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Comstock ML
Health Services, Consolidated Rail Corporation, Philadelphia, Pennsylvania, **USA.**

Doll's landmark 1959 study of the epidemiology of occupational lung cancer failed to find an increased risk in workers exposed to petrol fumes and **emissions.** In it, he pointed out a critical issue that is not resolved today. With theoretically increased risk based on biological plausibility but an absence of positive findings, epidemiologic methodology cannot reliably distinguish between no risk and very little risk. Despite the ensuing nearly **40** years of research, neither human epidemiologic studies nor animal studies can support a causal relationship between either lung cancer or noncancer respiratory health effects at current levels of occupational exposure. Even with statistically significant but low relative risks, neither evidence of causality nor level of risk can be definitively established. Epidemiologic data suggest that an increased risk of lung cancer for **diesel exhaust** exposed workers may be comparable with that for environmental tobacco smoke. Monitoring and control of the particulate is necessary. Prudent policy dictates continued efforts to reduce **emissions** of soot from **diesel** engines and decrease occupational exposure as a matter of good health and safety practice. Improvements in engine design, soot filters, and fuel modification will provide the best approach to exposure control. Further research is also needed in the areas of carcinogenic mechanisms and development and validation of biomarkers of exposure before reliable estimates of **risk** of human health effects in the occupational setting can be made.

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DIESEL EXHAUST IN THE OCCUPATIONAL SETTING

Current Understanding of Pulmonary Health Effects

Marcia L. Comstock, MD, MPH

Concern about potential carcinogenicity of diesel exhaust has existed for several decades. More recent widespread use of diesel equipment has intensified the debate about appropriate control of occupational exposure. Numerous cohort and case control studies of occupational exposure have been conducted over the past 20 years in industries with presumed high usage of diesel engines.

In 1988 National Institute for Occupational Safety and Health (NIOSH) recommended that whole diesel exhaust be regarded as a potential occupational carcinogen based on an association in some animal studies, although epidemiologic data were weak.[34] In 1989, the International Agency for Research on Cancer (IARC) classified whole diesel exhaust in Group 2A, probably carcinogenic to humans, concluding that there was sufficient evidence in animals. In humans they believed information was credible; however, chance, bias, or confounding information have not been ruled out.[23] The US Environmental Protection Agency (USEPA) has classified it into the equivalent B-1 category. Many authorities believe these decisions were premature at best.

Exposure criteria for diesel exhaust in the United States have not been defined. Establishing an exposure threshold presumes that investigators can define the level of human health hazard. Although a threshold limit value of 150 $\mu g/m^3$ has been proposed for submicrometer particu-

From Health Services, Consolidated Rail Corporation, Philadelphia, Pennsylvania

late by the American Conference of Governmental Industrial Hygienists (ACGIH), there is much uncertainty in its basis.-'

Particulate diesel exhaust, like particulate air pollution, has also been implicated in noncancer respiratory health effects. In 1993, USEPA established an inhalation reference concentration (RfC) of 5 $\mu g/m^3$ for noncancer effects of diesel exhaust. This was intended to be an estimate of daily human exposure without risk of deleterious effects. The basis for this derivation has been criticized as inaccurate extrapolation.

From the perspective of public health policy, there is a dilemma when facing the need to balance health concerns with the economic impact of regulations without proven scientific basis. Do investigators know enough about what is toxic and what causes health effects to properly regulate the matter? If not, premature action could have severe economic consequences.

This article reviews the literature on pulmonary health effects of diesel exhaust, with particular reference to occupational exposure. Neither animal data nor epidemiology can accurately define the toxic potential of diesel engine fumes under human exposure conditions.

GENERAL AIR POLLUTION

Severe air pollution has been known to have adverse health effects. Studies have also reported weak, but statistically significant acute health effects of particulate air pollution, even below the current standard of 150 $\mu g/m^3$ (24 hr). A 1995 review of the literature, however, concluded that studies are inconsistent, and the criteria for causality have not been met. Confounding by weather, other pollutants in the complex mixtures, or exposure misclassification could explain much of the positive association. Investigators do not yet know which constituents are most potent.[12]

The association of ambient particulate matter with serious health effects, however, should not overly influence consideration of the question of diesel exhaust effects. These studies did not examine diesel exhaust; its contribution to particulates in the studies is unknown, and in many investigations, the source was known to be something else.

