Health effects of diesel exhaust

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Abstract

This paper, based on a literary research, focuses on current knowledge of diesel exhaust (DE), from both carcinogenic and non cancer, epidemiological and experimental research.

DE is a pervasive airborne contaminant that continues to be widespread in industrialised and developing countries, and contributes significantly to outdoor pollution. In fact, in addition to occupational exposure, the wide use of diesel engines in transportation provides significant opportunity for environmental exposure to these emissions. Both the gaseous and particulate components contain mutagens and carcinogens, and for this reason most studies on the health effects of DE have focussed on the issue of its role in cancer. However, health concerns about diesel exhaust relate not only to cancer, but also to respiratory diseases, such as airway inflammation and the possibility of contracting asthma and chronic bronchitis. All of these have been investigated experimentally and epidemiologically. There are also observations supporting the hypothesis that persistent exposure to particulate air pollution from motor vehicles is an important factor contributing to the allergy pandemic.

1 Introduction

Air pollution is a highly relevant topic for public health, since all people are potentially exposed. Over the decades, outdoor air pollution has been shown to cause adverse health effects.

In London on 4 December 1952, during an increase in smog over the city, particulate and sulphur pollution rose greatly over the following three days, resulting in 4,000 excess deaths. Although acute exposures with dramatic
consequences occasionally still occur, nowadays epidemiologists are more concerned with chronic or repeated low-level acute exposures to outdoor pollutants as a cause of the more subtle excesses in respiratory morbidity and mortality.

The United Nation Environment Programme has identified particulate matter pollution as the most serious air pollution problem faced by many cities [1]. The particle and gaseous components of DE are "priority pollutants". They contain many mutagens, carcinogens and toxic substances and they are a major contributor to various types of air pollution, including smog-forming oxides of nitrogen (NOx) and fine particles (PM$_{2.5}$). Polycyclic aromatic hydrocarbons (PAHs) are found in both the gaseous and particulate fraction of diesel exhaust, that are produced as pyrolytic products during the combustion of any fossil fuel, including diesel fuel.

2 Diesel exhaust

Diesel fuel is widely used throughout our society, to power automobiles, trucks, buses, locomotives, off-road equipment, agricultural equipment, and electricity generators, and they all produce exhausts. DE is a complex mixture of thousands of gases and fine particles (commonly known as soot) that contains more than 40 toxic air contaminants. The gaseous constituents include carbon dioxide, carbon monoxide, nitric oxide, nitrogen dioxide, oxides of sulphur, and hydrocarbons (e.g., ethylene, formaldehyde, methane, benzene, phenol, 1,3-butadiene, acrolein, and polycyclic aromatic hydrocarbons). The particulate components: diesel exhaust particulate (DEPs), are composed of solid carbon cores that are produced during the combustion process and that tend to form chain or cluster aggregates, absorbed organic compounds and small amounts of sulphate, nitrate, metals, and other trace elements [2]. Nearly all DEPs fall within the PM2.5 size range, with mass median diameters ranging from 0.05 to 0.3 µm [3]. The human health effects of airborne particulate matter (PM) have been examined in numerous recent epidemiological studies [4-10], several of which highlight the special health significance of particles ≤ 2.5 in aerodynamic diameter (PM$_{2.5}$). PM2.5 are potentially more harmful than larger particles because they can reach deeper into the lower respiratory tract of the lungs. Recent electron microscopy studies suggest that over 80% of DEPs have a size ≤0.1 µm. The ultrafine particles (diameters <0.05-0.10 µm), are highly reactive and are present in large quantities in the urban environment. They are able to penetrate the epithelium and vascular walls and enter the bloodstream. Because diesel engines burn fuel more efficiently than conventional spark ignition gasoline engines, they offer better fuel economy. However, diesel engines emit 10 times more particles per mile than conventional gasoline engines and 30-70 times more than engines equipped with catalytic converters [11].

