fact that roughly half of the older workers were unexposed to diesel exhaust and those who were had relatively short exposures. This unsubstantiated assertion could be influenced by the classification of those employed before 1959 who were considered to be unexposed. Retrospective smoking histories are frequently inaccurate, especially when next of kin are used as the source of information. This is particularly true when compensation is involved and in up to
25% of subjects there is a complete turn with smokers and exsmokers becoming life long nonsmokers (Berry et al., 1985; Lapp et al., 1994).

Garshick et al. (1988) is of critical import in that an attempt was made to deal with most of the defects in their prior studies (Schenker et al., 1984; Garshick et al., 1987). An attempt was made to demonstrate a dose–response relationship between diesel exposure and an excess of lung cancer. The study was based on a cohort of over 55,000 white male railroad workers, aged 40–64 yr in 1959, who had started to work for the railroad 10–20 yr earlier and who were selected on the basis of their job in 1959. This cohort was followed until 1980. At the study period cut-off date, around 19,400 deaths had been reported to the Railroad Retirement Board. Death certificates were obtained for 17,120 subjects. Of these, 1,694 (8.7%) were attributed to lung cancer. Diesel exposure was assessed on the basis of annual job codes. Most workers with potential asbestos exposure were excluded. SMRs for deaths from lung cancer in diesel exposed and unexposed workers were computed for 5 yr age groups. In addition, proportional hazard models, time-dependent and nontime-dependent, were devised. The relative risk of diesel exposure adjusted for age was 1.45 for men aged 40–44 yr, and declined to 0.98 for men aged 60–64 yr. The time-dependent model(s) refers to the inclusion or exclusion of the exposures during the last 5 yr of life. When these latter years were included in the exposure estimates, no evidence of a consistent exposure–response relationship was evident. It should be noted that the referents used were an internal nonexposed group of workers.

The authors inferred that the data supported the proposition of a small but significantly elevated lung cancer risk related to diesel exposure. This study is one of the more carefully designed mortality studies that evaluate the suggested cause and effect relationship. The data, results, and inferences that were drawn, however, are by no means convincing. A crucial defect is the lack of information on cigarette smoking. In this regard, the work of Stellman et al. (1988) is enlightening. When the smoking habits of over 800,000 men and women in the U.S.A. were tabulated by occupation, railroad workers (men) were shown to have one of the highest rates of smoking of all occupations. Slightly over 80% of the workers admitted to having (at some time) smoked cigarettes on a regular basis; a much higher prevalence than exists in the general male population of the U.S.A. The possibility that the excess risk of lung cancer in those subjects with diesel exposure could be due to differences in smoking habits between diesel exposed and nonexposed groups was rejected by the authors on the basis that no such differences existed in a group of railroad workers previously evaluated for past asbestos exposure. This cannot substitute for an accurate and preferably prospective cigarette smoking history. Confounding by cigarette smoking can easily explain a SMR of 1.5–2 as shown in previous studies. The designation of the subjects into exposed and nonexposed subgroups and the cumulative lifetime exposures are both questionable since they rely on duration by job-years with no yardstick for intensity. Thus, misclassification of exposure is probable, along with possible confounding by asbestos exposure, and multicollinearity.

