Hypothesis

Particulate air pollution and acute health effects

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Summary

Epidemiological studies have consistently shown an association between particulate air pollution and not only exacerbations of illness in people with respiratory disease but also rises in the numbers of deaths from cardiovascular and respiratory disease among older people.

Meta-analyses of these studies indicate that the associations are unlikely to be explained by any confounder, and suggest that they represent cause and effect. We propose that the explanation lies in the nature of the urban particulate cloud, which may contain up to 100000 nanometer-sized particles per mL, in what may be a gravimetric concentration of only 100–200 μg/m3 of pollutant. We suggest that such ultra-fine particles are able to provoke alveolar inflammation, with release of mediators capable, in susceptible individuals, of causing exacerbations of lung disease and of increasing blood coagulability, thus also explaining the observed increases in cardiovascular deaths associated with urban pollution episodes.

This hypothesis is testable both experimentally and epidemiologically.

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In the 1940s and 1950s, coal was the major fuel for industrial and domestic use, and cities were frequently affected by winter smogs, when temperature inversions trapped smoke close to ground level and the air contained high concentrations of soot, sulphur dioxide, and other pollutants. One such episode, in London in 1952, was associated with excess deaths from respiratory and cardiovascular causes.[1] Research at that time, recently reanalysed,[2] showed an association between particle and sulphur dioxide concentrations in the air and risks of death and acute respiratory disease. The UK Clean Air Act in 1956 led to reduction in urban pollution and elimination of winter smogs. The causes of the excess deaths were never explained, but it was believed that the problem had been eliminated.

Two facts make it necessary to question this assumption: the increase in motor vehicles on roads world-wide with the consequent rise in exhaust emissions, and evidence of continuing associations between air pollution and ill-health. The former has resulted in a change in the type of pollution in cities, and the latter has shown effects on health at levels of pollution previously considered harmless. Associations have been shown between overall mortality and episodes of respiratory disease, and concentrations of small particles measured in the microgram range. These findings have encountered some scepticism, partly because the concentrations of particles at which effects seem to occur are low by comparison with those to which many people are exposed in industrial workplaces without apparent harm; and partly because no plausible hypothesis has yet been advanced to explain the associations. We propose such an hypothesis.

Studies in fourteen different locations have shown that overall daily mortality increases as the concentration of small particles in the air rises.[3,4] The relationship is present across a wide range of climatic conditions and meta-analysis has shown that atmospheric temperature or other pollutants are unlikely to explain the association.[3] Where specific causes have been examined, a significant excess of cardiovascular as well as respiratory deaths related to particulate pollution has been found.[5,6] The strongest associations are in older individuals and in smokers. There is also evidence linking particulate air pollution with acute attacks of asthma[7] and other respiratory diseases.[8–11]

Particles in the air

Particulate air pollution has been traditionally measured by drawing air through a filter paper and measuring the density of the black stain, the "black smoke method". However, most urban pollution is now derived from vehicle exhausts and is less black. Increasingly, therefore, it is being measured by the mass of particles that pass through a size-selective orifice with a 50% collection efficiency cut-off at 10 μm aerodynamic diameter (PM10), chosen to represent those particles most likely to reach the lung acinus. Measurements of black smoke or PM10 are both expressed in μg/m³, but do not measure quite the same thing. Nevertheless, the epidemiological relation discussed above in general hold true whichever method is used.

Studies of earlier London urban pollution showed particles to be predominantly very small; whilst half the mass comprised particles less than 1 μm in diameter, half by number were less than 0·1 μm.[12] As many as 150 000 particles were found per mL. They were predominantly acidic, the pH of smog during episodes sometimes being as low as 2. There are also large numbers of small particles in the rural atmosphere, averaging 5000–10 000 per mL and rising to 25 000–30 000 per mL when influenced by traffic 1 km distant.[13] Studies in the UK (Jones M, Harrison RM, Dept of Environmental Health, University of Birmingham, UK, personal communication), with a condensation nucleus counter, have shown particle counts in Birmingham of 1000–50 000 per mL, sometimes rising to 100 000 per mL. Taking the latter figure, we calculate that during a pollution episode each lung acinus could receive on average some 30 million particles and each alveolus about 1500 particles every 24 hours, about 50% being deposited. Since ventilation is not evenly distributed, especially in chronic lung disease, some alveoli would receive much larger doses.