3 People exposed to diesel exhaust

Exposure to diesel exhaust particles (DEPs) is both an environmental and occupational health concern. It occurs through inhalation rather than ingestion or
skin absorption. It is difficult to quantify exposure, as diesel exhaust is chemically complex and its components, particulates, oxides of nitrogen, and others, may also derive from many other sources. Individuals may be exposed to DE when they are in an area where diesel engines are in use and the exhaust mixture is breathable. Those most likely to be occupationally exposed to diesel exhaust include bridge, tunnel and loading dock workers, auto mechanics, toll booth collectors, truck and forklift drivers, and people who work near areas where diesel powered vehicles are used, stored and maintained. Farm workers and car, truck, and bus maintenance garage workers may also be subject to heavy exposure [11]. Air pollution from diesel-engine exhaust has been a major respiratory hazard for workers in underground mines. Jørgensen and Svensson [12] reported that underground miners often developed productive coughs and frequent respiratory infections, but they did not find any spirometric abnormalities. Wade and Newman attributed asthma amongst train crew to diesel exhaust [13]. A non-occupational setting that may have a higher than average ambient exposure could be, for example, among those who spend a notable part of their day in the vicinity of diesel roadway traffic, such as in or around highways or urban streets. Most people spend more than 22 hours each day indoors [14]. Indoor air contains DE at levels that are affected both by outdoor concentrations and by the type of building ventilation. Modern buildings with heating, ventilation and air conditioning (HVAC) systems sometimes have particle filtration systems that can reduce DE levels. Buildings with older or less expensive ventilation systems, though, usually lack particle filtration. Where building inhabitants open windows and doors to ventilate the building, indoor diesel exhaust concentrations have been found to be just as high as outdoor levels [15]. If loading docks or garages where diesel trucks may idle, are located near an air intake for the building, exposures may be greater than expected indoors, even in a tightly sealed building.

4 Lung cancer

4.1 Epidemiological evidence

Epidemiological studies of workers exposed to diesel exhaust have shown that small but significant elevation in the risk of lung cancer, even if it is difficult to correctly define and quantify occupational exposure. There are also concurrent workplace exposures, such as smoking [16]. A case-control study of deaths among U.S. railroad workers, conducted to test the hypothesis that lung cancer is associated with exposure to DE, showed that workers with at least 20 years of service were significantly more likely to die from lung cancer than were members of the general population [17]. A cohort study of over 55,000 railroad workers by the same researchers found that lung cancer risk increases with duration of exposure to DE, the relative risk was 1.72 among workers with the longest exposure (as much as 22 years). The cohort was selected to minimize the effect of past asbestos exposure. Workers with possible asbestos exposure excluded, analysis still resulted in a similarly elevated risk [18]. A case-control study of lung cancer deaths was conducted amongst the Teamsters Union to compare the risk of different occupations within the
Teamsters. Participants were controlled for smoking and other confounders. The study population consisted of 996 cases and 1,085 controls who had died in 1982 and 1983 after applying for pensions. The results suggest that diesel truck drivers have an excess risk of lung cancer compared to other teamsters in jobs outside the trucking industry. However, the findings were not uniformly consistent, and the data has many limitations, the most important of which is the lack of data on exposure to diesel fumes [19]. Still another two studies of teamsters also linked diesel exhaust exposure with lung cancer [20-21].

In 1982, the American Cancer Society enrolled over 1.2 million American men and women in a prospective study of cancer and other causes of mortality, in relation to different risk factors. The mortality over two years of 461,981 males aged 40-79 years with a smoking habit, has been analysed in relation to exposure to DE, and to employment in selected occupations related to DE exposure. Railroad workers, heavy equipment operators, miners, and truck drivers had a higher mortality rate, both from lung cancer and other causes of mortality, when compared to subjects with other occupations with no exposure to DE [22]. Two meta-analysis of epidemiological studies investigating the relationship between occupational diesel exhaust exposure and lung cancer, reached very similar conclusions: the pooled smoking-adjusted relative risk was 1.47 (95% CI= 1.29- 1.67) in one [23], 1.35 (95% CI=1.20-1.52) in the other [24].