A number of other concerns with this study need to be addressed. The authors decided to truncate the lower age at 40 yr, thereby excluding workers from 25 to 39 yr of age, which may partly explain the lower lung cancer risk in the older subjects. The use of job titles is far from ideal to determine exposures and no account was taken of exposure prior to and subsequent to 1959.
Garshick et al.'s (Garshick et al., 1988) choice of an internal group of reference is appropriate and permits directly adjusted risk rates to be derived. The original risk ratio trends, however, were not compared with those of an external source of referents that would rely on indirectly adjusted rates. Crum (1994) when evaluating the Garshick data compared them with those obtained from the U.S. white male population and found that the SMR (by age in 1959) for exposed and unexposed workers, particularly the former, demonstrated a trend counter to the relative risk that Garshick and co-workers had derived. When Crum calculated the risks for exposed and nonexposed railroad workers by age in 1959, the trends he found closely resembled those found by Garshick et al. (1988). Thus, if it assumed that there were no effects from misclassification or selection effects, the relative risks would be expected to be comparable and to show similar trends no matter whether internal or external referents were used. The unduly low SMRs of 63 and 69 derived by Crum (1994) for unexposed workers aged 40–44 and 45–49 yr are far too low to be credible suggesting that significant selection effects may be extant in the data of Garshick et al. (1988). Steenland et al. (1990) studied male deaths occurring in the Central States files of the Teamsters Union. There were 10,699 deaths in 1982 and 1983 amongst men with 20 yr of tenure in the union and who had claimed benefits. Death certificates were obtained for 98% of the subjects. Certificates relating deaths from lung cancer and controls were obtained using a systematic one-in-six sample of all social security numbers, excluding deaths from lung or bladder cancer and motor vehicle accidents. In all, there were 1288 lung cancer cases and 1452 controls. Occupational histories were obtained from Teamster records and from next of kin, and were analyzed separately. Information on smoking and other confounding factors was obtained from the next of kin. Interviews were conducted with the next of kin for 1085 (82%) cases and 1160 (80%) controls. Information on 77% of the study groups and 75% of the controls was available for analysis of occupation using Teamster records, and for 68% of the study group and 66% of the controls using next of kin data. Subjects were classified according to the job category in which they had worked longest, while those who had never worked in any of these job categories were classified as either nonexposed or potentially exposed. Several job categories in the exposed group had elevated lung cancer risks compared with unexposed workers, but none of the differences was statistically significant. Based on the Teamster history, however, a significant positive trend was observed with increasing years of employment as a long haul truck driver after 1959. Data derived from histories provided by the next of kin indicated that men who primarily drove diesel trucks showed a similar increasing lung cancer risk with duration of employment; but the trend was not significant. It was concluded that some types of truck drivers have an increased risk of lung cancer, and this excess seemed confined to truck driving after 1959 and specifically to diesel trucks. No quantitative environmental measurements were made in this study, thus the actual exposures of truck drivers are unknown. Here again, the reliability of the next of kin smoking data cannot be assumed.

Boffetta et al. (1988) reported on the mortality of men aged 40–79 yr who were enrolled in a prospective study sponsored by the American Cancer Society. This study dealt with occupations with possible or probable diesel exposure. After an adjustment for cigarette smoking, a relative risk of 1.05 for all causes of death and
1.18 for lung cancer was observed. A hint of a dose–response effect for lung cancer was detected, the risks being 1.05 for individuals with 1–15 yr exposure and 1.21 for individuals with 16 or more years exposure. Truck drivers, for example, who were exposed to diesel emissions were not at any increased risk of lung cancer when compared with truck drivers who were not thus exposed. All relative risks, however, were nonsignificant. Railroad workers, heavy equipment operators, miners, and truck drivers had higher mortality rates from all causes and also from lung cancer when compared with subjects with other occupations and no exposure to diesel emissions. However, internal comparisons by occupation revealed a quite different scenario. For example, truck drivers who were exposed to diesel emissions were not at any increased risk of lung cancer when compared to truck drivers who were not thus exposed. Accordingly, differences other than diesel exposure may have been responsible for the difference in risk of lung cancer between truck drivers and other men. In addition to these findings, workers categorized as having increased diesel exposure had significantly elevated risks of death from several nonmalignant conditions. Like most other studies, quantitative determinations of diesel exhaust exposure were lacking.

Boffetta et al. (1989, 1990) later reported on a lung cancer case–control study of workers with probable exposure to diesel exhaust emissions. Over 2500 incident lung cancer cases were matched with two controls per case. Information on probable exposure was obtained using a questionnaire relating to the duration of exposure to 45 groups of chemicals including diesel exhaust during work and with hobbies. Other information including smoking histories was obtained. While the crude odds ratio for those probably exposed to diesel exhaust was 1.31, this decreased to less than unity after accounting for the effects of cigarette smoking. Only one specific occupational category (truck drivers) was large enough to accommodate a separate analysis; the results resembled those of the overall analysis. Data on self-reported exposure for a subset of subjects revealed a crude odds ratio of 1.45, which after taking smoking into account decreased to 1.21.

