Non-biological particles and health / Committee on the Medical Effects of Air Pollutants ; chairman, Stephen Holgate ; chairman of the Sub-Group on Non-Biological Particles and Health, Robert Waller.

DEPARTMENT OF HEALTH

Committee on the Medical Effects of Air Pollutants

NON-BIOLOGICAL PARTICLES AND HEALTH

HMSO

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Chairman: Professor Stephen Holgate

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Figure 5.1 provided by Dr P Norman, CBDE.

Contents

Chapter 1

Executive Summary

1.1 The Department of Health (DH) asked the Committee on the Medical Effects of Air Pollutants (COMEAP) to advise on the possible effects of outdoor airborne non-biological particles on health. The Committee formed a Sub-Group which reviewed the literature in detail and drafted this report. The report has been endorsed by the Committee.

1.2 The terms of reference of the Sub-Group were to advise on:

a. The current state of knowledge of effects of variations in mass concentrations of suspended particles upon health (excluding occupational exposures).

b. The value of the measure of particle levels (PM_{10}) used by the Department of the Environment's (DoE) Automated Urban Network (AUN) monitoring sites as an index or indicator of levels of airborne particles of significance to health.

c. Gaps in current understanding and the need for future research.

1.3 The Sub-Group has reviewed in detail the available information on levels of particulate air pollution in the United Kingdom (UK) and the evidence available from epidemiological studies conducted mainly in other countries regarding the likely effects of such pollution on health. The Sub-Group has also reviewed evidence regarding the likely mechanisms of effect of such particles. The report has not dealt with occupational exposure to particles or to tobacco smoke. Having considered the Sub-Group's work, the Committee's conclusions are summarised below.

1.4 There is clear evidence of associations between concentrations of particles, similar to those encountered currently in the UK, and changes in a number of indicators of damage to health. These range from changes in lung function through increased symptoms and days of restricted activity to hospital admissions and mortality.

1.5 The evidence regarding these associations has been gathered from a range of well conducted epidemiological studies which have mainly been undertaken in the United States (US) and recently in Europe. The consistency of the associations demonstrated by these studies is notable especially as regards mortality, though the reported effects on health of day-to-day variations in concentrations of particles are small in comparison with other uncontrollable factors, eg, seasonal variations or variations in temperature. Considerable coherence of results across health endpoints has also been shown. The few studies which have been conducted in the UK have tended to confirm the findings of studies reported from other countries.

1.6 There is no clear evidence that associations with effects on health are restricted to specific types of particles. Epidemiological studies have demonstrated associations between effects on health and particles from a wide range of sources. These include primary emissions from motor vehicles, industrial sources or coal fires and secondary aerosols derived from gaseous emissions, including sulphur dioxide and oxides of nitrogen, from industrial and vehicular sources. In the absence of strong evidence on the relative effects of different particles within the respirable range, it seems reasonable, at present, to base policy on PM_{10} measurements.

1.7 The principal question to consider in reviewing the rapidly expanding literature on health effects of suspended particulate matter is whether the statistical associations demonstrated indicate a causal role. There is certainly a remarkable degree of consistency and coherence in the direction and magnitude of findings from a diversity of studies, carried out in different localities in the US and elsewhere, with a

range of different health indicators and varying sources of pollution. We consider that the reported associations between levels of particles and effects on health principally reflect a real relationship and not some artefact of technique or the effect of some confounding factor. The indications that the association is likely to be causal are certainly strong.

1.8 We conclude that, in terms of protecting public health it would be imprudent not to regard the associations as causal. We also believe that the findings of the epidemiological studies of the acute effects of particles, which have been conducted in the US and elsewhere, can be transferred to the UK, at least in a qualitative sense. However, we consider that there are insufficient UK data available to allow direct extrapolation and reliable estimation of the size of the effects in the UK.

1.9 It would be possible, for any health effect of interest, to take a weighted average of the results of well-conducted published studies and apply this to conditions in the UK. [This would usually imply conversion across different measures of particles.] Thus, the relative risk calculated by Schwartz[1] with regard to effects of particles on mortality was 1.06 (confidence interval [CI]: 1.05-1.07) for a 100 $\mu g/m^3$ change in total suspended particles, equivalent to some shortening of life in approximately 1% of daily deaths per 10 $\mu g/m^3$ increase in PM_{10}. Application to the UK of the results even of such structured meta-analyses does not formally take account of uncertainties in extrapolating to different air pollution mixtures (with generally lower concentrations of suspended particles), climate patterns and at-risk populations. Because of these uncertainties, we think it would be unwise to offer a single coefficient with regard to effects on mortality or any other index of ill health. The reader is referred to the tables in Annex 8A to Chapter 8 with the warning that the estimates based on studies reported in these tables are likely to provide only a first approximation to the actual effect. Studies should be undertaken urgently to allow better quantitative predictions to be made.

1.10 The only major difficulty in reaching any firmer conclusion about causality is the lack of any established mechanism of action. The mass of suspended particulate matter associated with adverse effects is very small, and while there is evidence relating to acute effects of some components, the fact that in epidemiological studies similar effects have been reported in localities with different types of suspended particulate matter suggests that particles may have a non-specific action. Reported studies indicate a range of effects, from small changes in ventilatory function or exacerbations of asthma through to increases in deaths among the elderly or chronic sick; it does not necessarily follow that the same components would be involved in each effect. The effects have not been explained in terms of the results of conventional inhalation toxicology studies, though few appropriate studies have been reported. It has been suggested, but by no means proven, that ultrafine particles (< 0.05 μm diameter) may play a role. These particles have been shown in recent animal studies to be unexpectedly capable of producing inflammatory reactions in the lungs. Concentrations of such particles would be higher close to sources in the environment because, with time, they would coalesce into larger and more stable forms. They would represent, therefore, only a small proportion of the mass of material measured as PM_{10}, though they would represent a high proportion of the number of particles present.

1.11 It is well established from the reported studies that people with pre-existing respiratory and/or cardiac disorders are at most risk of acute effects from exposure to particles. It has been suggested that these effects occur when air pollution aggravates an acute condition such as a respiratory infection, an attack of asthma or a heart attack in people with pre-existing chronic disease. There is no evidence that healthy individuals are likely to experience acute effects on health as a result of exposure to concentrations of particles found in ambient air in the UK.

1.12 Evidence regarding the effects of long term exposure to particles on health is even less well developed than that regarding the acute effects. The possibility of confounding in such epidemiological studies is considerable and it is difficult to

estimate the exposures of individuals over relevant time periods. Here again, the results of recent US studies reporting associations with mortality, respiratory symptoms and lung function are probably transferable to the UK in a qualitative sense, though confidence in the accuracy of the predictions is lower than for the acute effects of particles.

1.13 Although the evidence is limited, the Committee advises that it would be prudent to consider these associations between long-term exposure to particles and chronic effects as causal.

1.14 There is little evidence to show that exposure to atmospheric particles contributes significantly to the burden of cancer in the UK. The presence of genotoxic carcinogens in particles means that such a contribution cannot be ruled out, although it is likely to be very small.

1.15 In terms of monitoring levels of particulate air pollution in the UK, we support the continued use of automatic measurement of PM_{10}. Measurement of Black Smoke should also be continued. The need to determine the temporal and spatial mass and number distributions of particle sizes is stressed.

1.16 There is a need for research into the effects of particles on health. This research is needed both to improve the predictions of effects which can be made from currently available epidemiological studies and to investigate possible mechanisms of effect. A number of recommendations for research are provided in Appendix 1 of the report.

Conclusions

1.17 The Committee considers that the reported associations between daily concentrations of particles and acute effects on health principally reflect a real relationship and not some artefact of technique or the effect of some confounding factor.

1.18 In terms of protecting public health it would be imprudent not to regard the demonstrated associations between daily concentrations of particles and acute effects on health as causal.

1.19 We find it difficult to reach a firmer conclusion about causality due to the lack of any established mechanism of action.

1.20 We believe that the findings of the epidemiological studies which have been conducted in the US and elsewhere, of the acute effects of particles, can be transferred to the UK, at least in a qualitative sense.

1.21 It is accepted that insufficient UK data are available to establish the reliability of quantitative predictions of the effects of particles upon health in the UK.

1.22 We consider that results of recent US studies of the effects of long-term exposure to particles are probably transferable to the UK though confidence in the accuracy of the predictions is lower than with regard to the acute effects. Although the evidence is limited, we advise that it would be prudent to consider these associations as causal.

1.23 There is no evidence that healthy individuals are likely to experience acute effects on health as a result of exposure to concentrations of particles found in ambient air in the UK.

Reference

1. Schwartz J. Air pollution and daily mortality: a review and meta-analysis. Environ Res 1994; 64:36-52.

Chapter 2

Introduction

2.1 The present report is concerned with effects upon health of "suspended particulate matter" (SPM), comprising solid or liquid material present in the air in particles small enough to remain in suspension for some hours or days, and liable to travel considerable distances from the source. This implies an upper limit, in terms of equivalent aerodynamic diameter, of some 10 to 15 micrometres (μm) and this corresponds fairly closely with the upper limit of material capable of entering the respiratory tract and penetrating as far as the thoracic region. In most circumstances, the major proportion of SPM, in terms of numbers of particles, is present as fine particles with diameters up to a few μm, and much of this material comes directly or indirectly from combustion sources. The size range beyond SPM comprises particles having diameters of some tens of micrometres that will usually deposit close to the source, being referred to as "deposited matter". This is not of concern in relation to respiratory hazards, though some coarse material may at times be carried appreciable distances by the wind and be trapped by some sampling instruments.

2.2 A number of features make the assessment of effects of SPM on health especially difficult:

(i) SPM is not a defined entity—both chemical and physical characteristics vary widely with respect to source, location and time. While detailed studies can be undertaken as research tasks, routine monitoring relates only to some general characteristic, such as mass within a given size range.

(ii) There is no clear indication as to whether adverse health effects represent a non-specific particle effect or responses to particular components.

(iii) Because standard particle sampling devices do not distinguish between particles of biological and non-biological origin, we cannot say with certainty that effects on health seen at a given level of particles are not due to a biological component of the aerosol. However, for the purposes of this report, only non-biological particles are considered.

(iv) Adverse effects that have been reported in association with SPM could also arise through exposure to other pollutants, or be associated with other environmental factors.

(v) There are only limited opportunities for controlled exposure studies to investigate mechanisms and dose/response relationships in support of associations demonstrated in epidemiological studies. Animal experiments, and in some cases controlled human exposures, can be carried out with specific components or types of particulate matter, but it is difficult to simulate in the laboratory the material present in the ambient air.

2.3 Historically, the main component of SPM in urban areas of the UK has been smoke from the inefficient combustion of coal in industrial or, more particularly, domestic appliances. Apart from any rôle in adverse effects on health, it had a major effect on visibility and on the soiling of buildings, clothes and other fabrics. The traditional method of measurement in the UK, dating back to the early years of the present century, has been based on this soiling capacity. This "Black Smoke" assessment involved drawing a measured volume of air through a filter paper, then determining the darkness of the resultant stain, currently with a reflectometer. Concentrations, expressed as $\mu g/m^3$ "equivalent standard smoke" are then determined through the use of standard calibration curves. This remains the basic monitoring method for SPM in the UK and it was the principal measure used in the epidemiological studies carried out in the 1950s and 1960s.

2.4 At that time, 30 to 40 years ago, substantial effects on health were demonstrated in terms of day-to-day variations in morbidity and mortality and in the prevalence of respiratory disease, linked with the mixture of SPM, sulphur dioxide (SO_2) and other associated pollutants from the combustion of coal. These findings were reviewed in an earlier report[1] concerned primarily with the effects of exposure to episodes of high pollution of this type.

2.5 By now much has changed. In most, though not all major urban areas of the UK, coal smoke is no longer a problem, and concentrations of Black Smoke have fallen dramatically. What SPM remains has different origins, with motor vehicles making a proportionately larger contribution than before, along with secondary aerosols derived from reactions between SO_2, nitrogen dioxide (NO_2) and other gases in the air. In absolute terms, whether measured by the Black Smoke or more direct gravimetric methods, concentrations are far below the values commonly seen in former coal smoke days and benefits to amenity, with improved visibility, greater penetration of sunlight and reduced rates of soiling, have been clear-cut.

