Human health risks from diesel engine particles

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Summary

Evidence from toxicological and epidemiological studies indicates that human health hazards are associated with exposure to diesel engine particles (DEP), also called diesel particulate matter (DPM). The hazards include acute exposure-related symptoms, chronic exposure related non-cancer respiratory effects, and lung cancer (EPA 2002). As new and cleaner diesel engine and fuel technology, together with efficient exhaust aftertreatment, replace a substantial number of older engines, the general applicability of the health hazard conclusions will need to be reevaluated. With new engine and fuel technology expected to produce significantly cleaner engine exhaust, significant reductions in public health hazards are expected for those engine uses affected by the regulations. However, every newly developed technology has to be examined according to its influence on human health risks.

Keywords: diesel engine emissions, particles, polycyclic aromatic hydrocarbons, health risks, lung cancer, cardiovascular diseases, asthma

Characterization of DEP

The combustion of diesel fuel forms a complex mixture of hundreds of organic and inorganic compounds in the gas and particle phase of diesel engine emissions (DEE). Toxicologically relevant compounds in the gas phase of DEE – but not discussed in this review - are carbon dioxide, nitrogen oxides, carbon monoxide, sulfates, aldehydes (formaldehyde, acetaldehyde, acrolein), benzene, and 1,3-butadiene. Toxicologically most relevant compounds adsorbed onto surfaces of diesel particulate matter (DPM) are PAHs as well as their derivatives nitrated PAHs and oxidized PAHs. To a lesser extent (PAHs) and (nPAHs) are also found in the gaseous phase of DEE (Scheepers P. T. J. and Bos R. P. 1992a and 1992b, Health Effects Institute 1995).

The International Agency for Research on Cancer (IARC) classified DEE probably carcinogenic to humans (Group 2A) in 1989. This classification was confirmed by many other institutions.

Constituents

DEP contain a large variety of organic compounds adsorbed onto a center core of elemental carbon, as well as small amounts of sulfate, nitrate, metals, and other trace elements. DPM consists of fine particles (fine particles have a diameter <2.5 µm), including a subgroup with a large number of ultrafine particles (ultrafine particles have a diameter <0.1 µm). Collectively, these particles have a large surface area which makes them an excellent medium for adsorbing organic compounds. Also, their small size makes them highly respirable and able to reach the deep lung. A number of potentially toxicologically relevant organic compounds are on the particles. The organics, in general, range from about 20 % to 40 % of the particle weight, though higher and lower percentages are also reported. Many of the organic compounds present on the particle and in the gases are known for mutagenic and carcinogenic properties. Especially, PAHs, nitro-PAHs, and oxidized PAH derivatives are present on diesel particles, with the PAHs and their derivatives comprising about 1 % or less of the DPM mass (Scheepers P. T. J. and Bos R. P. 1992b, Health Effects Institute 1999).

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Exposure

Exposure to diesel engine emissions is ubiquitous. Highest environmental exposures occur in urban areas due to heavy traffic. All occupations where diesel engine powered vehicles or diesel engine powered machinery is in use can be potentially exposed to diesel engine emissions. Occupations with strong exposures are related to agriculture, transportation, construction, mining, and engine maintenance. Actual information on prevalence of occupationally DEE-exposed people is limited. For the total workforce in the European Union the number of exposed employees was estimated three millions based on information in the CAREX database from 1990 to 1993 (Kauppinen T., et al. 2000). In Italy, 500.000 subjects were estimated to work with exposure to DEE (Mirabelli D. and Kauppinen T. 2005). According to the Federal Agency for Work and Labour (Bundesagentur für Arbeit 2005) nearly two million employees are working under a probable exposure to DEE in Germany. The following numbers of employees in Germany are supposed to be substantially exposed to DEE:

On-road professional drivers	750,000
Off-road vehicle/machinery operators	50,000
Vehicle and machinery maintenance workers	645,000
Transportation workers	450,000
Miners	35,000

A detailed list of occupations with an assumption for probability and intensity of exposures to DEE is given in the appendix of a Swedish study (Bofetta P. et al. 2001).

