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Air pollution: The last 35 years

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Abstract

Perceptions of the effects on health of air pollutants have changed dramatically over the past thirty five years. It is now clear that current, historically low, concentrations of air pollutants have significant effects on health and that these effects bear most heavily on deaths and illness caused by cardiovascular diseases. Epidemiological studies have provided the evidence for these conclusions; toxicological studies have provided explanations, not yet complete, for these effects. Most emphasis has been placed on the effects of airborne particles and the evidence for their effects is convincing. Less attention has been paid to the effects of gaseous air pollutants: it may be that their effects have been, and are, under-estimated. Recent work has allowed the effects on health of air pollutants to be quantified at both a national and global scale. This work has led to the realization that the effects are large and that air pollutants continue to pose an important threat to health.

Keywords

air pollution, particles, nano-toxicology

Human and Experimental Toxicology first appeared in 1979 which was, by coincidence, about the time that the Medical Research Council's Air Pollution Research Unit, then based at St Bartholomew's Hospital in London, closed. The Unit had been established in response to the London Smog of 1952 in which over 4000 more deaths than usually occurred in a period of about 2 weeks in London were recorded.[1] That the smog was responsible for the majority of these deaths was immediately apparent and research into the toxicology of the London smog mixture ran hand in hand with the reductions in emissions of smoke that followed the introduction of the Clean Air Act in 1956. By the 1970s, it was concluded that levels of pollution had fallen dramatically, that epidemiological techniques could no longer demonstrate effects on health, and it was thought that the problem of air pollution in London had been solved.[2] This seemed a reasonable conclusion at the time but was, in retrospect, a mistake. British research into the effects of air pollutants on health ground to a halt. Workers in continental Europe and in the United States continued to study the problem and by the late 1980s it was clear that the then current levels of air pollution remained a hazard to health. Research into the effects of air pollutants on health has expanded exponentially since then, and it is no longer possible to review the entire field in a lengthy monograph, far less in a short paper. The present author joined the field in 1990 and retired in 2011: this article records some of the advances and surprises of those 21 years.

The impact of epidemiological studies

Many epidemiological methods have been applied to the problems of air pollution but time series studies and cohort studies have dominated the field and have had great influence on the development of policy. Time series studies appeared first and showed that daily variations in levels of air pollutants could be correlated with deleterious effects on health. Many hundreds of such studies have been published, and they have produced remarkably consistent results.[3] Studies have shown that effects fall more heavily on those with cardiorespiratory disease.[3] Those studies which bear on the effects of air pollution on cardiovascular disease are reviewed in detail in a publication of the UK Department of Health's Committee on the Medical Effects of Air Pollutants (COMEAP),

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and other reports by COMEAP will be referred to in this article.[4] These studies showed that effects on health occurred at very low concentrations of the pollutants studied. In fact no threshold of effect could be demonstrated; effects were found at the lowest concentrations studied, and these were in the range of from a few to a few tens of micrograms per cubic metre ($\mu g/m^3$). Such findings were startling and led to questions regarding their validity. Had confounding factors been taken, adequately, into account? Did the correlations reflect causal associations? Debate was brisk. It rapidly became clear that the consistency of the findings, their coherence across different end points and the temporal plausibility of the findings argued for a causal interpretation. Biological plausibility? Well, that was lacking; at least it was seen to be lacking by some.

Cohort studies followed: The Harvard Six Cities Study and then the American Cancer Society (ACS) cohort study led the way,[5,6] These studies showed that long-term exposure to low concentrations of fine particles was clearly associated with an increased risk of death from cardiopulmonary disease. These studies were reanalysed under the aegis of the US Health Effects Institute and found to be sound.[7] Furthermore, it was found that the burden of the effect fell on cardiovascular disease. This, too, was startling: it had been assumed that effects on the respiratory system were more likely, but it appeared that the lung was more the portal of entry for the toxicants, or perhaps the transducer, than as their target. Yet more surprising was the scale of the effects. It appeared that a 10 $\mu g/m^3$ increment in long-term average concentration of fine particles ($PM_{2.5}$: the mass concentration of particles generally less than 2.5 μm aerodynamic diameter) was associated with a 9% increase in the risk of death from cardiovascular disease at all adult ages. This coefficient was at least 10 times larger than the coefficient linking daily PM_{10} (the mass concentration of particles generally less than 10 μm aerodynamic diameter), and all, non-accidental, cause mortality. The availability of such coefficients led to estimates of the burden on public health imposed by exposure to air pollution, which is discussed subsequently.

The question of biological plausibility

Of all the common air pollutants, most emphasis has been placed on particles. This is unfortunate and has led to a lack of progress as regards the mechanisms of effects of low concentrations of the major gaseous air pollutants: nitrogen oxides, sulphur dioxide and ozone. What needs to be explained? Toxicologists think in terms of dose. Let the ambient concentration of particles monitored as $PM_{2.5}$ be 10 $\mu g/m^3$, and let the daily inspired volume be 20 m^3, then the daily dose, if all the inhaled particles were deposited (which they are not) would be 200 μg. That is, 200 μg/day of a mixture of carbon, inorganic salts, silicaceous material and traces of organic compounds including such known toxicants as polycyclic aromatic hydrocarbon compounds. To be asked to accept that such exposures can kill is to be asked to accept quite a lot. But what is the alternative? Are the results of all the epidemiological studies in some way false? This seems unlikely.