Lung cancer is the principal cancer linked to DE, but there is also suspicion that others cancers, especially those of the bladder, larynx, pancreas, and kidney, may be associated with DE [25]. The results of a large record-linkage study from Sweden to investigate the risk of cancer among male and female Swedish workers exposed to DE, provided evidence of a positive exposure-response relationship between exposure to DE and lung cancer risk among men. The positive results for other neoplasms, such as stomach, pancreatic, oral/pharyngeal, and cervical cancers, cannot be attributed to diesel exposure, but they deserve attention in future investigations [26]. A meta-analysis of bladder cancer and DE exposure was done to review and summarise the available epidemiological studies of bladder cancer and occupational exposure to diesel exhaust. This suggested that exposure to DE may increase the occurrence of bladder cancer, but the effects of misclassification, publication bias, and confounding cannot be fully taken into account [27].

4.2 Experimental evidence

Evidence for carcinogenicity of diesel exhaust has been demonstrated by several animal studies. A long term exposure study with hamsters, mice and rats inhaling filtered and unfiltered diesel engine exhaust was carried out. This was to investigate the effects of chronic toxicity and, predominantly, carcinogeneticity in the respiratory tract and, demonstrated that both types of diesel exhaust increased incidence of adenocarcinomas in the lungs of mice. In rats only the unfiltered diesel exhaust caused a lung tumor incidence. It amounted to 16% with no tumor in the controls [28]. Another study was carried out in rodents to examine the potential carcinogenic effect of inhaled automobile exhaust emissions. Both rats and hamsters were exposed to the emissions from a
gasoline engine, a gasoline engine fitted with a three-way catalytic converter, a
diesel engine and a diesel engine with particle filtration. An increased incidence
of lung tumours was found only in rats exposed to mean concentrations of diesel
soot particles of either 2200 or 6600 micrograms/m$^3$ [29]. Diesel exhaust inhaled
chronically at high concentrations proved to be a pulmonary carcinogen in the rat
[30]. In the above data Mauderly [31] and McClellan observed that lung cancer
in rats was probably due to particle overload in the lung after have inhaled high
concentration of particles [32]. The important role of the particulate matter in
diesel exhaust has also been demonstrated in an in vitro model of lung slices
in biphasic organotypic culture. Slices were exposed to a continuous flow of
diluted diesel exhaust with a $pO_2$ adjusted to 20% to avoid hypoxia-induced
effects. The results showed that whole diesel exhaust induced an inflammatory
response and DNA alterations which were reduced by filtration [33].
Based on such epidemiological and experimental evidence IARC rated diesel
exhaust as "probably carcinogenic to humans" (Group-2A) [34]. The
Environmental Protection Agency (EPA) considers DE "likely to be carcinogenic
to humans by inhalation at any exposure condition [35].

5 Non neoplastic effects

5.1 Epidemiological evidence
Many epidemiological surveys reported high acute and chronic disease morbidity
rates and decreased pulmonary function in populations occupationally exposed to
DE [36-37]. A study was carried out on tunnel workers to assess the occurrence of
respiratory symptoms and airflow limitation, and to relate these findings to
number of years of exposure. These demonstrated that exposure to dust and gases
from DE during blasting, drilling and rock transport in tunnel work, enhanced the
risk for an accelerated decline in FEV1, respiratory symptoms, and COPD in
tunnel workers compared with other heavy construction workers [38]. The others
Authors to assess the protective effect of exhausts pipe filters and respirators on
pulmonary function, studied 15 workers from a tunnel construction site, truck
and loading machine drivers, rock workers, and others. They found that the
respirators used to protect pulmonary function in workers exposed to diesel
exhausts, had no effect, probably because of the difficulties in correctly using
personal protection under the circumstances of the work [39]. Recently some
Italian experiences have also confirmed respiratory health damages from air
pollution, namely the prospective epidemiological studies on general population
samples of the Po Delta and Pisa areas; the cross-sectional study on
schoolchildren of the "Italian study on respiratory disorders in childhood and
environment" (SIDRIA); and a meta-analysis of the Italian studies short-term
effects of air pollution [40]. However despite reports suggesting an association
with DE, and of the motor vehicle generated air pollutants, diesel exhaust
particles (DEP) account for a highly significant percentage of the particles
emitted in many towns and cities [41-42], it is difficult to evaluate the
contribution of DE, because there are no specific markers of diesel particle
exposure.
Recently DEPs have been implicated to play a major role in rising prevalence of
392 Air Pollution XI