The chemical composition of urban particulate clouds varies considerably,[14] but the fine fraction, below about 2·5 μm diameter, to which PM10 approximates, is about half carbon and half salts, mainly ammonium sulphate and ammonium nitrate. In urban air, the particles are derived mostly from combustion, especially by diesel vehicle engines, and the carbon has chemicals adsorbed onto its surface. Very small particles, below about 1 μm in diameter, may remain suspended for weeks, whereas those greater than 2·5 μm are removed by settling and by rain in a matter of hours. A cloud of the finest particles will thus drift for many miles and may cause pollution across national boundaries. Moreover, very fine particles readily penetrate into buildings, and most indoor environments are unlikely to provide substantial protection from the risk of inhaling them. Indeed, it has been shown that indoor personal monitoring samples may contain as much chemical particulate matter as is found by outdoor fixed-point sampling in the same general area.[15]

At present, PM10 is measured in nine UK cities. Concentrations recorded to date indicate average values over a day of around 15–35 μg/m³ with daily maxima of up to 70 μg/m³. Meta-analysis of epidemiological data from the USA has suggested that rises of 10 μg/m³ are accompanied by an increase in relative risk of mortality of about 1% in the exposed population,[3,16] including elevated risks from both respiratory (around 3·4%) and cardiac (around 1·4%) causes. The lower percentage increase in cardiovascular deaths represents a higher absolute total, since these deaths are much more frequent. Other studies have shown rises in emergency-room visits for asthma and increases in hospital admissions for respiratory diseases when PM10 rises.[9,16,17] These findings imply an important effect on public health.[11] Much higher concentrations of particles occur in some of the world's largest cities, and here the effects on the health of populations already having a high prevalence of respiratory disease may be particularly important.

In general, studies of industrial cohorts have not shown increases in overall mortality rates even in workers exposed to high gravimetric concentrations of dust.[18,19] Any hypothesis explaining the observed associations between air pollution, morbidity, and mortality must take account of this fact. It must also explain the association of inhaled particles with cardiovascular and respiratory disease.

If epidemiological association between particulate pollution and disease is causal, it is likely that part of the explanation lies in the fact that the general population includes a much higher proportion of people who, by reason of arteriosclerosis or chronic airway disease, are at increased risk of death or exacerbation of their illness when subjected to environmental change than do industrial populations. The other part of the explanation must lie in the nature of the particles. A key point is that the urban pollution cloud comprises predominantly very small acidic particles, many of them in the nanometer range which readily penetrate indoors and persist for long periods in air, whereas industrial dust clouds consist mainly of much larger particles usually formed by the abrasion of rocks.

How particles may cause harm

About 50% of nanometer particles are deposited by brownian movement. Soluble particles will increase in diameter by absorption of water as they pass down the airway, but on reaching the alveoli they make contact with a water-repellant surface and will be handled by the lung's defences like other particles of similar size. Insoluble particles are predominantly carbon, of complex shape and high surface-to-volume ratio, and will be handled similarly. There is evidence that particles below about 100 nm in diameter behave differently from larger respirable ones and a particle which is non-toxic in the micrometer size range may be toxic in the nanometer range. Thus, rats exposed to equal weights of titanium dioxide in two aerosol size ranges, fine and ultra-fine (around 0·25 and 0·02 μm, respectively), retain more ultra-fine particles in the interstitial tissue of the lung, developing a marked airspace inflammatory response.[20,21] This interstitial retention probably arises from the failure of alveolar macrophages to phagocytose the large numbers of small particles, together with the action of surfactant in impelling them into the alveolar space.[22] These studies were carried out at a high airborne-mass concentration, but teflon fume particles, 30 nm in diameter at only 200 μg/m³, have also been shown to cause acute pulmonary toxicity in rats.[23] The teflon-generating system produces more ultra-fine particles than does the titanium dioxide system. It is part of our hypothesis that very small but chemically reactive particles in urban air pollution produce such a reaction in human beings. That transport of chemicals on the surface of particles may be important in the cause of lung inflammation has been shown in recent studies in which iron complexed on the surface of fly-ash particles promoted oxidative lung injury, and this effect was reduced after removal of surface iron by washing.[24]

Whatever the precise mechanism of induction, we propose that alveolar inflammation provoked by ultra-fine

particles, in addition to promoting exacerbations of lung disease, has an additional effect on the coagulability of blood, increasing the susceptibility of individuals to acute episodes of cardiovascular disease. Several haematological factors, including plasma viscosity, fibrinogen, factor VII, and plasminogen activator inhibitor, are not only known to be predictive of cardiovascular disease[25] but also rise as a consequence of inflammatory reactions. Such low-grade inflammation may in part be responsible for the otherwise unexplained variations in fibrinogen and white-cell counts seen in the general population.[26] Low-grade inflammation may be particularly important in altering the coagulability of blood as a result of activation of mononuclear cells in the lung.[27] Activated white cells have been shown to initiate and promote coagulation[28] by releasing tissue factor, which initiates the conversion of factor X to factor Xa, the first reaction of the final common clotting pathway.[29] Alveolar inflammation may also cause the release of interleukin-6 from macrophages and thus stimulate hepatocytes to secrete fibrinogen.[30]

The hypothesis

We propose that acidic ultra-fine particles characteristic of air pollution provoke alveolar inflammation which causes both acute changes in blood coagulability and release of mediators able to provoke attacks of acute respiratory illness in susceptible individuals. The blood changes result in an increase in the exposed population's susceptibility to acute episodes of cardiovascular disease; the most susceptible suffer the most.

This hypothesis, being based on the number, composition, and size—rather than on the mass—of particles, accounts for the observed epidemiological relations, and explains excess deaths occurring in people who may be indoors, and why similar serious effects are not seen in industrial workers exposed to much higher concentrations of dust measured by weight. By drawing attention to the possible effects of alveolar inflammation on blood coagulability, we propose an explanation of the observed and hitherto unexplained association of pollution episodes with cardiovascular deaths.