COMPOSITION OF DIESEL EXHAUST

Diesel emissions comprise a complex mixture that represents only a fraction of a broad array of air contaminants. Composition varies with fuel composition, engine type, operating conditions, and ambient air. Once emitted, transformation processes may alter the properties of the components, resulting in substances that may be more or less toxic than the original compound. Composition also varies with time of analysis. The chemical and physical composition of emissions has changed and will continue to do so with more stringent emission standards and evolving technology and fuel formulation.'"

The vapor phase contains gaseous components, such as oxides of carbon, sulfur, and nitrogen, and carcinogenic compounds, including benzene, formaldehyde, 1,3-butadiene, ethylene dibromide, and polycyclic aromatic hydrocarbons and derivatives.

The carbon core of fine submicrometer particles is coated with adsorbed trace metals, nitrites, and sulfites, in addition to organic compounds, many of which are cytotoxic or classified as possible human carcinogens or mutagens. Particulate aggregates comprise 60% to 80% elemental carbon by weight.

IN VITRO AND ANIMAL STUDIES

Particulate and gaseous fractions of diesel fumes have demonstrated direct-acting mutagenic activity with *Salmonella.* This is generally attributed to nitro polycyclic aromatic hydrocarbons.[30] Extracts from diesel exhaust have considerable mutagenic activity without exogenous metabolic activation, unlike extracts of cigarette smoke. No quantitative relationship between mutagenicity in bacteria and carcinogenesis in humans, however, has been established.

In a recent study, only the particle samples, not the semivolatile samples were mutagenic, and most of the mutagenicity was found in the polar fraction. The compounds causing mutagenesis are not polycyclic aromatic hydrocarbons because they require activation and are found in the aromatic, not the polar fraction.[18]

Inhalation of whole diesel exhaust results in DNA adduct formation in rats. Whole diesel exhaust and particles can also induce structural chromosome aberrations and sister chromatid exchange in cultured mammalian cells. These bioassays on the mutagenic effect of extracts of diesel exhaust are felt by Stobel and Abel[40] to be the only scientifically robust results supporting the conclusion that diesel exhaust is a borderline carcinogen by chemical carcinogenesis.

Evidence from animal studies also indicate that organic extracts of diesel particulate are genotoxic and carcinogenic, Inhalation of whole diesel exhaust resulted in DNA adduct formation in rats. Diesel exhaust was classified by IARC as a probable human carcinogen based on these inhalation rat studies, which also showed an increase in benign and malignant tumors after 2 years. This study period is essentially equivalent to lifetime exposure to high (2–8 mg/m^3) concentrations of unfiltered diesel exhaust.[27]

These results were not replicated in other animals. The phenomenon seems to be rat specific. The relationship between exposure levels and response is not clear cut. Data indicate that particle overload induces increased cell turnover, leading to inflammatory and proliferative changes that precede development of pulmonary tumors in rats. Chronic inhalation of high concentrations of whole diesel exhaust causes destruction of defensive pulmonary mechanisms, promoting development of primitive lung adenocarcinomas. Most studies support the observation

that whole diesel exhaust is the culprit, and filtering exhaust minimizes risk.

At lower exposure levels that do not reduce pulmonary clearance, diesel exhaust is not carcinogenic. This supports the notion that the mechanism of carcinogenic action is pulmonary overload and subsequent inflammation, not chemical carcinogenesis. The insoluble carbon core, specifically, is suspected because tumors of the lung have been experimentally induced following exposure to carbon black, which has the same carbonaceous core but no mutagenic adsorbates. Titanium dioxide, a chemically different but equally insoluble substance incapable of forming DNA adducts, also has provoked such tumors.[21]

Diesel particles also seem to be the main cause of noncancerous effects in animals. Concentrations at which effects are seen in these animal studies are orders of magnitude greater than those generally encountered in the workplace, but exposures shown to cause pulmonary injury in animals are lower than those that increase the incidence of tumors.[26]

Toxicity associated with acute exposure relates primarily to high concentrations of CO, NO_2, and aliphatic aldehydes. With short-term exposure, there are some toxic effects from high concentrations of particulate, but minimal effects on pulmonary function.

High concentrations over several months result in accumulation of particles and an increase in alveolar macrophages with aggregation. Decreased resistance to lung infection and behavioral, hematologic, and enzymatic changes, and reductions in growth rate have been noted with exposure of even longer duration.