In 1995, Seaton and his colleagues proposed a new theory: in essence, this stated that the number of particles inhaled rather than the mass of particles was important, that very small particles could either pass into the blood or trigger reactions in the lung with knock-on effects in the blood and that effects on the cardiovascular system should be expected .[8] Oberdörster, the doyen of particle toxicologists, together with his colleagues, proposed a similar theory at about the same time.[9] Evidence supporting this conjecture accumulated, and it would be fair to say that the current high level of interest in nanotoxicology has arisen from this work.[10] Modelling has supported the importance of dose expressed in terms of particle surface area rather than mass.[11]

Other workers have suggested that metallic species play an important role: Lippmann's studies of the importance of nickel have been instructive and may other workers have contributed.[12,13,14] Free radicals! These have been seen as the key extracellular or intracellular products which, when produced by particles, lead to pathological or at least pathophysiological effects.[15,16,17] Perhaps the metals act as catalysts, and if so, the mass of metal might be unimportant, that is, the catalyst need not be used up whilst catalysing the production of free radicals.

Other workers have focused on the effects on the heart that might be caused by changes in functioning of the autonomic nervous system. Changes in heart rate variability have been recorded in volunteers exposed to particles and in epidemiological studies of the effects of increases in ambient concentrations of particles.[18–20] In some studies, but not all, increases in ambient concentrations of particles have been linked with an increased frequency of triggering of implanted defibrillators.[21]

Blood viscosity and levels of fibrinogen and other plasma proteins have been related to ambient concentrations of particles.[22–25] Seaton and his colleagues

have shown that the red cell count is inversely related to ambient particle concentrations, suggesting trapping in the pulmonary circulation.[26] Künzli and colleagues have shown a link between exposure to air pollutants and the development of atherosclerosis: Lund et al. have investigated pathways that may account for such effects.[27,28]

All these results are reviewed in detail by Brook et al. in a series of definitive reports.[29] Encouraging though all this is, the exact mechanisms underlying the effects of particles reported in epidemiological studies remain unknown. Pope and Dockery have provided an overview of distinction.[30]

Implications for particle toxicology in general

The effects on health of short- and long-term exposure to low concentrations of ambient particles were not predicted by toxicological studies: toxicological studies have, rather, been helpful in suggesting mechanisms to explain the epidemiological findings discussed above. This observation may have far-reaching implications when particles of novel composition and size are introduced into the environment. As regards the nanoparticles, a cautious approach has been advocated, especially in the light of evidence to show that carbon nanotubes have asbestos-like activity.[31–33] In looking for the effects of exposure to ambient particles, one might wonder whether sentinel species could help. Not much work has been done on the effects of ambient particles on non-laboratory animals but Calderón-Garcidueñas and her colleagues have shown inflammatory and degenerative effects in the brains of dogs exposed to pollution in Mexico City.[34] Effects of nanoparticles on fish and on invertebrates have been discussed by Oberdörster et al.[10] Effects on plants are out with the scope of this article, but Manning and Feder have contributed a useful monograph on the subject that reports a wide range of effects.[35] It is interesting to note that plane trees were thought to withstand the smogs of London better than other trees on the grounds that they shed, periodically, their heavily contaminated bark thus removing the accumulating soot.

Counting the cost to public health

Let us accept that long-term exposure to 10 $\mu g/m^3$ $PM_{2.5}$ is associated with a 6% increase in the risk of all-cause mortality (other coefficients could be chosen). Let us assume that the annual average concentration of particles monitored as $PM_{2.5}$ is about 10 $\mu g/m^3$. Then we could say that 6% more deaths occur than that would occur if there were, or rather if there had been, no exposure to such particles. Simple calculation suggests that such exposure contributes about 29,000 deaths/year in the UK. If the time series coefficients are employed much lower figures are obtained: perhaps 6000 deaths/year. The figure of 29,000 deaths is described by epidemiologists as the 'attributable deaths': the effects that can be attributed to exposure to fine particles. But is this the best way of expressing the effect? COMEAP has argued that it is not and that more meaningful, albeit perhaps less striking, estimates can be produced by application of life table analysis. This is an actuarial approach in which cohorts of people are, so to speak, followed through time in an arithmetic calculation. The baseline hazard rates for each age group are known, and these can be increased or decreased according to the assumptions regarding levels of particles. These techniques were deployed in a major report published by COMEAP in 2010.[36] It was concluded that:

> As a central estimate we conclude that anthropogenic [man–made] PM2.5 at 2008 levels (8.97 $\mu g/m^3$ in the UK) is associated with an effect on mortality equivalent to nearly 29,000 deaths at typical ages of death in 2008 in the UK and an associated loss of total population survival of 340,000 years and an average loss of between three and four months of life expectancy in Scotland and Northern Ireland and between six and seven months in England and Wales, reflecting differences in the levels of anthropogenic PM2.5 to which these populations are exposed. (page 5, para 18)

These are striking findings. Yet more striking are the results of a calculation of the global burden of disease due to outdoor air pollution.[37]

Conclusions

It is clear from the above that current, historically low, levels of particulate air pollution in the United Kingdom have a major impact on public health. The effects of the major gaseous air pollutants have not yet been quantified. In addition, it has become clear that the concept of 'standards' taken as representing 'safe' levels of exposure is flawed: epidemiological studies suggest no thresholds of effect and thus no 'safe' levels can be proposed. Of course targets can be proposed and act as a spur to policy development. Further reductions in ambient concentrations of air pollutants may well be

expensive and a balancing of costs and benefits will be required. Only by better quantitative estimates of the impacts on public health of air pollutants will the benefits side of the equation be adequately represented.

Conflict of interest

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