2.6 While gross adverse effects on health, such as the large increases in daily deaths that stood out clearly in former "smog" episodes no longer occur, there has been increasing concern in recent years about associations demonstrated between current levels of air pollutants, including particles, and a range of health indices. Much of this evidence comes from studies in North America, and the ability to detect relatively small effects depends on careful monitoring of ambient concentrations of particles and the use of advanced statistical analyses of complex data sets.

2.7 Risks of confounding with other factors remain, but if the associations with SPM continue to be supported, the magnitude of some of the effects reported is larger than anticipated from simple extrapolation from those related to coal smoke. This could indicate a greater toxicity of current particles or simply the use of a more appropriate measure of them. There could also have been changes in the susceptibility of the population concerned.

2.8 Regarding the measurement of particles, a revised specification has come into use in the US and is being written into US Air Quality Standards regulations. This measure is referred to as "PM_{10}", the concentration of SPM as determined with sampling instruments having a 50% cut-off point at 10 μm. The need for this arose because earlier regulations were based on total suspended particulates (TSP) determined with high volume samplers that were capable of collecting particles with diameters well beyond 10 μm should they be present, as from wind-blown dust or some coarse industrial emissions close to such sources. Such coarse components, falling more in the range of deposited matter, are not of direct relevance to inhalation risks. Some of the more recent epidemiological studies have included PM_{10} monitoring data, while for some earlier ones, attempts have been made to convert from TSP, Black Smoke or other measures to PM_{10}.

2.9 It is important to recognise that PM_{10}, as with any other measure of SPM, is not a defined entity and under that "umbrella" there remains a wide range of physical and chemical characteristics. The particular problems associated with TSP have not arisen in the UK, since that measure never came into general use. In respect of the particle size range covered, Black Smoke measurements fall within the PM_{10} definition, the 50% cut-off point for the smoke samplers used in the UK having been estimated as 4.5 μm. PM_{10} is not in itself a new concept, but what constitutes this category of SPM has changed greatly over the past few decades.

2.10 Thus the problem of assessing possible effects on health of suspended particles is exceptionally difficult, for not only have confounding factors other than pollution to be considered carefully in each epidemiological study, but the nature of the particles monitored for each published study and the relevance to present day UK environments also have to be taken into account. Studies appearing in the international literature up to May 1995 have been examined for this report. In the succeeding chapters each aspect, including a review of the nature and current levels

of particles, the deposition of particles in the respiratory tract, biological effects of exposure and an appraisal of recent epidemiological studies, is considered to provide advice regarding the protection of public health and to identify research needs.

Reference

1. Department of Health. Advisory Group on the Medical Aspects of Air Pollution Episodes. Second Report: Sulphur Dioxide, Acid Aerosols and Particulates. London: HMSO, 1992.

Chapter 3

The Nature of Airborne Particles

Introduction

3.1 Airborne particles are probably the longest recognised kind of air pollution. Their visible nature, for example, in the form of smoke from fires, makes their presence clearly recognisable, unlike many of the gaseous emissions which do not absorb or scatter light and hence are unseen. Controls on smoke emissions are now rather effective and consequently smoke emissions from sources are less frequently visible, and indeed, visible "smoke" plumes are nowadays often comprised primarily of condensed droplets of water. However, most chimneys and all vehicle exhausts emit particles into the atmosphere during periods of operation, even though these may not be evident to the naked eye. Microscopic particles are very abundant in the atmosphere and although invisible on a very local scale, manifest their presence by their impact upon visibility. In a particle-free atmosphere, visibility would approach 300 kilometres, and reductions from this are the results of natural or man-made particles in the air. Natural particles include water droplets in mists and fogs, although their presence can be enhanced by emissions of particles which act as nuclei upon which the fogs condense.

3.2 Very high loadings of airborne particles can cause extreme reductions of visibility. There are two classic examples of this phenomenon which have very different causes, although both are termed smogs. Examples of the first occurred in London most notoriously during the 1950s and 1960s and arose from particle emissions, mainly from combustion of coal. During cold stagnant weather conditions, fogs condensed on the particles with extreme visibility loss. The simultaneous presence of large amounts of sulphur dioxide (SO_2) and its oxidation product sulphuric acid are thought to have contributed to the very well documented adverse health effects of the London smogs. The second classic case is that of Los Angeles. The Los Angeles smogs are mainly a summer event associated with chemical reactions promoted by sunlight in a mix of pollutants generated largely by motor vehicles and trapped by the topography. In the Los Angeles atmosphere, oxides of nitrogen (NO_x) and sulphur (SO_x) are rapidly oxidised to form nitrate and sulphate particles, which, together with high levels of nitrogen dioxide (NO_2) cause the formation of a dense, brownish haze, also termed a smog.

3.3 Nowadays, airborne particle concentrations in the United Kingdom (UK) are far lower than were present in the 1950s and 1960s and the chemical composition lies somewhere between that of the London smog and the Los Angeles smog. One major difference is that because of changing patterns of fuel use, the black coal smoke particles which were so prevalent in the 1950s now contribute little to urban pollution, whilst the even blacker fine particles from diesel vehicles now comprise the major dark component of the smoke. This is accompanied by sulphates and nitrates, largely generated from oxidation of SO_2 and NO_x, as in Los Angeles, together with industrially emitted particles and wind blown soils and dusts. In some areas, sea spray particles and suspended road salt may also contribute.

Terminology describing airborne particles

3.4 One of the most important distinctions to be drawn in relation to airborne particles reflects their origin. They may be either: *primary*—these are emitted directly from sources such as non-nuclear power stations, motor vehicles and cement factories; or *secondary*—particles formed within the atmosphere from condensation of vapours, or as a result of chemical reaction processes. The most abundant secondary constituent is frequently ammonium sulphate, formed from the reaction of ammonia gas with sulphuric acid, itself a product of atmospheric oxidation of SO_2 gas.

3.5 The main determinant of the behaviour of an atmospheric particle is its size. This is usually expressed in terms of the "aerodynamic diameter" which refers to unit density spherical particles with the same aerodynamic properties, such as falling speed. In practice, except for very dense materials and clusters, the aerodynamic diameter is very similar to the geometric diameter as might be measured with a light microscope or an electron microscope.

3.6 Over the years, many terms have been adopted to describe airborne particles. Some are linked to specific sampling devices, whilst others are connected with human respiratory exposure; not all have single explicit definitions. Terms used here are as follows:

Suspended Particulate Matter (SPM): a general term embracing all airborne particles.

Aerosol: a suspension of particles in a gas.

Total Suspended Particulates (TSP): a term describing the gravimetrically determined mass loading of airborne particles, most commonly associated with use of the United States (US) high volume air sampler in which particles are collected on a filter for weighing.

PM_{10}: particulate matter less than 10 μm aerodynamic diameter (or, more strictly, particles which pass through a size selective inlet with a 50% efficiency cut-off at 10 μm aerodynamic diameter).

Smoke: particulate matter, < 15 μm, derived from the incomplete combustion of fuels.

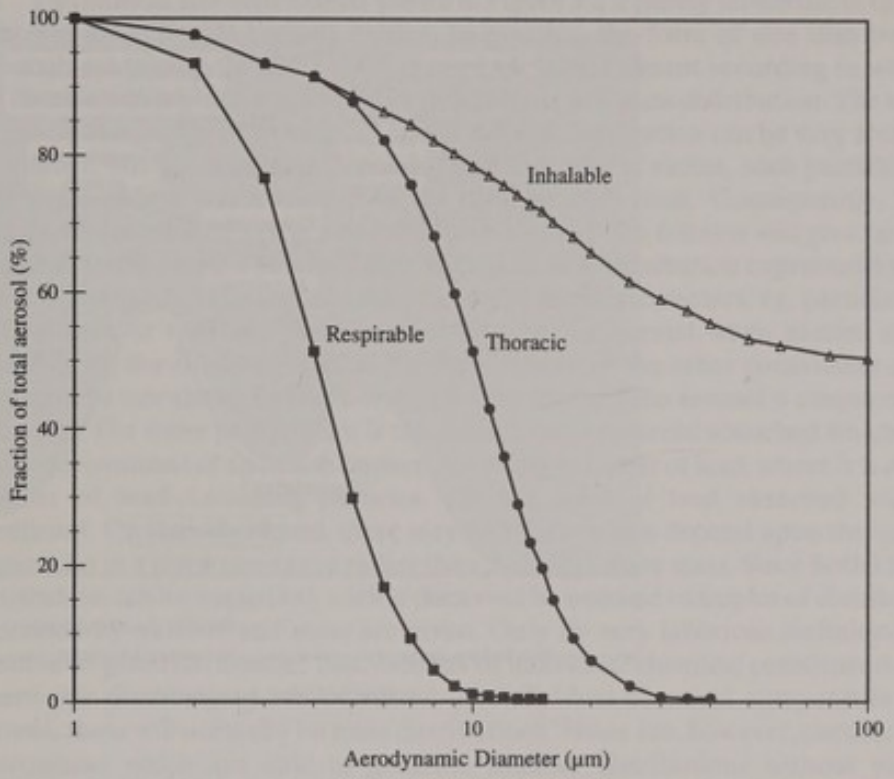
Black Smoke: non-reflective (dark) particulate matter, associated with the smoke stain measurement method, described later.

Inhalable Particles: (also termed inspirable), particles which may be breathed in—"inhalability" is the orientation-averaged aspiration efficiency for the human head.

Respirable Particles: particles which can penetrate to the unciliated regions of the deep lung.

Thoracic Particle Mass: describes that fraction of the particles which penetrates beyond the nasopharynx and larynx. A standard curve of thoracic aerosol as function of particulate aerodynamic diameter takes the form indicated in Figure 3.1.

Figure 3.1 **Curves defining respirable, thoracic and inhalable particle fractions**



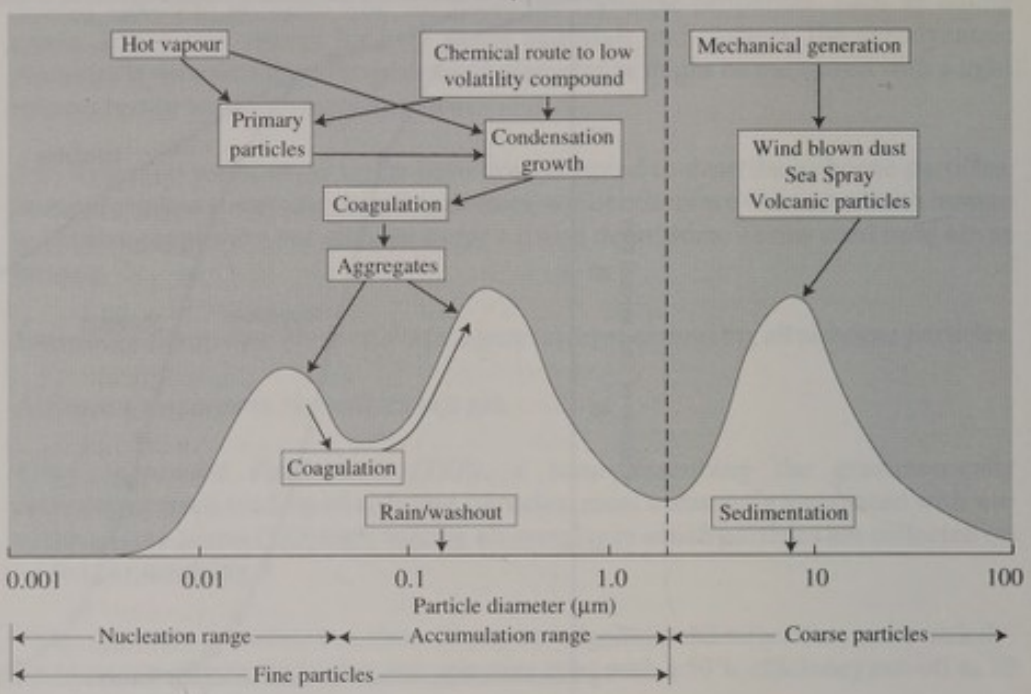
The difference between inhalable and respirable particles arises from their behaviour when they are inhaled. Because of inertial and gravitational effects, very large particles do not readily enter the human nose or mouth. Those that do enter during normal breathing are termed "inhalable". Figure 3.1 shows the efficiency with which particles of different size may be inhaled, according to the curve recommended by the International Standards Organisation (ISO). Particles which pass this first barrier to entry may then deposit in one of three regions, or be exhaled undeposited. The three defined regions of deposition are described as nasopharyngeal, tracheobronchial and alveolar. Both of the former regions are cleared (mixed with mucus) largely to the stomach and components of the particles may be absorbed in the gut or excreted. Particles which deposit in the alveolar, or deepest region of the lung are cleared less efficiently and may be absorbed into the blood stream (eg, lead), or if insoluble and inhaled in sufficiently large amounts, may cause lung disease eg pneumoconiosis, emphysema. Inhalation of some particles may lead to cancer as in bronchial carcinoma induced by inhaled asbestos fibres. Particles capable of entering the alveolar region are termed respirable and a curve indicating the extent to which different particle sizes are typically respirable appears in Figure 3.1. Whilst there is no agreed definition, particles of less than 2.5 μm aerodynamic diameter are frequently described as respirable.