Histologic studies show that chronic exposure to high concentrations of diesel exhaust can cause changes in respiratory tract tissue. Pathologic effects are dependent on relative rates of pulmonary deposition and clearance. With concentrations above 1 mg/m^3 and adequate duration of exposure, clearance is reduced because of impaired macrophage function.[31] Data for animals other than rats are limited.

EPIDEMIOLOGIC EVIDENCE

Epidemiologic studies of human exposure are of limited value because of numerous methodologic flaws. Exposure assessment is crude and imprecise. It is not based on actual measurement, but rather is generally limited to few qualitative categories based on occupational features or duration of employment as a surrogate. Surrogates for exposure, however, do not permit estimates of dose-effect relationships or quantification of absolute risk.

Confounding the studies by smoking, diet, and other lifestyle related factors or occupational exposures also seriously skews results. Inconsistencies in dose-effect relationships based on job category or duration of exposure are found in key studies. Preconceived bias for positive studies based on presumption of effect is common. Negative

studies, however, frequently suffer from size limitations that result in lack of statistical power to detect difference or insufficient follow-up in view of disease latency.[40]

Earliest studies undertaken to evaluate the relationship between occupational exposure to diesel emissions and lung cancer were negative; however, none were scientifically rigorous. Studies of railroad workers[11] and dock workers[15] found an association, but there was a definite suggestion that smoking confounded the results. A 1986 review by Steenland[39] of 14 studies on lung cancer in truck drivers revealed that none had measured exposure and few adjusted for smoking habits or other potential confounders. He concluded that the studies did not produce a definitive answer.

In 1992, Mauderly[25] surveyed the literature on effects of diesel exhaust up to 1990 but did not critically analyze the studies. He recognized that the epidemiology was incomplete and contradictory. Up to 1986, none of the epidemiologic investigations published met the methodologic criteria for reliable studies. It has been suggested, too, that results from earlier studies may be less relevant than recent ones because improvements in engine design and emission control technology have altered the chemical composition of diesel exhaust.

Mauderly concluded that weight of evidence suggested a possible, although small, carcinogenic effect. It is important to note that he was clearly influenced by investigations whose accuracy was subsequently challenged.[7]

Only since 1987 have there been studies suggesting an association after adjustment for smoking. These studies too have serious flaws, including design,[10] other potential confounding occupational exposure, potential exclusion bias, and misclassification.[6] Case control studies in which smoking habits were carefully assessed and controlled for in the analysis demonstrated increased odds ratios only in the crude analysis and disappeared when smoking was accounted for.[5, 16]

The Garschick investigation of American railroad workers[14] may be the best that exists of mortality studies evaluating the hypothesis of a causal link between diesel exhaust exposure and mortality from lung cancer. The investigation was previously thought to provide the most substantive evidence of a small but significant increase in lung cancer risk from diesel exhaust. Major concerns, however, relate to the classification of workers into exposed and unexposed and the methods used to evaluate and control for smoking, which were unsatisfactory based on established quality criteria. More importantly, a later reanalysis of the data requested by the Environmental Protection Agency (EPA) did not confirm the findings.[7]

Two significant statistical anomalies were found. First, data from the cohort study were not compatible with a dose-effect relationship. Second, relative risk tended to decrease with increasing duration of exposure within exposed workers. It was also discovered that follow-up between 1978 and 1980, the last 3 years of the study, was inadequate,

and a large number of deaths in the cohort went undetected. As a result, even the EPA admitted these studies do not provide reliable risk data.[35]

Perhaps the most important and balanced reviews on the association between emissions from diesel engines and risk of carcinogenicity in humans are the Health Effects Institute study published in 1995[29] and an extensive 1996 review, including meta-analyses, conducted by Stobel and Abel.[40] Despite the fact that investigators in this field are by no means neutral to the outcomes of their studies, the backgrounds and affiliations of these investigators help ensure a well-balanced interpretation.

These surveys conclude that all the studies have serious weaknesses and inconsistencies, many acknowledged by the authors. There is no consistency in findings, nor any good evidence of a dose-response relationship. Strength of association based on calculated relative risk is low, with no study finding relative risk in excess of 2. With such small risk, studies are sensitive to confounding variables and exposure uncertainties. Using commonly accepted criteria for determining causal associations, the evidence is insufficient to establish diesel engine exhaust as a human lung carcinogen at occupational exposure levels or to make quantitative risk assessments.[27, 28, 40]

RISK ASSESSMENT

Risk assessment for mutagenic or carcinogenic substances is complicated by long latency periods, synergistic or antagonistic actions of chemical mixtures, complex interactions with biologic systems, and difficulty in extrapolating from animal data.

