

EDITORIAL

Diesel exhaust particles and respiratory allergy

Air pollution is a subject of increasing concern throughout the developed and developing worlds. Historically, most concern has been directed towards acid aerosols and black smoke, which were the principal ingredients of the infamous smogs associated with coal burning. Since the introduction of clean air legislation in the 1950s and 1960s, emissions of these 'traditional pollutants' have declined substantially [1]. In their place we now see two new hazards: photochemical smogs and particulate pollution, both resulting from increased road traffic. Much has been written about photochemical pollutants, and especially ozone which has adverse effects on human airways at high ambient concentrations [2]. Patients with asthma and other airways diseases seem particularly vulnerable to ozone [3]. Ozone is generated by a complex photochemical reaction between oxygen, sunlight and volatile organic compounds (VOCs) released from the incomplete combustion of hydrocarbon fuels, and especially petrol used in internal combustion engines [4].

In the late 1980s, steps were taken to address this, with the compulsory fitting of catalytic converters. At the same time, fiscal incentives have made diesel-powered personal transport an increasingly attractive option. Diesel fuel is now widely available at car filling stations and the current generation of diesel-powered cars is much more efficient at the lower speeds (less than 40 mph) that are typical of modern urban and suburban motoring. In the 1989/1991 National Travel Survey, diesel cars were reported to have average consumptions of 41.4 miles per gallon against 28.7 miles per gallon for petrol-driven cars [5]. The net effect has been a progressive increase in the proportion of new car registrations with diesel power plants, until diesel-powered cars now account for over one-third of all new registrations in Europe [5,6]. In contrast, diesel cars are much less popular in the US where fuel costs are lower: new diesel registrations there reached 6% in 1981 during the height of the energy crisis, but in the 1990s only 0.1% of new US car registrations are diesel-powered [6].

Diesel exhaust consists of a complex mixture of nitrogen oxides, formaldehyde, carbon monoxide, hydrocarbons, ash, transition metals, and carbon particles. In the UK, diesel exhaust currently accounts for about 15 000 tons per year or 40% of all emissions, while in large cities like London, diesel exhaust accounts for 87% of all emissions [7]. Diesel engines also release over 100 times more particles per mile than petrol engines of equivalent power running on unleaded petrol [6].

A series of epidemiological studies in the United States has found a relationship between particulate pollution, in

particular particulate matter below 10 μm in diameter (PM_{10}), and cardiovascular morbidity [8,9]. Particulate matter concentrations have also been linked to the incidence of asthma and other respiratory diseases [10–12]. As particulate matter concentrations have already risen by 82% in the past decade [7] and diesel engines are an important contributor of PM_{10} , these findings have raised important and potentially embarrassing questions about the wisdom of encouraging the uptake of diesel engines in private vehicles. At the same time we are now aware that since the 1960s there has been a steady increase in the proportion of children suffering from atopic allergic diseases including asthma [13]. Epidemiological studies in Japan, where diesel-powered cars are even more popular than in Europe, have shown that people who live within 200 metres of main roads are much more likely to develop allergy to cedar pollen [14]. Taken together, these concerns have led to an intense research effort aimed at identifying the health hazards of modern forms of air pollution and in particular the ways in which particulate matter pollution might influence the airways, either directly or via perturbation of the immune system.

Several studies have suggested that diesel exhaust particles may act as adjuvants for pollen allergy, either by influencing antigen presentation, by modulating the downstream events such as IgE switching or by acting as vectors for submicronic fragments of pollen grains which would otherwise be too small to deposit in human airways. In mice, it has been shown that diesel exhaust particles administered by the nasal route enhance IgE production *in vivo* [15], while in man, aromatic hydrocarbons from diesel exhaust have a direct effect on B-cells, leading to enhanced IgE production *in vitro* [16].

Another possible mechanism by which pollution may influence the development of allergy is by physical interaction between pollutants and pollen grains. Behrendt has presented data suggesting that pollen from trees growing in cities may be more allergenic, and that the allergenic molecules are more readily released onto the surface of the pollen grain when these are exposed to gaseous pollutants [17].

The aerodynamic diameter of grass pollen grains is usually in the 20–50 μm range. Particles of this size impact in the upper airways and will not be carried out to the small airways where the asthmatic reaction typically occurs. It is now well established that pollen grains may disintegrate and release allergenic molecules of particles in the submicronic range [18–20]. In part these seem to arise from rupture of pollen grains on exposure to rain, yielding

starch grains of 0.5 to 2.5 μm diameter [21]. These can be inhaled but are too small to deposit in the airways. Relatively little grass pollen allergen can be found in the respirable range (2.5 to 10 μm) [18].

In this issue of the Journal, Knox and co-workers demonstrate that purified grass pollen allergen molecules (Lol pl) bind to DEP when incubated in fluid phase *in vitro* [22]. They postulate that this mechanism could allow grass pollen allergens to be concentrated onto DEP of respirable sizes and then be carried into the airways to induce allergic symptoms. Interestingly Lol p5 molecules did not bind to DEP. Lol pl molecules are more glycosylated than Lol p5 and negatively charged at pH 6.8, whereas Lol p5 is a basic protein and thus positively charged at pH 6.8, suggesting that either glycosylation or charge are important determinants of grass pollen allergen binding to DEP.

This study is important because it provides clear experimental evidence that DEP can bind pollen allergens and thus gives a firm basis for the theory that asthma outbreaks associated with thunderstorms [23] might be triggered by sudden exposure to pollen allergens carried into the lung on DEP and other particles. This study opens the door to further work to determine firstly whether this mechanism operates in the atmosphere and secondly whether cellular immune responses to the DEP-allergen agglomerates are skewed towards IgE production.