Size distributions of airborne particles

General

3.7 Measurements of particle size distributions usually show up to three groups of particles (or modes), shown schematically in Figure 3.2.

Figure 3.2 **Schematic diagram of a typical atmospheric aerosol particle size distribution, indicating formation pathways**



These are as follows:

— *nucleation mode, < 0.2 μm diameter.* These are particles recently emitted from processes involving condensation of hot vapours (eg, incinerators, smelters), or particles freshly formed within the atmosphere by gas to particle conversion (eg, sulphuric acid particles from SO_2 oxidation). Nucleation mode particles have a rather transient existence, as they rapidly coagulate into larger particles; hence in many situations the nucleation mode is not found;

— *accumulation mode, 0.2-2 μm diameter.* This mode comprises particles which have grown from the nucleation mode by coagulation or condensation of vapours. These are the most stable and long-lived of atmospheric particles with a lifetime of some 7-30 days, as they are not subject to efficient removal by gravitational settling, scavenging by rain, or any of the other mechanisms which remove smaller and larger atmospheric particles;

— *coarse mode, > 2 μm diameter.* These particles are mainly formed by mechanical attrition processes, and hence soil dust, sea spray and many industrial dusts fall within this mode. Because of their large size and high settling speeds, their atmospheric lifetime tends to be short.

A simple distinction is frequently drawn between fine particles, usually < 2 μm diameter and coarse particles, > 2 μm. The former are those most commonly associated with adverse health effects, whilst the latter may make a major contribution to soiling due to their rapid deposition, and to the disamenity consequent upon it. In years gone by, deposition of coarse particles from industry and mining activities was a major cause of local soiling problems; fortunately, due to stricter controls, such problems now occur infrequently.

Measurements of size distribution

3.8 The particle size distribution shown in Figure 3.2 is purely schematic in order to illustrate the different particle modes. In practice, the form of size distributions, although containing the same modes, can look very different according to whether the distribution is plotted as a number distribution or a mass distribution. The reason for this is that particles at the small end of the size distribution can be very abundant in number, but because mass depends upon the cube of radius, such particles may contribute only a small amount of the total aerosol mass. Consequently, a size distribution expressed as the number of particles per size fraction will give far more emphasis to the smaller particles than will occur in a distribution expressed by mass per size fraction. Given that the distribution of some parameters, eg, particle mass, surface area or number, of an aerosol may be log normal when plotted against particle size, the characteristics of the distributions of the other parameters can, in principle, be calculated. In practice, this is difficult since the aerosol is commonly not unimodal. For some pollutants it is the mass of toxic material absorbed which is the major determinant of an health impact. An example is that of lead, where it is not the number of lead-containing particles, but the mass of lead absorbed which is significant. On the other hand, there may be effects which depend upon the number of particles in a given size range rather than their aggregate mass. Since both kinds of distribution can be important, each is discussed below, and examples of distributions expressed by number and mass are given. Only by very laborious techniques is it possible to generate number distributions of individual chemical constituents; thus, where size distributions are expressed for individual chemical components of an aerosol, these will normally be mass distributions. There are, however, particle sizing instruments which are able to generate number distributions without yielding chemical information, and hence it is perfectly possible to express size distributions for the total particle content of an aerosol in terms of number per increment of size.

3.9 Some examples of measured size distributions are presented. Figures 3.3a and 3.3b shows mass distributions for TSP and for lead measured in Cricklewood, North London.[1]

Figure 3.3a **Mass size distribution of total suspended particles, sampled in North London (from Biggins, 1979[1])**

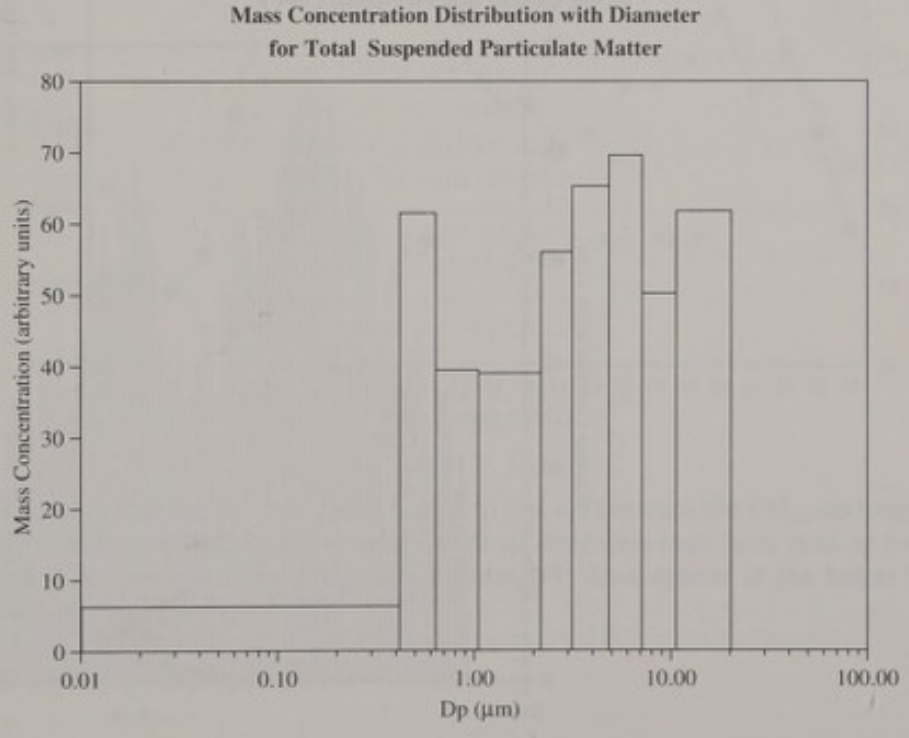
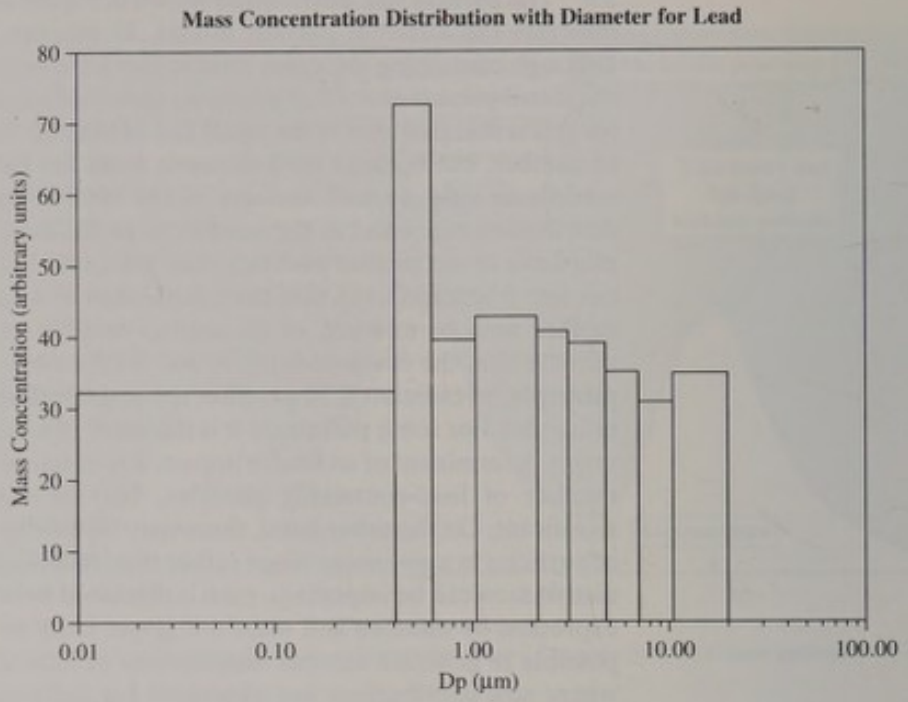
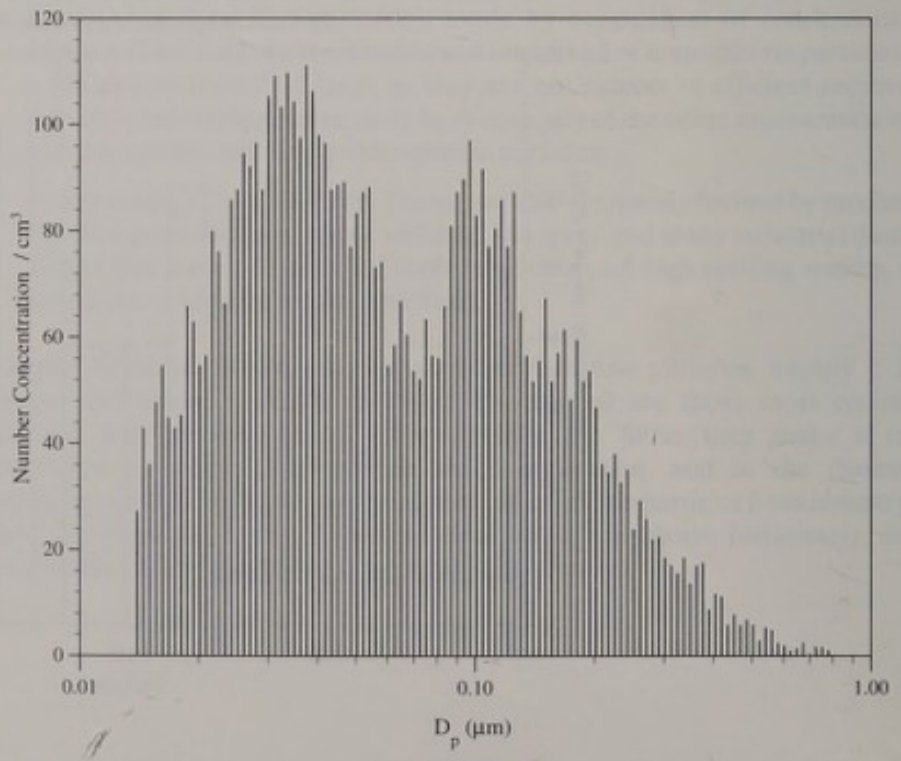


Figure 3.3b **Mass size distribution of lead, sampled in North London (from Biggins, 1979)**



Both particulate matter and lead approximate to a log normal distribution of mass. The lead, which is expected to be in the nucleation and accumulation modes is smaller in size than the total particulate matter as the latter contains a significant proportion of particles in the coarse mode. The mass median aerodynamic diameter is the size below which 50% of the mass of lead or TSP is present, and in this example, the mass median diameter for lead was 0.8 μm and for TSP 2.8 μm. Figure 3.4 shows a number size distribution of total aerosol sampled on the University of Birmingham campus.[2]

Figure 3.4 **Typical number size distribution of airborne particles sampled in Birmingham (from Collins and Harrison, 1994[2])**



This shows two modes centred on 30 nm and 120 nm. Number median diameters vary somewhat with time of day, but are typically of the order of 40-50 nm. A study in

London used electron microscopy to characterise airborne particles, and reported mass median diameters in normal urban air and street samples ranging from 0.4 to 0.8 μm and number median diameter from 0.09 to 0.13 μm.[3]