DPM mass (expressed as µg DPM/m^3) has historically been used as a surrogate measure of exposure for whole DEE. Although uncertainty exists as to whether DPM is the most appropriate parameter to correlate with human health effects, it is considered a reasonable choice until more definitive information about the mechanisms of toxicity or modes of action of DEE becomes available. In the ambient environment, human exposure to DEE comes from both on-road and non-road engine exhaust. A large percentage of the population also is exposed to ambient PM2.5, of which DPM is typically a significant constituent. Exposure estimates for the early to mid-1990s suggest that annual average DEP exposure in the U.S.A. from on-road engines alone was in the range of about 0.5 to 0.8 µg DPM/m^3 of inhaled air in many rural and urban areas, respectively. For localized urban areas where people spend a large portion of their time outdoors, the exposures are higher and, for example, may range up to 4.0 µg DPM/m^3 of inhaled air (EPA 2002). In Europe, existing occupational exposure levels (OELs) for DEP are based on the measurement of elemental carbon (EC). An inter-comparison showed that existing analytical procedures for the determination of diesel particulate matter at workplaces fulfil the requirements of European standard EN 482 (Hebisch R. et al. 2003).

Some 3,500 measurements of DEE at enclosed workplaces were performed in 1.070 German work sites in 1990 to 2000 (Mattenklott M. et al. 2002), comprising results for elemental carbon (EC) and total carbon (TC). Mean exposures at workplaces under roof varied between 0.018 and 0.027 mg/m^3 for EC (0.026 and 0.047 mg/m^3 for TC). The corresponding 90 %-values were 0.055 up to 0.100 mg/m^3 for EC (0.088 and 0.150 mg/m^3 for TC). Means of exposures at underground workplaces varied between 0.095 and 0.150 mg/m^3 for EC (0.165 and 0.210 mg/m^3 for TC). The corresponding 90 %-values were 0.226 up to 0.406 mg/m^3 for EC (0.373 and 0.498 mg/m^3 for TC).

Due to the high relevance of DEE in many occupations and environmentally exposed subjects very effort is put to the development of specific and sensitive biomarkers of exposure to DEE and their health effects, especially according to PAHs (Angerer J. et al. 1997, Scheepers P. T. J. et al. 2002, Seidel A. et al. 2002, Rossbach B. et al. 2007, Wilhelm M. et al. 2007).

Health effects of DEP

Diesel exhaust particles (DEP) contribute considerably to the ambient air pollution from particulate matter, which causes acute and chronic effects in mucosal membranes, in the respiratory tract including lung cancer, and in the cardiovascular system. Due to their median aerodynamic diameter (0.01 - 0.3 µm) these particles are readily inhaled and about 10 % are deposited in the alveolar region of the lung (Scheepers P. T. J. and Bos R. P. 1992b, Health Effects Institute 1995). Number and size of the particles as well as the type and amount of combustion compounds vary in a wide range depending on the engines, fuels, and driving parameters. Although the epidemiological evidence is strong, there are until now no established biological mechanisms to fully explain the toxicity of DPM to humans (Salvi S. et al. 1999).

Non cancer effects

Acute and subacute effects

First recognized during smog episodes in London during the 1950´s, subsequent epidemiologic studies have noted that short-term increases in ambient levels of particulate matter (PM) are associated with hospital admissions and deaths from cardiovascular and respiratory disorders. These acute effects were observed in patients with chronic obstructive pulmonary disease, chronic bronchitis, asthma and cardiovascular disease (Dockery D. W. and Pope C. A. III 1994, Samet J. M. et al. 1995, Katsouyanni K. et

al. 1997). However, the biologic mechanisms that underlie this association and the role that the composition and size of PM may have in causing adverse health effects are not well understood (Salvi S. et al. 1999, Holgate S. T. et al. 2003).

Recent experimental studies in healthy human volunteers showed increases of many parameters of systemic and pulmonary inflammation but no measurable effects on lung function after exposure to DEP (Salvi S. et al. 1999, Nordenhall C. et al. 2000, Pourazar J. et al. 2005). Furthermore, there is broad evidence that DEP inhalation causes vascular dysfunction and impaired endogenous fibrinolysis (Mills N. L. et al. 2005).