These effects are over and above the direct effects of diesel exhaust on human airways. In collaboration with colleagues at the University of Northern Sweden and St Thomas Hospital, London, we have recently shown that 1 hour's exposure to diluted fresh diesel exhaust causes an influx of neutrophils and upregulation of endothelial adhesion molecules in bronchial biopsies obtained from normal, non-asthmatic volunteers 6 hours after exposure [24]. The timing of the rise in allergic disease is not consistent with being caused by diesel exhaust as the increase in allergies preceded the recent increase in new diesel cars, but taken together, the scientific evidence is beginning to suggest that diesel engines may not be the solution to our concerns about emissions from petrol-driven cars. Doctors and legislators should be careful about making public policy changes in this area as it is clear that there is still a lot to learn about the relative risks of different types of motor vehicle emissions.

References

- Dept of Health Advisory Group on the medical aspects of air pollution episodes. Second report: sulphur dioxide, acid aerosols and particulates. London: HMSO; 1992.
- Aris RM, Christian D, Hearne PQ et al. Ozone-induced airway inflammation in human subjects as determined by airway lavage and biopsy. *Am Rev Respir Dis* 1993; 148:1363–72.
- Balmes JR, Chen LL, Scannell C et al. Ozone-induced decrements in FEV1 and FVC do not correlate with measures of inflammation. *Am J Respir Crit Care Med* 1996; 153:904–9.
- UK Quality of Urban Review Group. Ozone in the United Kingdom 1993. London: Dept of the Environment; 1993.
- Royal Commission on Environmental Pollution. Eighteenth report: transport and the environment. London: HMSO; 1994.
- Diesel working group. Diesel exhaust: a critical analysis of emissions, exposure and health effects. Cambridge, Massachusetts: Health Effects Institute; 1995.
- UK Quality of Urban Air Review Group. Urban air quality in the UK. London: HMSO; 1993.
- Dockery DW, Pope CA, Xu XP et al. An association between air pollution and mortality in six US cities. *N Engl J Med* 1993; 329:1753–9.
- Dockery DW, Pope CA. Acute respiratory effects of particulate pollution. *Annu Rev Publ Health* 1994; 15:107–32.
- Pope CA, Thun MJ, Namboodiri MM et al. Particulate air pollution as a predictor of mortality in a prospective study of US adults. *Am J Respir Crit Care Med* 1995; 151:669–74.
- Pope CA, Dockery DW. Acute health effects of PM10 pollution on symptomatic and asymptomatic children. *Am Rev Respir Dis* 1994; 145:1123–8.
- Dept of Health Committee on the Medical Effects of Air Pollutants. Non-biological particles and health. London: HMSO; 1995.
- Ninan TK, Russell G. Respiratory symptoms and atopy in Aberdeen schoolchildren: evidence from two surveys 25 years apart. *Br Med J* 1992; 304:873–5.
- Ishizaki T, Koizumi K, Ikemori R, Ishiyama Y, Kushibiki E. Studies of the prevalence of Japanese cedar pollinosis among residents in a densely cultivated area. *Ann Allergy* 1987; 58:265–70.
- Takafuji S, Suzuki S, Koizumi K et al. Diesel exhaust particulates inoculated by the intranasal route have an adjuvant activity for IgE production in mice. *J Allergy Clin Immunol* 1987; 79:639–45.
- Takenaka H, Zhang K, Diaz-Sanchez D, Tsien A, Saxon A. Enhanced human IgE production results from exposure to the aromatic hydrocarbons from diesel exhaust: direct effects on B-cell IgE production. *J Allergy Clin Immunol* 1995; 95:103–15.
- Behrendt H, Becker WM, Friedrichs KH, Darsow U, Tomingas R. Interaction between aeroallergens and airborne particulate matter. *Int Arch Allergy Appl Immunol* 1992; 99:425–8.
- Spieksma FTM, Kramps JA, van der Linden AC. Evidence of grass pollen allergenic activity in the smaller micronic atmospheric aerosol fraction pollen concentration. *Clin Exp Allergy* 1990; 20:273–80.
- Spieksma FTM, Nikkels BH, Dijkam JH. Seasonal appearance of grass pollen allergen in natural, pauci-micronic aerosol of various size fractions. Relationship with airborne grass pollen concentration. *Clin Exp Allergy* 1995; 25:234–9.
- Emberlin J. Plant allergens on pauci-micronic airborne particles. *Clin Exp Allergy* 1995; 25:205.
- Sulphioglu C, Singh MB, Taylor P. Mechanism of grass pollen-induced asthma. *Lancet* 1992; 339:569–72.

- 22 Knox RB, Sulphioglu C, Taylor P et al. Major grass pollen allergen Lol p1 binds to diesel exhaust particles: implications for asthma and air pollution. *Clin Exp Allergy* 1997; 27:246–51.
- 23 Wallis DN, Webb J, Brooke D et al. A major outbreak of asthma associated with a thunderstorm. *Br Med J* 1996; 312:601–4.
- 24 Salvi SS, Blomberg A, Rudell B. et al. Acute inflammatory response in the airways and peripheral blood after exposure to diesel exhaust in healthy human volunteers. *Eur Respir J* 1996; 9(S23):415s.

A. J. FREW & S. S. SALVI
Air Pollution Group
University Medicine (810)
Southampton General Hospital
Southampton
SO16 6YD, UK