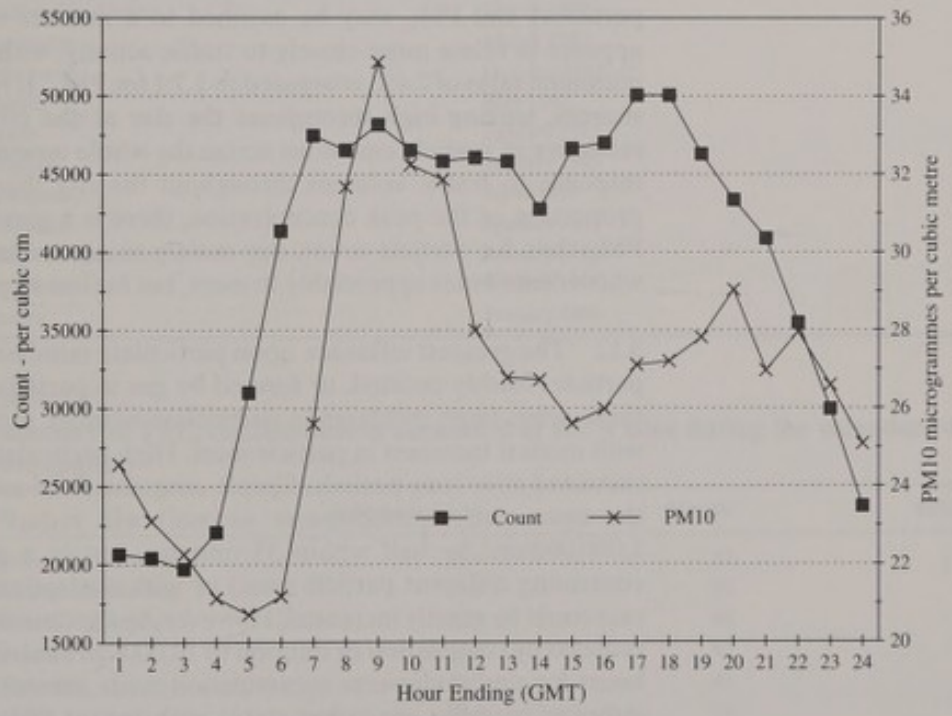
Concentrations of airborne particles

Particle number density

3.10 Number densities can vary enormously depending on the age and source of the airborne particles. Measurements on the west coast of Ireland indicate that "clean" maritime air entering western Europe can contain as little as 200 particles/cm^3. Once over the land there are many sources of primary particles and secondary particulate precursor emissions, and typical number densities of particles measured with a condensation nucleus counter in Birmingham air are of the order of 1000/cm^3 to 50,000/cm^3, although on occasions, concentrations can exceed 100,000/cm^3.[4] Measurements made in London by Waller using electron microscopy revealed concentrations of the order of 10,000/cm^3 at background sites, 30-50,000/cm^3 in street samples, and up to 160,000/cm^3 in samples taken in tunnels and urban fogs.[3]

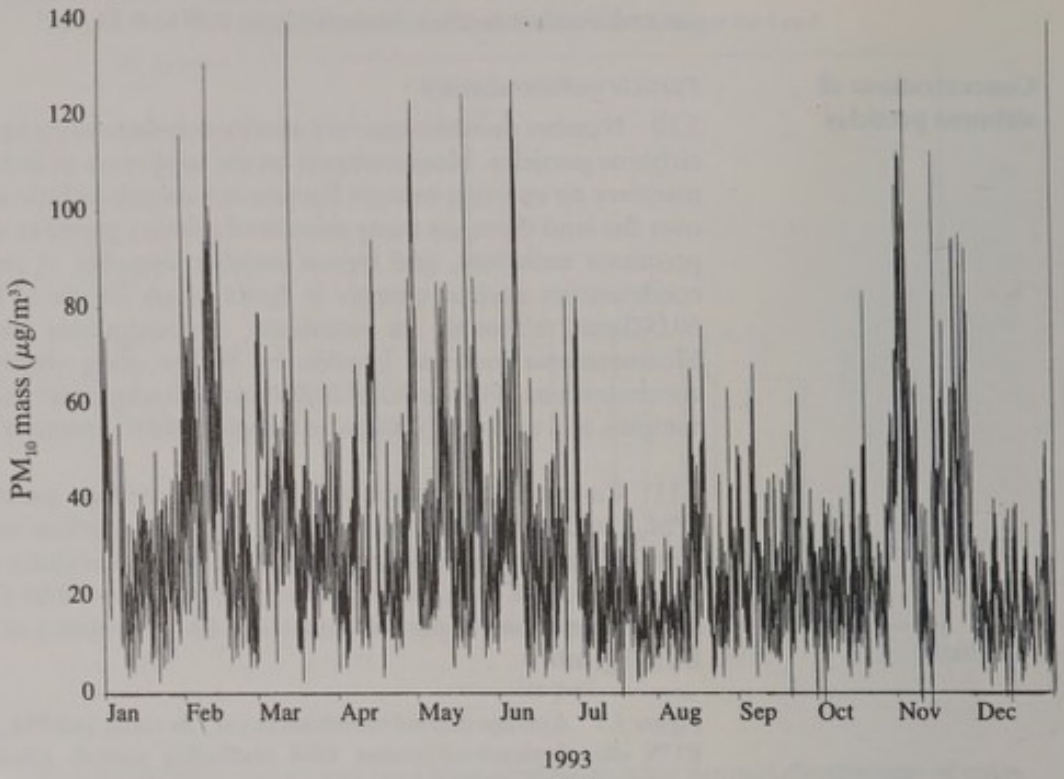
3.11 Co-located measurements of hourly average particle mass concentrations (PM_{10}) and particle number density (by condensation nucleus counter) made in Birmingham reveal a fairly close relationship (correlation coefficient, r = 0.52). For 24-hour average data, this correlation improves to r = 0.64. Figure 3.5 shows averaged diurnal variations of particle count and PM_{10} measured at the same time in central Birmingham.

Figure 3.5 **Average diurnal variations in particle count and PM_{10} at the Birmingham Central EUN site, September/October 1994 (excluding periods when the count exceeded the instrument limit of 10^5/cm^3)**



It is notable that the particle count begins to rise earlier than the PM_{10}, and appears more closely to reflect traffic volumes, with an afternoon rush hour peak at 5-6 pm which is not seen in these PM_{10} data (although it does appear in the larger PM_{10} dataset averaged in Figure 3.7).

Figure 3.6 **Time series of hourly mean PM_{10} concentrations at the London, Bloomsbury site for 1993**



The differences in behaviour between particle count (dominated by ultrafine particles) and PM_{10} may be ascribed to a number of causes. The particle count appears to relate more closely to traffic activity, with a daytime peak to nocturnal minimum ratio of 2.4:1, compared to 1.7:1 for PM_{10}. It responds rapidly to local traffic sources, staying high throughout the day at the city centre site. PM_{10}, which is reflective of particle emissions across the whole upwind urban area, shows a greater response to traffic volumes throughout the city than to very local sources. As a proportion of the peak concentration, there is a greater nocturnal background for PM_{10} than for particle count, due mainly to accumulation mode secondary aerosol which contributes appreciably to mass, but far less to particulate number.

3.12 The greatest influence upon particulate numbers is made by nucleation mode particles freshly emitted, or formed by gas to particle conversion processes. When these arise, large increases in particulate number density are observed, associated with modest increases in particle mass. High particulate number densities cannot be sustained over long periods. Simple coagulation of accumulation mode particles of the same size (monodisperse aerosol) will reduce an initial concentration of 1,000,000/cm³ by half within 33 minutes, but in a polydisperse aerosol (ie, one containing different particle sizes) or with nucleation mode particles present, this rate could be greatly increased. However, by the time that particle concentrations are reduced by coagulation or dilution to 10,000/cm³, halving of number density takes 15 hours for a monodisperse accumulation mode aerosol. Thus at this number density, airborne particles are rather stable with regard to loss by coagulation with other particles. Undoubtedly, coagulation of particles is a major influence upon the particulate number counts shown in Figure 3.5, and it is likely that counts of very fine particles are much greater close to sources such as motor traffic, than at more distant locations.

Particle mass concentration

3.13 Mass concentrations of airborne particles have proved quite difficult to measure reliably and hence, over the years, a number of techniques have been used. The largest database in the UK derives from the use of the smoke shade reflectance technique which depends on the estimation of the darkening of a filter paper by collected particles. It is not now helpful as a measure of gravimetric particle mass, but will be discussed in paragraph 3.16.

3.14 In North America, for many years airborne particle loadings were determined as TSP, estimated by weighing a large glass fibre filter before and after drawing a volume of around 2,000 m^3 of air through it. This technique has been criticised because of the variable characteristics of the sampler inlet with respect to large particles which are collected with different efficiencies in different wind speeds and directions. The very large particles which the sampler could collect under certain conditions were also of little relevance to health or environmental effects. Consequently, the US moved to the sampling of PM_{10}, which is the gravimetrically determined mass of particles passing an inlet with a cut-off at 10 μm aerodynamic diameter and corresponds approximately to the "thoracic" curve in Figure 3.1. This provides a greater consistency of measurements as the inlet particle size cut-off is not appreciably affected by wind speed or direction and the very large particles of no health significance are eliminated. When the UK Enhanced Urban Network (EUN) was planned it was decided to incorporate continuous monitors of PM_{10} based upon the tapered element oscillating microbalance (TEOM) principle. After some initial problems, these have proved operationally sound and have generated high quality datasets. Table 3.1 lists the sites currently equipped with continuous PM_{10} monitors and their date of commencement, and Table 3.2 gives a breakdown of the data collected in the calendar year 1993 for the sites operational throughout that year.

Table 3.1
Enhanced urban network (EUN) stations measuring PM_{10} concentrations

Site	Date operational
London, Bloomsbury	January 1992
Birmingham, Central	March 1992
Birmingham, East	December 1993
Belfast, City Centre	March 1992
Newcastle	March 1992
Edinburgh	October 1992
Cardiff	May 1992
Leeds	January 1992
Bristol	January 1993
Liverpool	April 1993
Leicester	January 1994
Kingston-upon-Hull	January 1994
Southampton	January 1994
Bexley	January 1994

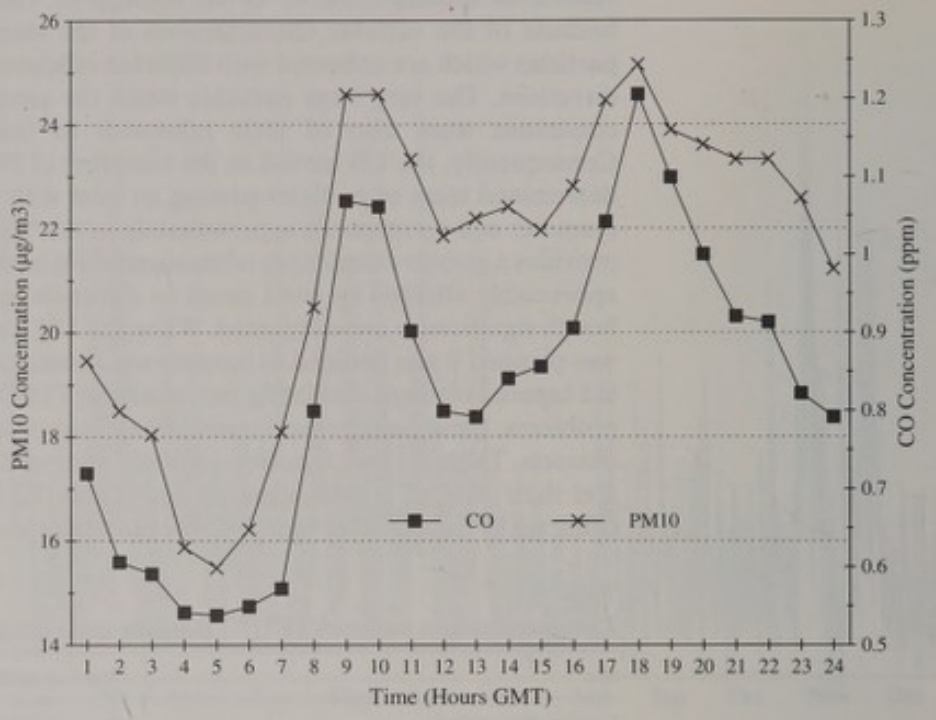
Table 3.2
Summary of PM_{10} concentrations measured at EUN sites during the calendar year 1993 ($\mu g/m^3$)

Site	Arithmetic Mean	95% ile	99% ile
London, Bloomsbury	26.6	63	87
Birmingham, Central	24.4	60	85
Belfast, City Centre	31.4	68	141
Newcastle	29.8	65	104
Edinburgh	21.7	43	62
Cardiff	29.0	44	106
Leeds	25.1	61	87
Bristol	25.1	63	87

Figure 3.6 shows a time series of hourly mean PM_{10} concentrations from the London Bloomsbury site throughout 1993. This clearly shows the considerable temporal variations in levels of PM_{10}. PM_{10} data collected by the UK EUN are summarised in Annex 3A.