In 1986, Gustafsson et al. (1986) reported on the mortality of Swedish dock workers. This was a retrospective cohort study meant to evaluate mortality and cancer incidence amongst Swedish dock workers between 1961 and 1981 in several different locations. The investigators relied on matching locally compiled personal data with information from two Swedish Central Registers on cancer and cause of death. The data consisted of employment records and the port of employment. No information on cigarette smoking habits was collected, and neither quantitative estimates nor measurements of diesel exhaust exposure was available. It was assumed that all of the dock workers were exposed to diesel exhaust to some extent. Over the period of observation, a total 6071 workers with an average tenure of around 16 yr were admitted to the cohort. At the close of the study, 1062 dock workers had died; 292 from cancer. Seventy of the 292 cancer cases were diagnosed as lung cancer. Seventy lung cancer deaths represent around 6.5% of the total deaths, a number which is close to expected. While the lung cancer deaths were distributed in various ports, around half of them were found in three locations. Expectations of lung cancer death were obtained by calculating age and calendar specific lung cancer rates from the general populations of the applicable metropolitan areas. Thus, differences in lung cancer rates by geography were
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Gustavsson et al. (1990) investigated the occurrence of lung cancer amongst 695 workers employed in five bus garages in Stockholm between 1945 and 1970. Both cohort mortality and case referent analyses were performed. Some general records of exposure to diesel fumes were available relating to the number of units, size, ventilation and other engineering controls but quantitative exposure assessments were scanty. Nonetheless, an exposure index was devised based on extant information. This less than precise rank scale was then related to the time spent in various jobs. Cause specific expectations of death were derived from Stockholm rates with adjustments for occupational activity. There were 17 lung cancer deaths suggesting a marginally increased but not significant risk of lung cancer (SMR = 122). Increasing exposure was not associated with a demonstrable increased risk. The case–control portion of the analysis involved 20 lung cancer cases with 6 controls per case. Calculated odds ratios showed an increasing risk of lung cancer to increments in the exposure index. In the most exposed group, the relative risk was around 2.4. When case–control is being related to a cohort analysis, it is essential not only to have information on the suspected carcinogen but also on other confounding factors, and in particular, cigarette smoking. These were absent from the case referent portion of the study. While the authors imply that these data are consistent with the hypothesis that diesel exhaust is carcinogenic, the omissions noted above seriously detract from their conclusions. Lastly, the fact that the case referent analysis is not consistent with the overall cohort analysis casts grave doubt on any causal connection between diesel exposure and lung cancer mortality.

Siemiatycki et al. (1988) carried out a case referent study in several Montreal hospitals of over 3700 cancer patients, aged between 30 and 70 yr. For patients with site-specific cancers, controls were selected from patients with other site cancers. The odds ratios for patients with squamous cell lung carcinoma who were rated as exposed to either gasoline or diesel fumes was increased to 1.2. This modest increase in the relative risk is unimpressive in view of the inexact projection exposure and an absence of cigarette smoking histories.

In contrast, a case–control study by Benhamou et al. (1988) involved 1625 histologically confirmed cases of lung cancer and nearly double the number of controls matched for age, sex, and hospital admission. Smoking habits and occupational histories were available for evaluation. A significantly elevated odds ratio (1.42) existed for motor vehicle drivers. The risk, however, was not specific for diesel exposure, and there was no relationship between risk and duration of exposure.

A case–control study by Buiatti et al. (1985) examined the relationship between cancer and occupation. In the case of lung cancer, 376 cases and 892 controls were involved. Cigarette smoking histories were available. While marginally increased
odds ratios existed in transportation workers and train conductors, neither was statistically significant. Moreover, the assumption that there was a consistent relationship to diesel exposure between the various subgroups cannot be sustained. Other published studies are not reviewed in detail as they add little to our knowledge regarding lung cancer mortality and diesel exhaust emissions. For example, Damber and Larsson (1985) found a moderately raised relative risk of lung cancer amongst professional drivers who were nonsmokers. Unfortunately the smoking histories were obtained from the next of kin, an unreliable method. In those said by their next of kin to be smokers, the effects were obvious. Luepker and Smith (1978) and Nokso-Koivisto and Pukkala (1994) also studied the effects of diesel exposure with inconclusive or negative findings. Lastly, Edling et al. (1987) studied bus garage workers in Sweden and found no differences between observed and expected cancer deaths in total or with regard to different degrees of exposure or various requirements of exposure and induction latency time.

DISCUSSION

The work of Wynder and Higgins (1986) provides an instructive dissertation as to how to control for multiple confounding factors in interpreting cancer epidemiology studies, as does a further review from the same investigators (Wynder et al., 1990). Had their recommendations been applied to many of the studies discussed there would have been many fewer publications on this topic.

Epidemiological studies are used to provide evidence for making decisions about cause and effect. Bradford Hill, in his 1965 address to the Royal Society of Medicine listed the following criteria: temporality, biological gradient, strength of association, consistency, plausibility and coherence. These criteria provide the statistical and scientific wherewithal to indicate a probable cause and effect association (Hill, 1965).