allergic diseases [42-44]. A number of epidemiological studies conducted in different parts of the world have reported a clear association between the prevalence of allergies and road traffic-related air pollution [45-47]. The first report implicating occupational exposure to diesel exhaust as a cause of reactive airways disease, is by Wade et al. [13]. They reported the development of asthma in three railroad workers who were exposed to excessive amounts of diesel fumes while riding immediately behind the engine of a caboose-less train. In loading dock workers exposed to diesel fumes due to use of diesel-powered equipment, an increase in the proportion of IgE was found [48]. Polosa et al. reported in traffic wardens with a well-defined occupational history a positive increase in the proportion of positive skin prick tests [49]. Regarding the role that diesel exhaust may play in other health problems, associations between day-to-day particulate air pollution, (to which diesel exhaust contribute significantly), and increased risk of cardiopulmonary diseases [50], and recently, of adverse central nervous system effects have been found [51].

5.2 Experimental evidence
Epidemiological evidence suggest a link between chronic bronchitis-like symptoms and asthma-like symptoms, reduced pulmonary function, ischaemic heart disease, and levels of particulate matter in the atmosphere. There have also been reports from human, animals and in vitro experiments, suggesting that diesel particles are related to asthma, chronic obstructive pulmonary disease (COPD), and allergic susceptibility.

5.2.1 Human studies. An experimental study carried out in twelve healthy non-smoking volunteers, has shown that exposure to DE caused symptoms and bronchoconstriction which were not significantly reduced by a particle trap [52]. Ten non-smoking healthy volunteers exposed to DEPs at high ambient concentration, had an airway inflammatory response characterised by an influx of activated neutrophils accompanied by an increase in exhaled CO levels, indicative of oxidant stress [53]. Most in vivo studies in man demonstrated that DEPs potentiate IgE production in the respiratory mucosal surface (54-55), can strongly enhance mucosal allergic inflammation and specific Ig responses in already sensitised subjects, and that they are able to drive sensitization to neoantigen [56-57].

5.2.2 Animal studies. The effect of long-term (24 months) inhalation of diesel exhaust, on the bronchoalveolar region of the respiratory tract of rodents, was assessed by serial analyses of the bronchoalveolar lavage fluid (BALF). There were found dose-dependent increases in inflammatory cells, cytoplasmic and lysosomal enzymes, and protein in BALF, demonstrating that, for non the carcinogenic health effects, there is a threshold exposure below which adverse effects were not observed [58]. A study conducted on rats and mice exposed to DEPs by inhalation, demonstrated respectively, decreased ability of alveolar macrophages to produce antimicrobial reactive oxidant species in response to zymosan (a fungal component), and decreased ability of the lung to produce the antiviral agent interferon and increased viral multiplication in the lung. These results support the hypothesis that exposure to DEPs increases the susceptibility
of the lung to infection by depressing the antimicrobial potential of alveolar macrophages [59]. Fibrogenic effect on lung: peribronchiolar fibrosis associated with significant increase in lymphocytes, fibroblasts, and interstitial macrophages, following chronic exposure to DEPs was found in cats [60]. In mice, following repeated intratracheal instillation of DEPs, asthma-like symptoms, marked infiltration of inflammatory cells, proliferation of goblet cells, increased mucus secretion, airway constriction, and increased airway responsiveness were all observed [61]. Air pollution by DEPs is a cause for serious concern for our health, but the toxicological mechanism should be clarified. Recent reports suggest that oxygen-derived free radicals and their metabolites, reactive oxygen species (ROS), are important mediators of pulmonary injury. These include asthma [62], pulmonary fibrosis and inflammation caused by exposure to asbestos [63-64], quartz and silica [65-66], and adult respiratory distress syndrome [67-68]. The first direct evidence of $\cdot$OH generation from $O_2^\cdot$ through a Fenton-like reaction in the lungs of mice 1 d after exposure to DEP, is provided by using L-band spectroscopy and a membrane-impermeable nitroxyl probe. This technique is non invasive and enables one to make a time-resolved analysis of in vivo free radical reactions with individual animals [69].