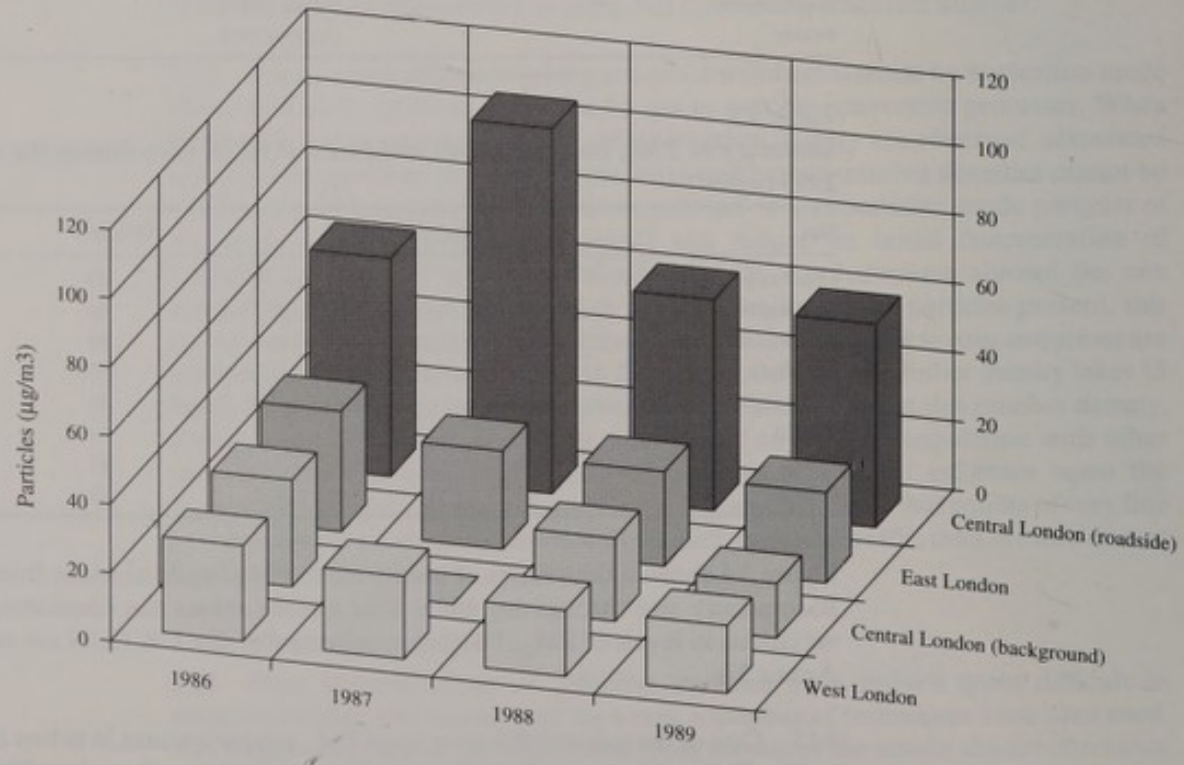
3.15 One of the major influences upon PM_{10} concentrations in urban areas is motor traffic. This is shown clearly by Figure 3.7 in which winter diurnal profiles of PM_{10} and carbon monoxide (a good indicator of traffic activity) are plotted and show very similar behaviour.

Figure 3.7 **Average diurnal profiles of PM_{10} and carbon monoxide at the Birmingham, Central EUN site, December 1993 to February 1994)**



Despite the fact that carbon monoxide is generated mainly by petrol vehicles and PM_{10} by diesels, the high correlation of the activity of the two kinds of vehicles leads to a close relationship of the pollutants. Another indicator of the impact of motor traffic is shown in Figure 3.8 which shows concentrations of particulate matter measured with a sampler with characteristics similar to that of the PM_{10} devices at four sites in London.

Figure 3.8 **Annual mean concentrations of suspended particles at four sites in London (1986–1989) (from London Scientific Services, 1989)**



Comparison of the central London (roadside) and central London (background) sites clearly indicates the strong impact of the road upon airborne particle loadings.

One consequence is that rural concentrations of PM_{10} are appreciably lower than urban concentrations, perhaps by a factor of two. There are, however, very few rural data.

Black Smoke

3.16 As mentioned above, there is a large base of data for Black Smoke in UK urban air. The method was developed when the main source of particles in urban air was the burning of coal and depends upon the ability of the particles to blacken the surface of the filter paper, the extent of blackening being determined by reflection of light. Originally, the technique was calibrated by comparison of light reflectance measurements with the gravimetrically determined mass of particles from urban sites. At that time, concentrations derived from smoke stain reflectance and reported as "standard smoke" were almost identical with gravimetrically measured particle masses. However, since that time, the make-up of particles in urban air has changed greatly and the two types of measurement have diverged appreciably. The major factor influencing the smoke shade measurement is the concentration of elemental carbon in the airborne particles. Nowadays, the main source of elemental carbon is diesel vehicle emissions and it has been shown that, in London, concentrations of lead in air (emitted from combustion from leaded petrol) correlate closely ($r = 0.68$) with measurements of Black Smoke, attributed to diesel vehicles. At the London Bloomsbury site, using data from summer 1992, the relation between Black Smoke and PM_{10} was as follows:

$$BS = 0.33\ PM_{10} + 3.0\ \mu g/m^3$$

The correlation coefficient was 0.68 and the correlation is significant at the 95% level. The winter data at the same site gave the relationship:

$$BS = 0.72\ PM_{10} - 2.78\ \mu g/m^3$$

The correlation coefficient in this case was 0.79, significant at the 95% level. Comparable relationships are observable at other city centre sites, and hence it appears that Black Smoke is reasonably well correlated with PM_{10}, but the relationship is far from 1:1. The gradient of the relationship at different sites is thus highly site-specific, presumably reflecting the influence of local sources, particularly for Black Smoke.

Sources of urban particulate matter

Primary particulate matter

3.17 Emissions may arise from both stationary and mobile sources.

— *Mobile sources*. These are both petrol and diesel vehicles, the latter being responsible for the majority of Black Smoke.

— *Stationary sources*. These fall into two groups:

  — controlled emissions from chimney stacks;

  — uncontrolled or "fugitive" emissions.

  Fugitive emissions are both difficult to measure and control, and may include:

  — wind blown dusts from open storage areas and spoil heaps;

  — emissions from buildings via natural or fan-assisted ventilation;

  — emissions from roadways as a result of local air turbulence;

  — emissions from the handling of materials, eg, when loading/unloading.

Secondary particulate matter

3.18 Particles are formed when gas phase species react to give rise to a product with a very low vapour pressure which hence condenses. Such a product is described as a secondary particle in order to differentiate it from primary material emitted directly from sources. The main source of secondary particles is the atmospheric oxidation of SO_2 to sulphuric acid, and of NO_2 to nitric acid. Whilst sulphuric acid exists in air in

particle form, nitric acid is present as a vapour. Both nitric acid and hydrochloric acid vapour, the latter arising mainly from refuse incineration and coal combustion, react reversibly with ammonia gas, largely arising as a product of decomposition of animal urine, to form ammonium salts.[5] Ammonium nitrate and sulphate exist in air as solid particles at low humidities, or as solution droplets at higher humidities.

$$NO_2 \rightarrow HNO_3$$

$$HNO_3 + NH_3 \gtrless NH_4NO_3$$

$$HCl + NH_3 \gtrless NH_4Cl$$

Sulphuric acid reacts irreversibly in two stages to form either ammonium bisulphate or ammonium sulphate.

$$SO_2 \rightarrow H_2SO_4$$

$$H_2SO_4 + NH_3 \rightarrow NH_4HSO_4 + NH_3 \rightarrow (NH_4)_2SO_4$$

These ammonium salts formed progressively as SO_2 and NO_2 are oxidised on a timescale of hours, and ammonia becomes available for neutralisation. They are not, therefore, a specifically urban problem, but are part of a regional-scale pollution phenomenon affecting both rural and urban sites. Ammonium salts comprise a major part of the accumulation mode particles in the UK air.

3.19 A national inventory of PM_{10} emissions appears in Table 3.3(a) and an inventory for London in Table 3.3(b).

Table 3.3a
UK Emissions of PM_{10} (kTonnes)

	Source	1970	1980	1990	1991	1992	1993	1993 as %
1	Public power etc	41	58	39	39	39	40	15%
	Coal	38	57	38	38	38	38	14%
	Fuel Oil	3	1	1	1	1	1	0%
	Other	0	0	0	0	0	0	0%
2	Commercial Institutional &							
	Residential Combustion Plants	226	96	45	47	45	42	16%
	Domestic	210	88	39	41	39	37	14%
	Other	16	9	6	5	5	5	2%
3	Industrial Combustion Plants							
	& Processes with Combustion	131	60	46	45	44	44	17%
	Refineries	10	10	6	6	6	7	3%
	Iron and Steel	56	17	21	21	20	20	8%
	Other	65	33	19	19	18	18	7%
4	Non-Combustion Processes	85	39	63	63	63	63	24%
	Construction	4	4	4	4	4	4	2%
	Industrial Processes	30	30	30	30	30	30	11%
	Mining and Quarrying	29	29	29	29	29	29	11%
5	Extraction & Distribution							
	of Fossil Fuels	0	0	0	0	0	0	0%
6	Solvent Use	0	0	0	0	0	0	0%
7	Road Transport	47	57	73	73	71	70	26%
	Petrol Exhaust	11	12	17	16	14	13	5%
	DERV Exhaust	34	39	52	53	53	52	20%
	Tyre and Brake Wear	2	3	4	4	4	4	2%
8	Other Transport	18	7	5	5	5	5	2%
9	Waste Treatment & Disposal	0	0	0	0	0	0	0%
10	Agriculture	2	1	1	1	1	1	0%
11	Nature	0	0	0	0	0	0	0%
	TOTAL	**550**	**318**	**272**	**273**	**268**	**265**	

Table 3.3(b)
Emissions of PM_{10} in London in 1990

	Emissions (Tonnes)		Emissions as %	
	1×1 km	Greater London	1×1 km	Greater London
Cars	6.3	1,334	16%	18%
Taxis	4.0	193	10%	3%
LGV	3.0	608	7%	8%
MGV	7.9	1,841	20%	24%
HGV	2.6	1,569	6%	21%
Buses	5.7	610	14%	8%
Motorcycles	0.1	14	0%	0%
Trains	0	16	0%	0%
Water	0	3	0%	0%
Air	0	558	0%	7%
Domestic	0.1	12	0%	0%
Industrial	0.2	219	0%	3%
Commercial & Institutional	3.4	327	8%	4%
Construction	7	220	17%	3%
TOTAL	**40.4**	**7,524**		

(1×1 km = Central London)

These are of limited value as they do not include secondary sources of PM_{10}. It should be noted also that urban as opposed to national inventories show a much greater influence of motor traffic[6].