The hypothesis is testable epidemiologically, by investigating relations between blood coagulability and changes in air-particulate concentrations; and experimentally in rats by studying the airspace inflammation induced by ultra-fine particles and its effects on mediator release and coagulation factors.

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Functional psychiatric disorders of the elderly

Edited by Edmond Chiu and David Ames. Cambridge: Cambridge University Press. 1994. Pp 623. £65/$100. ISBN 0-521431603.

To outsiders, psychogeriatrics without dementia is like a burger without beef. There are two main reasons why dementia, particularly Alzheimer's disease, has been centre stage since the emergence of old-age psychiatry as a subspecialty. First, the morbidity of dementia is not only massive but overt. Second, there has been fundamental and clinically important progress in understanding the molecular genetics and neurobiology of Alzheimer's disease. As a result, dementia has grabbed the headlines, the funding, and the book market. However, the prevalence of other psychiatric disorders does not as a rule decline as people get old. Depression in particular remains extremely common, is often unrecognised, and is treated inadequately if at all. This volume seeks to redress the perceived imbalance by creating a vegetarian burger based upon the neglected functional psychiatric disorders of old age. For the book's purposes, "functional" means everything except dementia and delirium.

Surprisingly few epidemiological, aetiological, or even therapeutic studies have focused on functional psychiatric disorders in the elderly. Thus, much of the text details syndromes and issues that are common to adult psychiatry and the reviews are largely descriptive. Where there are opportunities to expand upon elderly-specific data, these are well taken. The chapters on late-onset schizophrenia, pseudo-dementia, and affective disorders after stroke are especially good. It may not be fortuitous that these are the syndromes sitting closest to, if not yet defecting into, the organic domain, allowing for a welcome feeling of substance. Elsewhere the book is unnecessarily long. This is exemplified by 12–20 pages each on family therapy, group psychotherapy, and music therapy for the elderly—treatments that seem to lack any evidence for efficacy. By comparison the 12 pages on drug treatments are inappropriately brief given their undoubted importance. The discursive approach may strengthen the book's appeal to non-medical members of multidisciplinary teams for whom the lack of data and hard science may be less disconcerting.

There are other multiauthor texts on psychogeriatrics, notably *Psychiatry in the Elderly*, edited by Jacoby and Oppenheimer (Oxford University Press, 1991). In many ways the texts are similar in terms of clarity, breadth, and depth of coverage. The glaring difference is, of course, the inclusion of organic disorders in the Jacoby and Oppenheimer book which makes it a genuine psychogeriatrics textbook. Chiu and Ames' text ultimately suffers by comparison; its restricted scope is not compensated for by the greater space it can devote to the functional disorders since there is much prose but little valuable information in the extra pages.

To return to the metaphor, the chefs have few tasty ingredients (data) to work with and the fare is therefore generously portioned but nutritionally weak. However, for a departmental library, a combination of this book with an organic counterpart such as *Dementia,* edited by Burns and Levy (Chapman and Hall, 1994) would provide truly comprehensive coverage of both facets of psychogeriatrics.

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Unhealthy charities

Hazardous to your health and wealth.—*James T Bennett, Thomas J DiLorenzo. New York: Basic Books. 1994. Pp 269. $25. ISBN 0-465029108.*

Coming in the wake of financial scandals concerning one of the world's biggest charities, the United Way of America (UWA), this book's title and subtitle promise more of the same in its investigation of the three large American voluntary health organisations or "charities" as the authors like to call them: the American Cancer Society (ACS), the American Heart Association (AHA), and the American Lung Association (ALA). Unfortunately, if there are some substantial, although not always original, criticisms of these three health charities, the best documented evidence of scandal in the book comes from largely rehashed information concerning the UWA and not-for-profit American hospitals.

The book's greatest use is in focusing critical evaluation of these charities in several areas including public education, professional education, research, public service, and community service. It then looks at how money is spent in each area. In the professional education area, for example, the authors properly criticise subsidising the education of American physicians, whose average net income is well above $150 000 a year, with health charity money, most of which comes from people of far smaller financial means. In the area of disease research, the authors point out the tight interlock between the ACS and the federal National Cancer Institute (NCI), finding that ACS funding of research mainly goes to give seed grants to investigators who will thereby be more able to tap into NCI funding. At the level of finances, there is sharp criticism of all three charities' desperate appeals for contributions despite 1991 fund balances or net worth of $491·7 million (ACS), $264·6 million (AHA), and $136·2 million (ALA).

The main proposed remedy—making public more of the data on programmes and finances of these organisations—is an important one. Public accountability, the relative lack of which is at the core of the problems of these organisations, is not really possible without more of this information being easily available.

There are four areas of greatest weakness in *Unhealthy Charities.* First is the view that, in contrast to these charities, the for-profit sector is a model of efficiency and accountability because, ultimately, "The captain is the consumer". Second is the belief that the "charity" or services-to-the-needy function of these organisations