Quantitative risk assessment for diesel exhaust using in vitro studies, animal studies, and epidemiology has been attempted, but present scientific data cannot support its accuracy because of major uncertainties.[24, 27] Each source of potential data is plagued by inaccuracy and extrapolation problems. Regulatory agencies and the scientific community have acknowledged the severe limitations of unit-risk estimates.

In vitro data are based on diesel particles from which adsorbed organic compounds have been removed by solvent extraction. The clinical relevance of these data to human inhalation exposure to whole diesel exhaust is unclear. Most particulate matter is removed from conducting airways in 24 hours, allowing little time for phagocytotic extraction of organics from particles. Yet some carbonaceous particles deposited in the alveolar region may be rapidly phagocytosed by macrophages.[41] Many biologic fluids are ineffective in releasing adsorbed mutagens, but alveolar macrophages are more so. The question of bioavailability remains unanswered.[27, 28]

Analysis of unit-risk estimates for diesel exhaust using animal bioassays similarly is problematic. As stated earlier, rat tumorigenesis seems to result from an epigenetic mechanism of submicron-sized, insoluble particles in the lungs and not chemical carcinogenesis. The mechanism

is likely nongenotoxic and related to a finite dose threshold.",[41] Exposure scenarios and emission products differ between laboratory studies and human exposure. Data from animals suggest a threshold effect that may be caused by a volume of particulate matter that ultimately overwhelms the natural clearance defense mechanisms of the lung. High-dose to low-dose linear extrapolation ignores this threshold issue and is inappropriate." Some debate exists about whether or nut large species experience impairment of alveolar clearance, even with extremely large lung burdens, that nonetheless is unlikely to be replicated in occupational settings.

Combined with cross-species extrapolation and what may be the unique sensitivity of the rat lung to inert particles, which cause chronic inflammation and alveolar epithelial cell proliferation, there is clear compromise of the use of animal results in drawing conclusions about human effects. Even the primary author of the rat studies has cautioned against their use in risk assessment for human pulmonary carcinogenesis.[27]

Given all this uncertainty in extrapolation from animal studies, some investigators have attempted to base recommended unit risk on human epidemiology. As pointed out earlier, dose-response curves cannot be generated from available data; therefore, an acceptable risk estimate cannot be derived. This has been acknowledged by authors of key studies who admitted their original calculations were no longer valid.[29] The Health Effects Institute concluded that lack of definitive exposure data for occupationally exposed populations precludes the use of the available epidemiologic data to develop quantitative estimates of cancer risk.[20]

NONCANCER HEALTH EFFECTS OF DIESEL EXHAUST

In addition to concerns about carcinogenicity, 'components of complete carbon combustion and incomplete combustion may be associated with other respiratory symptoms and health effects. The diesel particulate is also believed to be the main cause of noncancerous effects in animals. Concentrations at which effects are seen are orders of magnitude greater than those generally encountered in the workplace.[27]

Studies in humans have looked at symptoms, acute and chronic, pulmonary function tests, and radiograph evidence of pneumoconiosis, which has been described in workers exposed to carbon black, graphite, and similar materials. The studies are plagued by the same problems that impair evaluation of potential for carcinogenic effects: poor exposure characterization, thus misclassification; lack of control for confounding variables; and short duration with low intensity of exposure.

Acute respiratory effects of diesel engine exhaust have been examined in studies of several occupationally exposed groups, including railroad yard workers, coal miners, salt miners, diesel bus garage me-

chanics, and stevedores.',[3, 11, 13, 36] Although no significant respiratory symptoms were noted, more than half reported eye irritation, apparently associated with measurable levels of NO, and particulate levels, but more likely caused by aldehydes, such as formaldehyde and acrolein, and phenols.

The studies generally found no pattern or minimal changes in respiratory function over the course of a shift. When NO_2, however, exceeds 5 ppm, a reduction in FEV, and FEF_{50} has been shown." In a salt miner study, however, it was later determined that before-to-after shift changes in pulmonary function only occurred in smokers. Pulmonary changes at NO, levels less than 5 ppm, the current OSHA standard, are minimal and similar in exposed and unexposed controls. Thus, it seems that acute symptoms, particularly eye irritation, are more reliable and sensitive indicators of exposure than acute changes in PFTs over the shift.[13]

There has been a suggestion that acute high-dose, long-duration exposure to diesel exhaust could result in persistent airflow obstruction.[42] As there are many components of diesel exhaust that could cause pulmonary irritation, such as aldehydes, carbonaceous particulate, or oxides of nitrogen or sulfur, it is not possible to know which components might be causative. The mechanism may be irritant or allergic.