Chemical composition of airborne particulate matter

3.20 Figures 3.9a-3.9c present a typical breakdown of the composition of TSP for an urban area, based largely upon data collected in Leeds 1982- 3.[7]

Figure 3.9a **Composition and major source categories for atmospheric particles sampled in Leeds, (1982–1983): total particles (from Clarke, 1992[7])**

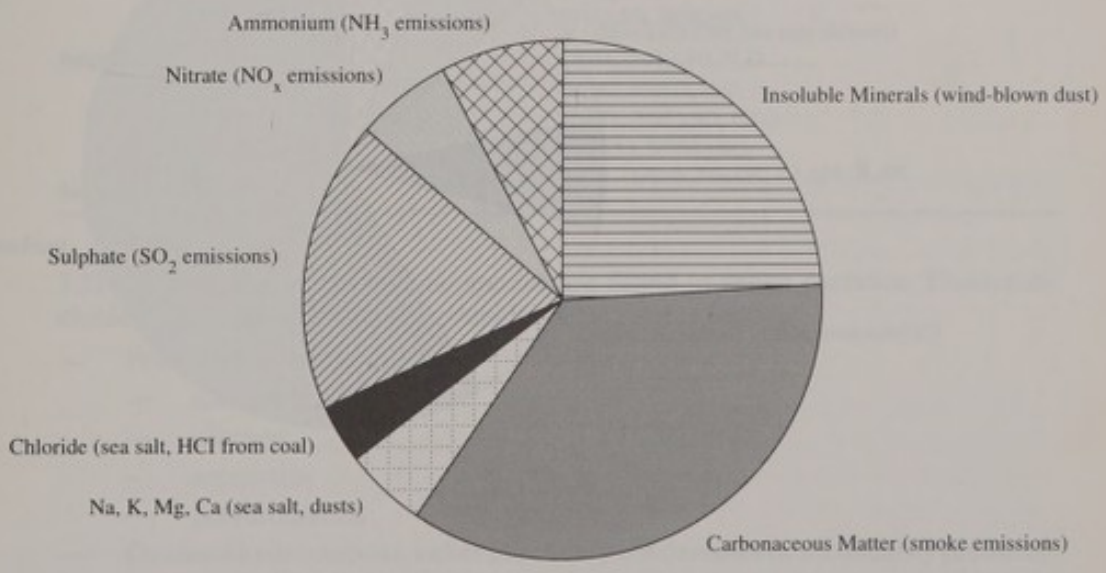


Figure 3.9b **Composition and major source categories for atmospheric particles sampled in Leeds, (1982–1983): fine fraction (< 2.5 μm) (from Clarke, 1992[7])**

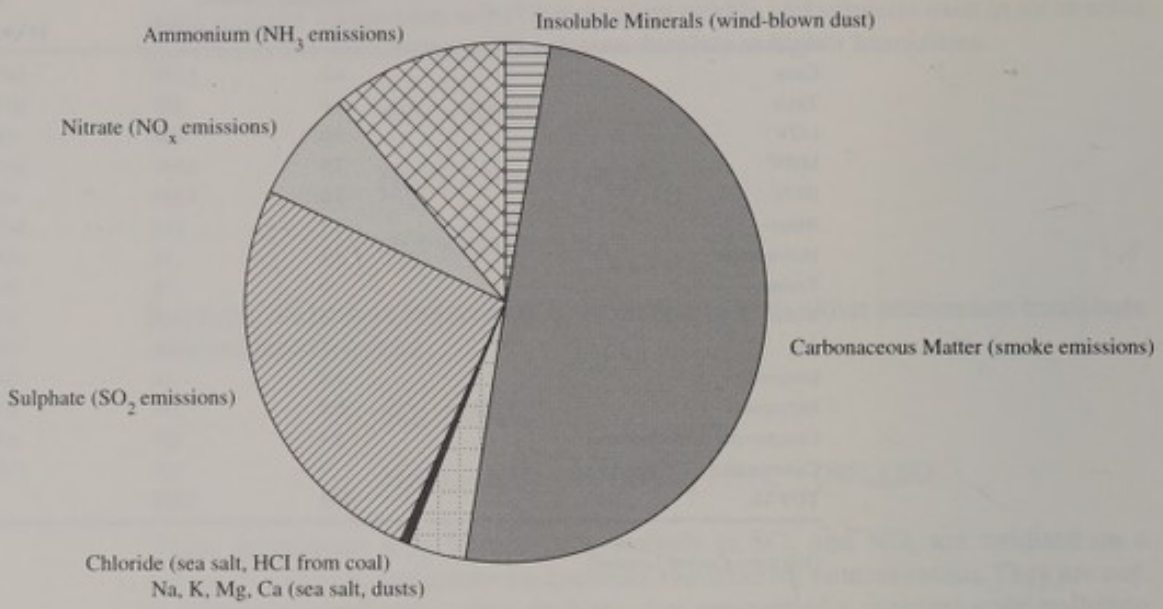
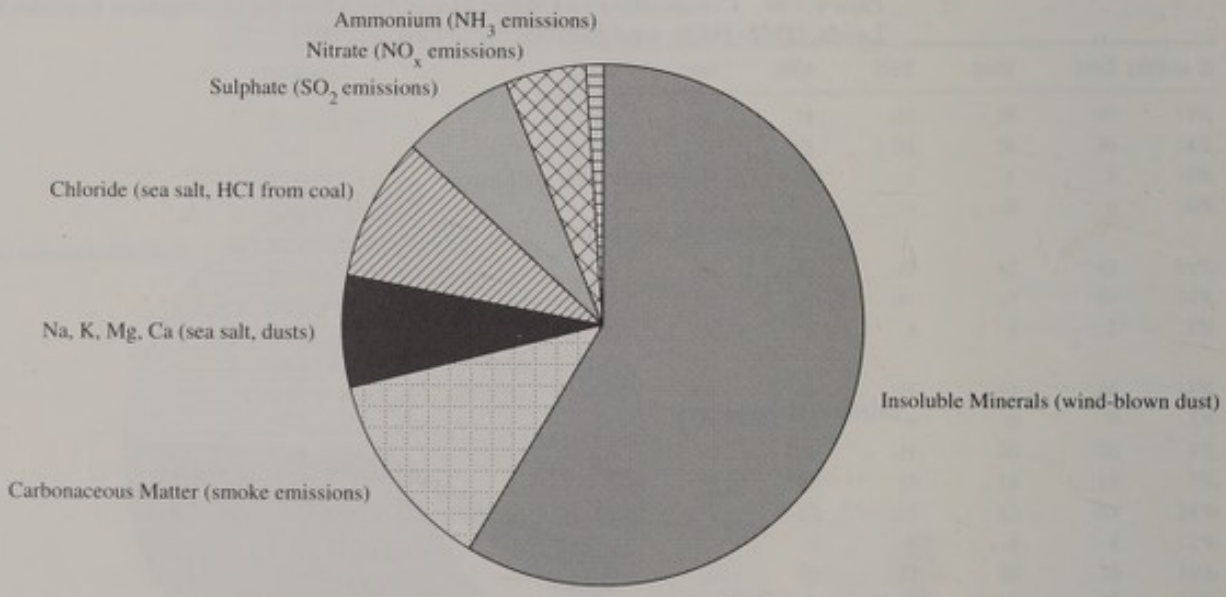


Figure 3.9c **Composition and major source categories for atmospheric particles sampled in Leeds, (1982–1983): coarse fraction (2.5-15 μm) (from Clarke, 1992[7])**



The main components are:

— soil-derived minerals, due to resuspension;

— elemental carbon, from combustion processes;

— organic compounds, mainly partially or unburned combustion products;

— ammonium salts, from ammonia neutralisation of airborne acids;

— sodium and magnesium chloride, from marine sources;

— calcium sulphate, from building materials and rocks/soils;

— sulphates from SO_2 oxidation;
— nitrates from NO_x oxidation;
— trace metals from industry and combustion of leaded petrol;
— biological particles, such as pollen grains, spores, small insects, etc, which are not revealed by traditional chemical techniques.

3.21 One approach to identifying chemical substances in atmospheric particles involves using X-ray powder diffraction (XRD). This technique identifies only crystalline components, representing about 50% of urban particle mass. One important finding is that many of the compounds are found in many different parts of the world.[8] Table 3.4 shows a summary of published data indicating the ubiquitous nature, particularly, of rock/soil minerals such as α-quartz, calcite, dolomite, gypsum and feldspar, ammonium salts and lead salts (from leaded petrol combustion).

Table 3.4
Compounds identified in UK urban air using X-ray powder diffraction

	Compounds
Natural minerals	α-Quartz (SiO_2)
	Calcite ($CaCO_3$)
	Epsomite ($MgSO_4.7H_2O$)
	Gypsum ($CaSO_4.H_2O$)
	Feldspar ($KAlSi_3O_8$)
	Chlorite (clay mineral)
	Kaolinite (clay mineral)
	Montmorillonite (clay mineral)
Lead compounds	$PbSO_4.(NH_4)_2SO_4$
	$PbSO_4$
	PbBrCl
Ammonium salts	$(NH_4)_2SO_4$
	NH_4HSO_4
	NH_4NO_3
	NH_4Cl
	$(NH_4)_2SO_4.2NH_4NO_3$
	$(NH_4)_2SO_4.3NH_4NO_3$
Sulphates	$CaSO_4.(NH_4)_2SO_4.H_2O$
	$Na_2SO_4.NaNO_3.H_2O$
	$Na_2SO_4.(NH_4)_2SO_4.4H_2O$
	$Fe_2(SO_4)_3.3(NH_4)_2SO_4$
Sea salt/road salt	NaCl

3.22 A wide variety of organic species are found in urban particles. These sub-divide approximately into two groupings, which are as follows:

— Primary condensates:
  — alkanes (C_{17}-C_{36});
  — alkenes;
  — aromatics;
  — polyaromatics.
— Oxidised hydrocarbons, either as primary condensates or secondarily produced as a result of atmospheric oxidation reactions:
  — acids;
  — aldehydes;
  — ketones;
  — quinones;
  — esters;
  — phenols;
  — dioxins;
  — dibenzofurans.

In addition, trace nitro-organics and heterocyclic sulphur compounds may be found in particulate material. Other than for specific groups of compounds (eg, polynuclear aromatic hydrocarbons, dioxins) there is little systematic information upon the organic content of atmospheric particles in the UK.

Approximate quantitative breakdown of chemical composition of UK airborne particulate matter

3.23 Airborne concentrations are liable to change considerably from place to place, and from day-to-day. Such changes may be accompanied by changes in composition, although the same components generally remain present, but in varying proportions. No UK research to-date has sought to quantify day-to-day variation of suspended particulate composition in a systematic manner. A typical breakdown of the measured components of UK urban particles is given in Table 3.5, derived from a survey of relevant literature.

Table 3.5

Representative concentrations of individual chemical components of airborne particulate matter

Typical analyte	Typical fraction of concentrations	Percentage found in total	Fine fraction	Studies (see table 3.6)
PM_{10}	30 $\mu g/m^3$	N/A	~60%	1
TSP	35 $\mu g/m^3$	N/A		14
Soluble ionic species:				
Sulphate	5-10 $\mu g/m^3$	20-25%	~85%	2-6
Nitrate	2-10 $\mu g/m^3$	10-20%	60-70%	2-6
Chloride	1-3 $\mu g/m^3$	< 10%*	~10%	2-6
Ammonium	2-6 $\mu g/m^3$	< 15%	> 95%	2,3,5
Strong acid (H^+)	0.1 $\mu g/m^3$	Trace	~100%	6,15
Carbonaceous:				
Elemental carbon	3 $\mu g/m^3$	10%	~80%	14
Organic carbon	5 $\mu g/m^3$	15%	~80%	14
Minerals:				
Natural minerals	5-15 $\mu g/m^3$	20-25%	~5%	12,13
Metals:				
Sodium	1 $\mu g/m^3$	2%*	21%	3
Magnesium	0.1 $\mu g/m^3$	0.2%*	19%	3
Calcium	0.4 $\mu g/m^3$	0.8%*	25%	3
Potassium	0.1 $\mu g/m^3$	0.2%*	44%	3
Lead	0.1 $\mu g/m^3$	0.2%	~90%	7,8
Other trace metals	5-50 ng/m^3	Trace	Most	7,8
Iron	0.5 $\mu g/m^3$	1%	35%	7
Toxic organic micropollutants:				
Dioxins	4 pg/m^3	Trace	Most	9,10,11
PCBs	1 ng/m^3	Trace	Most	9,10,11
PAH	150 ng/m^3	Trace	Most	9,10,11

* Surveys carried out in areas with abnormally high marine aerosol.

In rural air, secondary components such as ammonium sulphate and nitrate may be almost as abundant, but some primary materials (eg, vehicle-generated lead) will have lower concentrations than at urban sites. The data in Table 3.5 have been compiled using results of a large number of separate studies, summarised in Table 3.6.[6, 8-21] To-date, no comprehensive study of particulate composition at individual locations has been performed. Least is known about the organic carbon and insoluble inorganic fractions.