Information is limited for characterizing the potential health effects associated with acute or short-term exposure. However, on the basis of available human and animal evidence, it is concluded that acute or short-term (e.g., episodic) exposure to DEE can cause acute irritation of the eyes and upper airways, neurophysiological symptoms (e.g., lightheadedness, nausea), and respiratory symptoms (cough, phlegm). The lack of adequate exposure-response information in the acute health effect studies precludes the development of recommendations about levels of exposure that would be presumed safe for these effects (EPA 2002).

Chronic effects

In long-term studies a significant association of mortality has been reported with air pollution from PM less than 10 µm in aerodynamic diameter (PM10) (Schwartz J. 1993, Dockery D. W. et al. 1993, Pope C. A. III et al. 1995, Abbey D. E. et al. 1999). The Working Group on Public Health and Fossil-Fuel Combustion (1997) estimated 8 million additional deaths globally until 2020 due to PM exposure if the air pollution increases to the same degree as hitherto. Recently, special attention has been focussed on the respiratory effects of fine (PM2.5) and ultrafine particles (PM0.1) (Peters A. et al. 1997, Schwartz J. and Neas L. M. 2000).

Information from human studies is solely inadequate for a definitive evaluation of non-cancer health effects from chronic exposure to DEP. However, on the basis of extensive animal evidence, DEP is judged to pose a chronic respiratory hazard to humans. Chronic-exposure, animal inhalation studies show a spectrum of dose-dependent inflammation and histopathological changes in the lung in several animal species including rats, mice, hamsters, and monkeys (EPA 2002).

Sensitization

There also is evidence for an immunologic effect–the exacerbation of allergic responses to known allergens and asthma-like symptoms (EPA 2002). Several large epidemiological studies have demonstrated a strong association between exposure to motor vehicle traffic emissions and allergic symptoms and reduced lung function (Brunekeef B. et al. 1997, Brauer M. et al. 2002, Janssen N. A. et al. 2003, Mc Connell R. et al. 2006), although the singular results differ in detail. Laboratory studies in humans and animals have shown that particulate toxic pollutants-particularly diesel exhaust particulates-can enhance allergic inflammation and can induce allergic immune responses (Li N. et al. 2003, Siegel P. D. et al. 2004). Most of these immune responses are mediated by the carbon core of diesel exhaust particulates. However, also PAHs from DEP enhance the production of immunoglobulin E (Mastrangelo G. et al. 2003).

While the evidence for the exacerbation of immunologic effects in already sensitized subjects is good, evidence for the development of allergic sensitization from diesel exhaust particulates is less abundant. Comparisons of the prevalence of hay fever, as well as positive skin-prick tests, between citizens of former West and East Germany and between Hong Kong and China civilians, have demonstrated marked differences. Crucial variations in the level of particulate air pollution from motor vehicles in these countries may account for the observed increased prevalence of atopy. In a review from 2002 Polosa and coworkers stated that allergic susceptibility associated with diesel exhaust particle exposure is clear as mud (Polosa R. et al. 2002). Two years later Heinrich and Wichmann wrote that the evidence for an increased risk for asthma and hay fever is still weak but seems to be strengthened a little (Heinrich J. and Wichmann H. E. 2004).

Cancer and mutagenic effects

Cancer

An association of increased risks for lung cancer associated with exposure to DEE has been observed in the vast majority of over 30 epidemiologic cohort and case control studies published in the literature. Distinct populations of occupational groups were studied, including railroad workers, truck drivers, heavy-equipment operators, farm tractor operators, and professional diesel vehicle drivers. Three meta-analyses confirmed the relationship of diesel exhaust exposure and lung cancer (Cohen A. J. and Higgins M. W. P. 1995, Bhatia R. et al. 1998, Lipsett M. and Campleman S. 1999).