Most epidemiologic data do not demonstrate an increase in chronic respiratory disease. A few show higher prevalence of pulmonary symptoms, such as phlegm and persistent cough, not associated with definite functional decrements. No effects were attributable specifically to diesel exhaust, but many studies involved miners with confounding exposure to mine dust or salt.[2, 11]

A 1987 study of diesel bus garage employees using tenure as a surrogate for exposure showed dose-response relationships were inconsistent for various symptoms, but dyspnea showed a moderate association with employment. The study concluded that the potential for diesel engine exhaust to increase respiratory symptoms and reduce function is biologically plausible at some levels of exposure but revealed no convincing evidence of a causal relationship. Smoking was the strongest and most consistent risk factor for symptoms.[13]

Prevalence of pneumoconioses in several populations studied has been low and in all cases could be related to other exposures, such as coal dust or grinding dust.[2, 13] At the present time, epidemiologic studies do not provide solid evidence for noncancerous respiratory effects of diesel exhaust at occupational exposure levels.

EXPOSURE MONITORING

Because diesel exhaust is a very complex mixture of chemical compounds, there is considerable interest in identifying markers to monitor individual exposure and relate it to internal dose.

An appropriate marker must be sufficiently specific and detectable

at low levels. The method used must be replicable, suitable for personal sampling, and practical for field use. Past studies have assessed gaseous and particulate fractions.[45] Selection of the best marker requires careful review of the specific job tasks and exposures, including sources of emissions, to determine appropriate sensitivity and specificity.'"

Attempts to assess gaseous components failed because oxides of sulfur or nitrogen cannot be reliably detected, and CO_2 cannot be used for breathing zone sampling. Because tumor induction in animals is associated with unfiltered exhaust, a measure of exposure to the carbonaceous aerosols in the particulate fraction is most relevant.[34]

Several strategies have been used to select out the nonrelevant components of particulate soot to provide a more accurate measure of exposure to diesel exhaust.[17, 43, 44]

Size selective sampling for total respirable particulate matter (RSP)
Elimination of contribution of environmental tobacco smoke (ETS) to obtain the adjusted respirable particulate (ARP)
Determination of the mass extractable in dichloromethane to eliminate inorganic respirable aerosol and produce the adjusted extractable mass (AEM)

Other methods of exposure monitoring focus on more specific measurement of carbon components. Use of total carbon, elemental plus organic, results in tobacco smoke bias. Determination of submicrometer elemental carbon using thermal–optical analysis is an excellent indicator of exposure, with high sensitivity, specificity and precision, permitting identification of organic and elemental carbon at environmental background levels. In most workplaces the diesel engine is the only significant source of elemental carbon. The method, generally using open-face cassettes for routine monitoring and evaluation of control technology, is inexpensive and practical. In at least one study there was a highly significant relationship between elemental carbon and respirable dust, with elemental carbon averaging slightly less than 20% of corresponding respirable dust level.[45]

Efforts to use a chemical component, such as one of the polycyclic aromatic hydrocarbons as a marker of exposure requires that it be present at levels detectable by routine analysis and that there not be other sources for the compound. Phenanthrene was found promising as a marker for diesel exhaust because it is the PAH found in the highest concentration in diesel exhaust. It correlated with known exposure by job grouping. The study found phenanthrene concentrations near the limit of detection, but a fairly constant ratio of phenanthrene to respirable particulate concentration on samples, suggesting the compound should be pursued as a possible marker of exposure.[38]

BIOLOGICAL MONITORING

In addition to being flawed by exposure estimates that are imprecise, epidemiologic studies of diesel exhaust also suffer from failure to

accurately quantify the biologically effective internal dose of a substance received. Age, gender, diet, and other nonoccupational exposures can affect dose received. Biological markers can increase the accuracy of exposure assessment and enhance the power and sensitivity of epidemiologic studies.