Table 3.6

Summary of the studies to provide data for Table 3.5

Sampling Study	Species analysed	Method	Location	Reference
1 EUN	PM_{10} and gaseous pollutants	Tapered Element Oscillating Microbalance	City Centre Sites	QUARG[8]
2	SO_4^{2-}, NH_4^+, NO_3^-, Cl^- and sampled mass	Dichotomous sampler. (Coarse and fine fractions)	Simultaneous measurements at urban and rural sites near Leeds	Clarke et al[10]
3	Soluble ionic species as above plus Ca, K, Na, Mg	Cascade impactor (7 size fraction)	Lancaster	Harrison and Pio[11]
4	SO_4^{2-}, NO_3^-, NH_4^+, TSP at one site	No size discrimination	Five sites near Lancaster	Colbeck and Harrison[12]
5	SO_4^{2-}, NH_4^+, NO_3^- and Cl^-	No size discrimination	Essex, five sites urban and rural	Harrison and Allen[13]
6	SO_4^{2-}, NH_4^+, NO_3^- and H^+	No size discrimination	Essex, four sites, urban and rural	Kitto and Harrison[14]
7 Multi element survey	16 trace metals	No size discrimination	The five urban sites exhibited the highest concentrations among the original 20	McInnes[15]
8	Lead, cadmium		Lancaster, urban and rural	Harrison and Williams[16]
9 Toxic Organic micropollutant network	Dioxins, PAH and PCBs	No size discrimination	Cardiff, London Manchester and Stevenage	Clayton et al[17]
10	PAH	Some use of cascade impactors	Exhibition Road, London	Baek et al[18]
11	PAH	No size discrimination	Birmingham	QUARG[8]
12	Crystalline species	No size discrimination	NW England	Sturges et al[8]
13	Elemental analysis of individual particles	Mostly PM_{10}	Antwerp, urban	Van Borm et al[19]
14	Elemental and organic carbon	TSP and PM_{10}	Birmingham University	Pio et al[20]
15	H^+ and other soluble ions	PM_{10}	Birmingham	Archer et al[21]

3.24 There are systematic variations in mean particulate composition between different urban sites. For example, coastal towns will have higher concentrations of marine sodium, magnesium and chloride. There are also within-town gradients in concentrations relating to the influence of point source emissions and road traffic. In general, however, these have been rather little studied, and are poorly described by quantitative measurements of particulate composition.

3.25 It must be borne in mind that the chemical composition data in Table 3.5 relate to the *bulk* particles. Some chemical species by virtue of their mode of attachment to atmospheric particles may reside predominantly on the *surface* and hence be more immediately available for leaching into solution if the particle deposits in the respiratory system. Whilst techniques of surface analysis have clearly demonstrated surface enrichments of chemicals which have condensed on to particle surfaces or been formed there by chemical reaction, quantitative data upon their extractability, particularly by biological fluids, are lacking.

Correlations of PM_{10} levels with other pollutants and with temperature

3.26 Frequently, the main controls upon pollutant concentrations in ambient air are meteorological factors which determine the rate of atmospheric dispersal. There is thus a tendency for concentrations of one primary pollutant to correlate with those of another, particularly if they have a common source, frequently motor traffic in urban areas. This is shown in Table 3.7 which presents a correlation coefficient matrix for 24-hour average concentrations of pollutants measured at the Birmingham Central EUN site in 1993.

Table 3.7

Correlation coefficients for 24-hour average pollutant concentrations measured at Birmingham, Central in 1993

	PM_{10}	CO	NO	NO_2	NO_x	O_3	SO_2
PM_{10}	1.0						
CO	0.42	1.0					
NO	0.59	0.75	1.0				
NO_2	0.74	0.54	0.64	1.0			
NO_x	0.69	0.74	0.97	0.81	1.0		
O_3	–0.37	–0.67	–0.69	–0.58	–0.71	1.0	
SO_2	0.73	0.36	0.50	0.64	0.58	–0.43	1.0

Positive correlations are seen, except for the secondary pollutant ozone which is negatively correlated with all other pollutants measured. PM_{10} particulate matter is rather well correlated with other primary pollutants. Correlation coefficients of hourly-average PM_{10} concentrations with those of other pollutants appear in Table 3.8 and indicate positive associations between all pollutants at all sites, except again for ozone.

Table 3.8

Correlation coefficients between hourly average concentrations of PM_{10} and other pollutants at various EUN sites for 1993

Pollutant	Belfast	Edinburgh	Newcastle	Birmingham	Cardiff	London
SO_2	0.68	0.27	0.48	0.58	0.42	0.51
NO	0.69	0.40	0.68	0.58	0.36	0.50
NO_2	0.64	0.41	0.63	0.64	0.44	0.61
CO	0.63	0.41	0.56	0.47	0.32	0.34
O_3	–0.36	0.26	–0.36	–0.33	–0.12	0.01
NO_x	0.73	0.43	0.70	0.66	0.41	0.57

3.27 All primary pollutant concentrations show a negative correlation with mean temperature (levels rise as temperatures fall), but ozone shows the reverse trend. Correlation coefficients for 24-hour average data appear in Table 3.9, and indicate that the variables are rather poorly correlated, with PM_{10} showing the weakest negative association with temperature, presumably due to high concentrations during summer photochemical pollution episodes.

Table 3.9

Correlation coefficients between mean air temperature and concentration for primary pollutants (Birmingham, Central 1993)

Pollutant	Correlation coefficient
CO	–0.43
NO	–0.37
NO_2	–0.34
NO_x	–0.39
SO_2	–0.26
PM_{10}	–0.20
O_3	–0.34

Recommendations

3.28 Compared with most gaseous pollutants, particulate matter is a complex mixture and there are many questions still to be answered. These include:

(a) How do particle mass loadings and number counts vary across urban areas and between urban and rural areas?

(b) What is the chemical composition of size fractionated PM_{10} and how does it vary spatially and temporally? In particular, the composition of the nucleation mode of ultrafine particles is very poorly understood.

(c) What is the size distribution of PM_{10}? What proportion of particles by number are less than 50 nm diameter?

(d) What are the sources of PM_{10} in the UK atmosphere and what strategies would be most cost-effective at limiting them?

(e) What processes are responsible for events leading to extreme concentrations of airborne particles?

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Annex 3A

Summary of PM_{10} data from the Enhanced Urban Network, 1992–1994 ($\mu g/m^3$)

1992 (from 01/07)							
Location	10%*	50%*	90%*	Mean	Max	% Data capture	
Belfast	9	20	90	31.0	871	98.5	
Edinburgh	10	20	39	22.2	127	47.8	
Newcastle	11	21	50	26.6	215	99.4	
Birmingham	9	18	42	21.2	195	99.5	
Cardiff	9	20	42	23.3	296	99.4	
London	11	22	44	26.1	153	98.8	
1993							
Belfast	10	25	60	31.4	445	97.3	
Edinburgh	10	20	39	21.7	691	97.9	
Newcastle	10	25	58	29.8	236	96.5	
Birmingham	10	20	48	24.4	186	98.8	
Cardiff	10	22	54	29.0	667	98.1	
London	10	22	50	26.6	139	97.2	
Leeds	8	20	52	25.1	162	98.7	
Bristol	8	20	53	25.1	201	97.9	
Liverpool	12	26	62	34.2	330	99.7	From 01/10
Birmingham East	5	19	52	24.1	172	99.4	From 27/10
Southampton	4	17	37	23.1	709	96.0	From 01/12
Leicester	8	18	30	17.0	67	94.7	From 08/12
Hull	6	19	38	20.0	129	93.3	From 16/12
1994 (to 31/10)							
Belfast	10	20	42	24.7	391	93.6	
Edinburgh	10	19	34	20.0	693	97.0	
Newcastle	10	21	50	26.2	296	94.1	
Birmingham	9	20	41	22.4	156	96.2	
Cardiff	10	25	63	35.3	564	96.0	
London	11	24	45	26.4	307	97.3	
Leeds	10	20	44	25.2	215	95.8	
Bristol	10	20	42	23.6	612	96.9	
Liverpool	10	20	44	24.4	537	95.7	
Birmingham East	10	18	37	20.2	2230	97.0	
Southampton	10	20	41	22.9	291	97.2	
Leicester	10	19	37	20.6	164	94.7	
Hull	10	20	41	25.5	548	97.9	

Contains some provisional data

* Percentiles of hourly means

Chapter 4

Particle Dosimetry

Introduction

4.1 Assessing the degree of exposure to environmental particles should not simply involve a consideration of airborne concentration of particles or their chemical constituents, but should take into account the individual or population dose of the appropriate fraction of the ambient aerosol. Dose relates to the deposition, uptake and retention of each component of the ambient aerosol, but may be affected by a number of factors. These include:

particle size, shape and solubility;

chemical composition of the aerosol;

local environment, ie, temperature, humidity, ventilation and lifestyle;

anatomical and physiological factors such as inter-subject variability, gender, age, physique and disease;

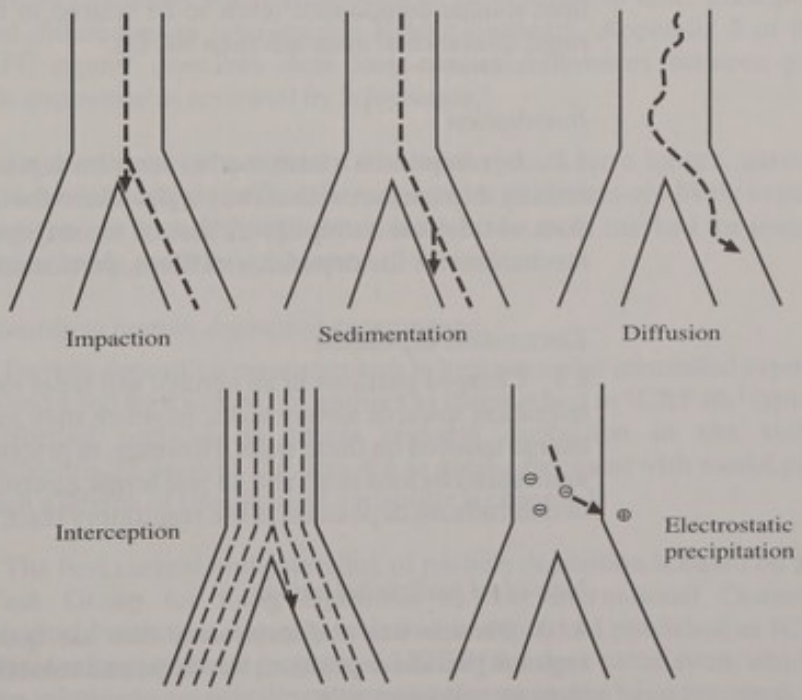
personal exposure relative to area sampling concentrations.

Interaction of these variables gives rise to a complex matrix in terms of absolute dose determination at the population level but a pragmatic approach may be adopted to estimate how these factors may influence relative dose, and hence the sensitivity of dosimetric models to these variables. This approach is already being addressed in more recent models of particle deposition where lifestyle factors and biological variability are taken into account.

Mechanisms of particle deposition

4.2 Five principal mechanisms of particle deposition exist based on the physical properties of the aerosol, as described below and illustrated in Figure 4.1. These mechanisms have been reviewed.[1]

Figure 4.1 **Mechanisms of particle deposition in the respiratory tract**



Impaction

4.3 Impaction, due to the inertia of the particles, occurs when the air undergoes a change of direction such as in the pharynx or at a bifurcation of the airways. This is important for the deposition of larger particles (> 1 μm) in the upper airways and the nasopharyngeal region. Clearance of such particles, where insoluble, occurs primarily via the mucociliary escalator.

4.4 There is additional experimental evidence from deposition measurements in early generations of human airways that vortices are set up downstream from bifurcations leading to regions of concentrated particle deposition rather than uniform deposition for that particular airway generation.[2]

4.5 Deposition by impaction increases as momentum of the particle increases, ie, with increased air flow and particle size. Bronchial dimensions are strongly dependent on physique; on average the side to side diameter of the adult male trachea is about 2 cm, that of the adult female about 1.5 cm. Since the velocity of air and hence the momentum of any particle is inversely proportional to the square of the airway diameter, deposition by impaction in the upper airways will show clear differences between men and women, as impaction efficiency increases at a given flow, and this has been observed.[3]

Sedimentation

4.6 Sedimentation is an important mechanism of deposition in parts of the respiratory tract where air flow velocity is low: it plays an important part in deposition in the bronchioles. The efficiency of sedimentation as a mechanism of deposition is dependent upon the terminal settling velocity of the particle concerned which is dependent on the square of its radius. In practice, deposition efficiency is low relative to impaction, although it becomes more significant for particle sizes in the 0.5-1 μm region. The low efficiency of deposition by this mechanism is reflected by the minimum of particle deposition, in adults, occurring for 0.5 μm particles.