Risk assessment data based on actual exposures to DEE was not available. Elevated risks were estimated in epidemiological studies on the basis of historical exposure scenarios. The Cohen and Higgins report (1995) is a qualitative review of 35 epidemiologic studies (16 cohort and 19

case-control) of occupational exposure to DEE published between 1957 and 1993. The evidence suggests that occupational exposure to DEE from diverse sources increases the rate of lung cancer by 20 % to 40 % in exposed workers in general, and to a greater extent among workers with prolonged exposure. Bhatia R. et al. (1998) found a small but consistent increase in the risk for lung cancer among workers with exposure to DEE, in a quantitative meta-analysis of 23 studies. The pooled RR weighted by study precision was 1.33 (95 % CI = 1.24-1.44). Lipsett and Campleman (1999) performed a quantitative meta-analysis. Pooled RRs for all studies and for study subsets were estimated using a random effect model. A pooled smoking-adjusted RR was 1.47 (95 % CI = 1.29-1.67). Although the results of these analyses were called into question by several authors (Stöber W. and Abel U. R. 1996, Muscat J. E. 1996, Crump K. S. 1999, Hesterberg T. W. et al. 2006), another recent study added new evidence for an increased lung cancer risk from exposure to DEP (Parent M. E. et al. 2007).

Risk assessment data for specific occupations based on actual exposures to DEE was not available. A pooled study based on exposures in East and Western Germany some decades ago showed the following odds ratios (Brüske-Hohlfeld I. et al. 1999):

Heavy equipment operators
OR = 2.31 (95 % - CI 1.44 - 3.70)
Tractor drivers (exposure >30 years)
OR = 6.81 (95 % - CI 1.17 - 39.51)
Professional drivers (West Germany)
OR = 1.44 (95 % - CI 1.18 - 1.76)
Other traffic related jobs
OR = 1.53 (95 % - CI 1.04 - 2.24)

Most assessments conclude that DEP is “likely to be carcinogenic to humans by inhalation” and that this hazard applies to occupational and environmental exposures (IARC 1989, EPA 2002). This conclusion is based on the evidence from human, animal, and other supporting studies. There is considerable evidence demonstrating an association between DEP exposure and increased lung cancer risk among workers in varied occupations where diesel engines historically have been used. The human evidence from occupational studies is considered strongly supportive of a finding that DEP exposure is causally associated with lung cancer, though the evidence is less than that needed to definitively conclude that DEP is carcinogenic to humans. There is some uncertainty about the degree to which confounders are having an influence on the observed cancer risk in the occupational studies, and there is uncertainty evolving from the lack of actual DEP exposure data for the workers (EPA 2002).

In addition to the human evidence, there is supporting evidence of DEP’s carcinogenicity and associated DEP organic compound extracts in rats. The experiments showed a consistent dose-dependant incidence of lung tumors after a chronic exposure to high concentrations of DEE (Heinrich U. et al. 1986, Ishinishi N. et al. 1986, Iwai K. et al. 1986, Mauderly J. L. et al. 1987). But these results were criticized since concentrations led to an “lung-overload” with particles in the animals (EPA 2002).

Mutagenicity

Other supporting evidence includes the demonstrated mutagenic effects of DEP and its organic constituents. A high mutagenic potency of extracts of DEP was described by Huisingh J. et al. (1978) using the Salmonella typhimurium/mammalian microsome assay (Ames-Test) and has been confirmed in multiple further studies (Clark C. R. and Vigil C. L. 1980, Claxton L. D. and Barnes H. M. 1981, Belisario M. A. et al. 1984). The direct-acting mutagenicity of DEP is ascribed to substituted PAHs, e. g. nitro-PAHs (Wang Y. Y. et al. 1978, Pedersen T. C. and Siak J. S. 1981, Ohe T. 1984), while not substituted PAH require metabolic activation by S9 (IARC 1983). In recent years renewable sources, especially vegetable oils, were used to create biogenic diesel fuels. According to results using the Ames-Test, DEP extracts of plant oil derived methyl esters e.g. (SME, RME) are less mutagenic (Bagley S. T. et al. 1998, Bünger J. et al. 1998, Bünger J. et al. 2000a, Bünger J. et al. 2000b, Bünger J. et al. 2006) compared to common diesel fuel, while the combustion of crude rape seed oil resulted in an extreme increase of mutagenicity in an actual study (Bünger J. et al. 2007).

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