Although a standard biomarker has not been identified, potential approaches range from analytical assays tailored to detect specific classes of compounds or evidence of cytogenetic damage to non-selective bioassays, such as mutagenicity assays that may detect unidentified substances.[35]

As electrophilic compounds are detoxified by reaction with glutathione, conjugates such as mercapturic acid or other thioether products can be detected in the urine. These nonselective assays may be the most practical for screening, especially in developing countries.[9]

Measures of urinary mutagenicity are inexpensive and convenient. Positive findings have been noted with some occupational exposures and with cigarette smoke. Although urinary mutagenicity may be useful for mixtures like diesel exhaust, usually analytic assays must be tailored. To control for smoking, biochemical markers like cotinine and nicotine are more accurate than questionnaires.

Studies thus far, however, have failed to find an independent association of diesel exhaust exposure with urinary mutagenicity. It is possible that this could relate to technical factors, such as the need for greater study power, and higher exposure levels or greater detection sensitivity would be necessary.[37, 38]

1-Hydroxypyrene (1-POH), a metabolite of the polycyclic aromatic hydrocarbon pyrene, which is emitted in significant amounts in diesel exhaust, has also been studied as a possible biomarker of exposure to PAHs. It was found in elevated amounts in residents in Japan exposed to significant automotive air pollution.[21]

Recently, Nielson studied urinary 1-hydroxypyrene (HPU) as a biomarker of genotoxicity in workers with occupational exposure to diesel fumes using high performance liquid chromatography analysis and found significantly higher levels than in controls. He points out that HPU is highly influenced by diet and smoking. In this study of nonsmokers, the issue was not specifically addressed.

Nielson also looked at cytogenic effects. After activation by cytochrome P450 enzymes, resulting electrophilic substances in diesel exhaust can bind covalently to DNA. Workers exposed to polycyclic aromatic hydrocarbons have an increased DNA adduct level. Using DNA from lymphocytes rather than from total white blood cells (WBCs) reveals higher levels of adducts and enhances the distinction between exposed persons and nonexposed persons, for example, smokers and nonsmokers.

Nielson's study examined lymphocyte DNA adducts using the 32P-postlabeling method, which requires less than 10 μg DNA and is highly sensitive, with butanol and P1 enrichment procedures. He demonstrated qualitative and quantitative differences in DNA adducts between occu-

pationally exposed and control individuals exposed to ambient air pollution. He did note, however, large interindividual differences, perhaps reflecting differences in the uptake and metabolism of genotoxic compounds.

Hydroxyethylvaline (HOEtVal) adducts in hemoglobin were also measured by gas chromatography–mass spectrometry (GCMS). Hemoglobin adducts reflect exposure to ethene from tobacco smoke or engine exhaust. Significantly higher levels of these biomarkers were also found.

Although all three methods detected low-level environmental exposure, postlabeling, and GCMS provided the most sensitive assays. Hydroxypyrene in the urine (HPU), being a metabolite, is a marker of recent exposure. DNA adducts reflect cumulative mixed exposure, whereas hemoglobin adducts result from a more specific compound interaction. Because these adducts estimate cumulative exposure to the protein or cell over its lifetime, they differ from air sampling, which gives a snapshot of exposure but says little about biologic relevance.[33]

SUMMARY

Doll's landmark 1959 study of the epidemiology of occupational lung cancer failed to find an increased risk in workers exposed to petrol fumes and emissions. In it, he pointed out a critical issue that is not resolved today. With theoretically increased risk based on biological plausibility but an absence of positive findings, epidemiologic methodology cannot reliably distinguish between no risk and very little risk.[5]

Despite the ensuing nearly 40 years of research, neither human epidemiologic studies nor animal studies can support a causal relationship between either lung cancer or noncancer respiratory health effects at current levels of occupational exposure. Even with statistically significant but low relative risks, neither evidence of causality nor level of risk can be definitively established.[32,40] Epidemiologic data suggest that an increased risk of lung cancer for diesel exhaust exposed workers may be comparable with that for environmental tobacco smoke.[4]

Monitoring and control of the particulate is necessary.[28] Prudent policy dictates continued efforts to reduce emissions of soot from diesel engines and decrease occupational exposure as a matter of good health and safety practice. Improvements in engine design, soot filters, and fuel modification will provide the best approach to exposure control. Further research is also needed in the areas of carcinogenic mechanisms and development and validation of biomarkers of exposure before reliable estimates of risk of human health effects in the occupational setting can be made

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Address reprint requests to

Marcia L. Comstock, MD, MPH
1157 Lafayette Road
Wayne, PA 19087–2110