5.2.3 In vitro studies. The involvement of DEPs in respiratory diseases, and their biological mechanism through which they act, were also evaluated by studying their effects in vitro. In a study conducted on pulmonary alveolar macrophages and RAW 264.7 cells, it was been demonstrated that methanol extracts made from diesel exhaust particles (organic component), induce ROS production and apoptosis via a toxic effect on mitochondria [70]. It has been demonstrated that organic DEP extracts induce a stratified oxidative stress response leading to heme oxygenase 1(1OH -1) expression at normal GSH/GSSG ratios. This proceeds to Jun kinase activation and interleukin8 (IL-8) production at intermediary oxidative stress levels, and culminates in cellular apoptosis in parallel with a sharp decline in GSH/GSSG ratios [71].

The cytotoxicity of DEPs, their phagocytosis, and the resulting immune response were investigated in a human bronchial epithelial cell line (16HBE14o-) as well as in human nasal epithelial cells in primary culture. DEP exposure induced a time- and dose-dependent membrane damage. Transmission electron microscopy showed that DEPs underwent endocytosis by epithelial cells and translocated through the epithelial cell sheet. Flow cytometric measurements allowed establishment of the time and dose dependency of this phagocytosis and its nonspecificity with different particles (DEPs, carbon black, and latex particles). DEPs also induced a time-dependent increase in interleukin-8, granulocyte-macrophage colony-stimulating factor, and interleukin-1beta release. This inflammatory response occurred later than phagocytosis, and its extent seems to depend on the content of adsorbed organic compounds because carbon black had no effect on cytokine release. Furthermore, exhaust gas posttreatments, which diminished the adsorbed organic compounds, reduced the DEP-induced increase in granulocyte-macrophage colony-stimulating factor release. These results suggest that DEPs could be phagocytosed by airway epithelial cells and induce a specific inflammatory response [72].
Air Pollution XI

To investigate the mechanisms underlying DEP-induced airway disease in humans, human bronchial epithelial cells (HBEC) from surgically obtained bronchial explants have been cultured and investigated for effects of purified DEP on the permeability and ciliary beat frequency (CBF) of HBEC, and on the release of inflammatory mediators from these cells. The results of this study demonstrated that exposure of HBEC to DEP leads to an attenuation of ciliary activity of HBEC and release of proinflammatory cytokines, such as IL-8, granulocyte-macrophage colony stimulating factor (GM-CSF) and soluble intercellular adhesion molecule-1 (sICAM-1). These results suggest that exposure of HBEC to DEP may lead to adverse functional changes and release of proinflammatory mediators from these cells, and that these effects may influence the development of airway disease [73]. A recent study has been carried out to compare the effects of native DEP (nDEP), organic extracts of DEP (OE-DEP), and carbonaceous particles, represented by stripped DEP (sDEP) and carbon black particles (CB), in order to clarify their respective roles. It has been demonstrated that OE-DEP and nDEP induce granulocyte macrophage colony-stimulating factor (GM-CSF) release, NF-kB (nuclear factor \(\kappa B\)) activation, and MAPK (mitogen-activated protein kinase) phosphorylation. The carbonaceous core generally induces less intense effects. Reactive oxygen species are produced in 16HBE cells and are involved in GM-CSF release and in stimulation of NF-kB DNA binding by nDEP and OE-DEP. It has been also demonstrated that nDEP induce the expression of the \(CYP1A1\), a cytochrome P450 specifically involved in polycyclic aromatic hydrocarbons metabolism [74].

6 Concluding remarks

Exposure to diesel exhaust is an environmental and occupational health concern because the particle and gaseous components of DE contain many mutagens, carcinogens and toxic substances. Epidemiological studies have demonstrated an association between different levels of air pollution and various health outcomes including mortality, exacerbation of asthma, chronic bronchitis, respiratory tract infection, ischaemic heart disease. In addition, recent human and animal laboratory-based studies have shown that DEPs can enhance allergic inflammation and induce the development of allergic immune responses. Much of research on adverse effects of DE, both in vivo and in vitro, has been conducted in animals. However, since the animal experiment data were obtained as the result of exposure to considerably higher concentration than usually observed, it is unknown whether the effects observed at high concentrations occur at environmental level. It is very important to further assess acute and chronic effects of DE with careful consideration of exposure levels to understand the relevance of association found in the epidemiological studies.

References


398 Air Pollution XI

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