Strength of association

This is a reflection of the magnitude of the risk of lung cancer in the exposed and reference populations. An association of greater than 3 is likely to be causal, while a risk of 1.5–3 is suggestive, that is associations below 1.5 are often weak and explicable by bias and other confounding factors (Monson, 1980). Most of the studies referred to earlier with higher risk estimates (that is around 1.5) are prone to error due to flaws of one type or another. Thus, taking into account methodological quality, strength has been singularly lacking.

Consistency

The term consistency indicates the repeated observation of an association under different conditions of study. A repeated association (or lack of it) strengthens (or weakens) a causal hypothesis in that it is unlikely that confounding or bias or some other factors would consistently be present in different populations or would introduce bias that resulted in the same flawed inference. Similarly diverse results argue against a causal interpretation and in the case of the carcinogenic effects of diesel, diversity has been the only consistency. There is little to no consistency at all regarding the studies reviewed.
**Temporality**

This is the only criterion that may provide indisputable evidence that an association is not causal (Rothman, 1986). The cause must precede the effect, or it cannot be considered a cause. In the case of diesel exposure this criterion is present.

**Biological gradient**

This refers to the presence of an exposure–response curve. While some (true) causal relationships may not show an apparent trend with exposure, the existence of a biological gradient with exposure adds weight to a presumed effect. A few of the studies reviewed were analyzed on the basis of this factor. Although some studies show an apparent trend, the accuracy of the exposure classifications remain questionable and confounding factors such as smoking cloud the issue.

**Plausibility and coherence**

These criteria relate to the notion that the interpretation of a cause and effect relationship should not seriously conflict with our knowledge of the natural history and biology of the disease. It may be intuitively reasonable to suggest that whatever is breathed into the lung, for example diesel emissions, can affect its well-being and could cause cancer. IARC and NIOSH have relied on animal studies in support of this hypothesis. Thus Mauderly et al. (1993) performed studies on rats comparing the carcinogenic potential of diesel exhaust and mutagen poor carbon black. Tumors occurred equally frequently in the rats whether exposed to carbon black or diesel particulate. Based on lung burden, carbon black was actually more carcinogenic than diesel emissions. It is tempting to equate mutagenicity with carcinogenicity but Ames himself has deplored many of the tendentious associations and frightening pronouncements that have been made as a result of a positive Ames assay. Sugimura and Nagao (1979) using the Ames test found that onions contain a substance which makes up 1–2 of their weight and is carcinogenic for animals. Why did IARC and the U.S. Consumer Protection Agency not ban the consumption of onions?

**Experimental evidence and analogy**

Two other guidelines used to determine cause and effect are experimental evidence and analogy. The former relates to whether or not there is evidence that removal from exposure or reduction in exposure levels changes the situation and lowers the incidence of the effect. This factor cannot be addressed with the studies reviewed owing to the absence of accurate quantitative exposure data.

**CODA**

Summing up, in spite of the vast number of published epidemiological studies, none has provided convincing evidence that there is an increased risk of cancer from diesel exhaust emissions. It is possible that various flaws in the methodology could explain the lack of a consistent association, but this appears improbable. The vagaries of assumed factors, that is smoking habits and exposure information could easily explain the modest increases in relative risk that have been observed in many
studies. It is abundantly evident that there is no consistency in the various mortality studies that have been reviewed; moreover, the strength of the various associations found was low. The modest excesses in relative risk around 1.3–1.8, a range in which it is virtually impossible to assign a cause and effect relationship because of confounding factors. There have been no recent publications that permit more definite conclusions.

The importance of adequate and accurate information on cigarette smoking habits of any cohort used to assess mortality from lung cancer cannot be overemphasized. An editorial in the *Lancet* (1978) pointed out that lung cancer is responsible for just under 40% of all male cancers in the Western world and that smoking habits have a disproportionately high effect. In Britain it was noted that in 1978 manual laborers had a 22% greater lung cancer risk than administrative and clerical workers and the difference was attributable to their respective smoking habits. This emphasizes the need for prospective smoking histories. Since many workers who are exposed to diesel fumes and other suspected carcinogens have been and are undergoing pre-employment physicals, including smoking histories, it should be possible to gather sufficient data to give a definite opinion in the not too distant future. Meanwhile the tendency to publish poorly controlled studies replete with inaccurate data and spurious conclusions is to be deplored.

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Health effect of diesel emissions


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