Brownian motion

4.7 Particle deposition by Brownian motion occurs due to the bombardment of small particles (< 0.1 μm) by air molecules. This is most important for the deposition of small particles which penetrate to the alveolar region. This region has a high surface area allowing rapid dissolution and uptake of soluble particles. For insoluble particles, macrophage clearance predominates. The rate of subsequent clearance of lipid soluble compounds tends to be related to their molecular weight, with more rapid clearance at mass less than 300 Da.[4]

Interception

4.8 Interception is a term used to describe deposition of particles as a result of their coming into contact with airway walls where the direction of movement of particles does not deviate as rapidly as that of the air stream. Interception is an important mechanism for the deposition of fibres, particularly at airway bifurcations.

Electrostatic deposition

4.9 Charged particles in an aerosol will repel each other leading to an increase in migration towards airway walls, to which they may also be attracted as a result of charge induced on these walls. However, in practice, most ambient particles become neutralised by ions in air and, in real terms, electrostatic deposition plays a small role in determining deposition in the respiratory tract.

Non-ideal particle behaviour

4.10 Particle size and inspiratory flow are two of the principal determinants of regional particle deposition, but shape and solubility of the inhaled particle may also have an important role.

Particle shape

4.11 The majority of environmental aerosols encountered by the population will be sufficiently spherical to be considered to behave as spherical particles in deposition models. The exceptions are fibrous aerosols, such as asbestos and man-made mineral fibres (MMMFs). Fibrous materials tend to align with airflow so that aerodynamic diameter is not strongly dependent on length, and fibres of up to 360 μm in length have been found to penetrate to the human alveoli. It is not possible for lung clearance mechanisms to deal with fibres of this type, and defence mechanisms rely on depositing a proteinaceous covering on the fibres.

Particle solubility

4.12 Solubility may be significant for some components of the ambient aerosol where, on entering the high humidity of the respiratory tract, water vapour will condense on particles and form droplets of solution. If soluble, the particle hydrates, eventually forming a solution. As the vapour pressure of a solution is less than that of the pure solvent, the particle may swell to a droplet several times its initial size, a phenomenon known as hygroscopic growth. This topic was considered in detail in a report of the Advisory Group on the Medical Aspects of Air Pollution Episodes.[5]

4.13 In the most extreme case for sodium chloride, an aerodynamic growth factor of 4.5 is observed leading to a marked shift in the deposition pattern of sub-micron particles; lower factors have been reported for sulphate based aerosols. Soluble particles which deposit will dissolve in the lining fluids of the respiratory tract and so will not be cleared by the mechanisms involved in the clearance of insoluble particles.

Deposition models

Basis of human lung deposition models

4.14 Human lung deposition models are based typically on estimation of the physical behaviour of aerosol particles in a simplified anatomical model of the lung, that is, as a series of branching cylinders with bifurcations of known angles allowing calculation of deposition by impaction, sedimentation and diffusion. These models are generally weighted to take account of experimental data. The most widely used models of lung structure are based on a simplified branching model of the respiratory tract as published by Weibel;[6] the most widely used models of particle deposition are those published by the International Task Group on Lung Dynamics,[7] and more recently, ICRP 66.[8]

Animal deposition models

4.15 Animal models of the effects of inhaled particles upon the lung must be interpreted cautiously when attempting to extrapolate to man, principally due to marked differences in inter-species airway geometry. Appendix 3 of the second MAAPE report[5] describes clear inter-species differences between patterns of particle deposition as reviewed by Schlesinger.[9]

4.16 To summarise, the majority of animal species have longer, narrower nasal turbinates relative to man. Thus, fewer particles of all sizes are likely to penetrate to the lung than in man, although this is likely to be most marked for penetration of nucleation mode particles < 0.1 μm.

Relationship to human deposition experiments

4.17 Particle deposition measurements in humans under controlled exposures have been conducted by a number of authors as summarised in ICRP 66,[8] typically using radio-labelled particles to assess regional deposition in the various lung compartments. In general, the data are in good agreement with model predictions, although a degree of inter-subject variability is observed.

ICRP 66 Lung model [1995][8]

4.18 The best current understanding of particle deposition is based on a report of the Task Group for Lung Dynamics to the International Commission for Radiological Protection, recently reviewed in depth and published as ICRP 66.[8] In addition, a microcomputer program, LUDEP[10] for dose calculation, which includes modules relating to particle deposition and clearance, has been prepared.

4.19 The ICRP 66 model extends the scope of the earlier model and considers variation in deposition through factors such as anatomy/physiology (including age, gender and race), ventilation rate and pattern, nature of exposure and particle size.

Anatomy and physiology of the respiratory tract

4.20 The respiratory tract in the lung model is greatly simplified with division into 4 main regions: extrathoracic (ET), bronchial (BB), bronchiolar (bb) and alveolar-interstitial (AI) with simplifying assumptions for clearance broken down into simple considerations of mechanical clearance and translocation. Symmetrical airway branching and ventilation are assumed throughout the deposition models, although this is not observed. A summary of morphological and physiological parameters for both genders and various ages is shown in Table 4.1.

Table 4.1
Morphological and physiological parameters (Rudolf *et al*, from ICRP 66[8])

Parameter	Man	Woman	10y	5y	1y	0.25y
FRC (cm^3)	3300	2700	1500	770	250	150
V (cm^3) Sleep	625	450	305	175	75	40
Rest	750	460	330	210	100	—
Light exercise	1250	1000	580	245	125	65
Heavy exercise	1920	1610	760	—	—	—
Q (cm^3s^{-1}) Sleep	250	180	175	135	85	51
Rest	300	215	210	175	200	—
Light exercise	833	700	620	320	190	105
Heavy exercise	1670	1500	1140	—	—	—
No. alveoli (ICRP 23)	296×10^6	280×10^6	257×10^6	129×10^6	77×10^6	—

where: FRC = Functional Residual Capacity
V = Tidal Volume
Q = Volumetric flow rate

Extrathoracic regions

4.21 The choice of nasal versus oral breathing is largely determined by the relative resistance of the two pathways with respect to ventilatory needs. Nasal breathing, which conditions the temperature and humidity of the inhaled air and filters larger particles, predominates in healthy subjects at rest, with oronasal breathing increasing in response to exercise. The anatomical structure of this region is characterised by airflow resistance of approximately 0.15 $kPa.l^{-1}s$, equivalent to half the total airway resistance.

4.22 In most healthy individuals, a nasal cycle is observed, with an anatomical and resistance asymmetry through nasal congestion and decongestion. This causes an approximate 3 hour cycle with airflow distribution changing as much as 20 to 80% between nostrils without subjective discomfort, the effect disappearing in elderly people and during exercise. The introduction of turbulent flow through this asymmetry is likely to increase deposition efficiency.

4.23 Studies of deposition efficiencies in the extrathoracic region using a combination of volunteer studies and studies involving the use of nasal casts have been extensively reviewed by Cheng *et al*.[11] However, there remains a need for further comparative data for nasal and oral breathing.

Bronchial and bronchiolar regions

4.24 These regions comprise what is known as the classical "tracheobronchial tree" or "conducting airways" where inspired gases are transported but do not interchange with blood. The model is based on a branching structure from Generation 0 (trachea) to Generation 26 (last of branches), although the number of generations present varies significantly in different parts of the lungs. The bronchial region comprises airways greater than 1 mm diameter (to about Generation 8-10) with bronchiolar airways having diameters of less than 1 mm.

4.25 The region is characterised by a rapid clearance phase for deposited particles via a mucociliary escalator, which is generally complete within 24 hours. A slower compartment of bronchial clearance has been observed in both animals[12] and man.[13]

Alveolar-interstitial

4.26 This, the gas-exchange region, is comprised of respiratory bronchioles through to alveolar sacs. Alveolar deposition in this region is modelled by assuming an inflatable ¼ spheroid as a model of the alveolus with deposition by a combination of settling velocity and diffusive flux. Clearance of particles from this region is principally by phagocytosis with substantially longer clearance times, dependent to some extent on particle deposition. In a review by Bailey *et al*,[14] slow half-times of clearance range from 300 days to a number of years, which has implications for long-term particle retention.

Age

4.27 Age groups addressed in the ICRP 66 (1995) model[8] include adult male, adult female, 15 year old male, 15 year old female, 10, 5, 1 year and 3 months old male and females.

Ventilation

4.28 Ventilation data for various age groups, genders and ethnic groups have been reviewed by Roy *et al*,[15] with selected Caucasian data from the LUDEP model shown in Table 4.1.

Lifestyle

4.29 Ventilation data are chosen by the LUDEP model as appropriate for periods of sleep, rest, light and heavy exercise dependent on whether occupational or environmental exposures (indoor or outdoor) are taking place based on a review of lifestyle data from activity diaries.

LUDEP computer model

4.30 LUDEP[10] is a microcomputer based model which has been developed as a means of predicting regional particle deposition in the human lung based on the criteria published in ICRP 66,[8] and as such, offers a useful route in determining differences in deposition pattern across different groups.

General model predictions

4.31 A plot of particle deposition versus particle size for an adult male is shown in Figure 4.2. Tables 4.2-4.5 and Figures 4.3-4.6 show equivalent deposition data for particle sizes characteristic of the ambient nucleation (0.05 μm), condensation (0.2 μm), droplet (0.7 μm) and coarse (2.0 μm) modes.

Figure 4.2 **Lung deposition v particle size**

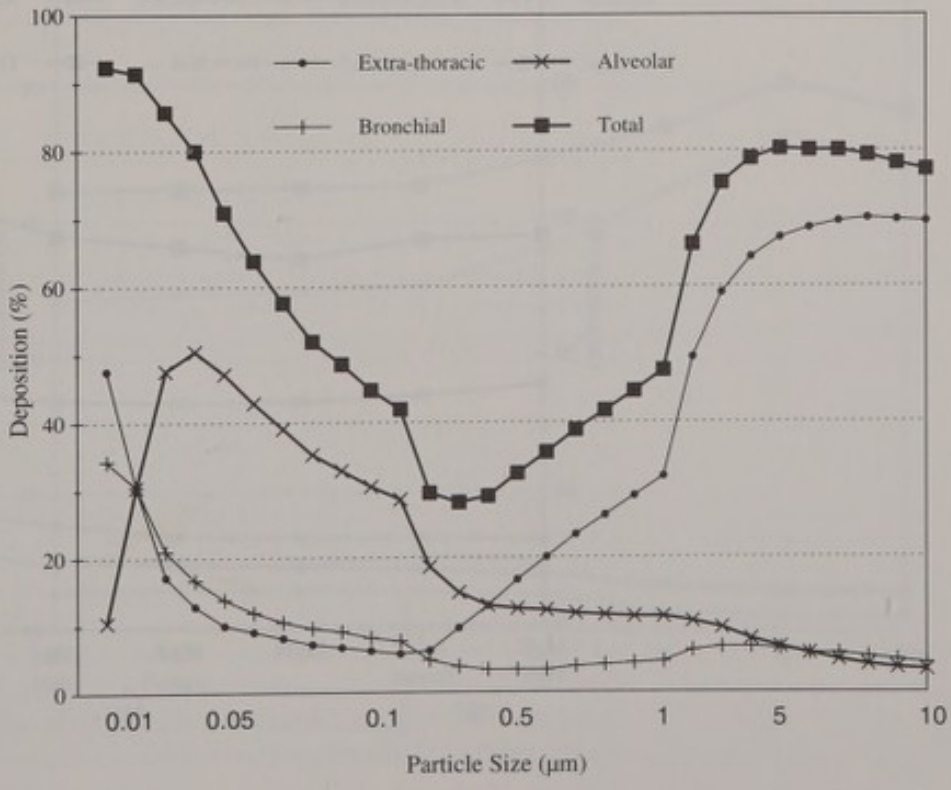


Figure 4.3 **Lung deposition v age (0.05 μm)**

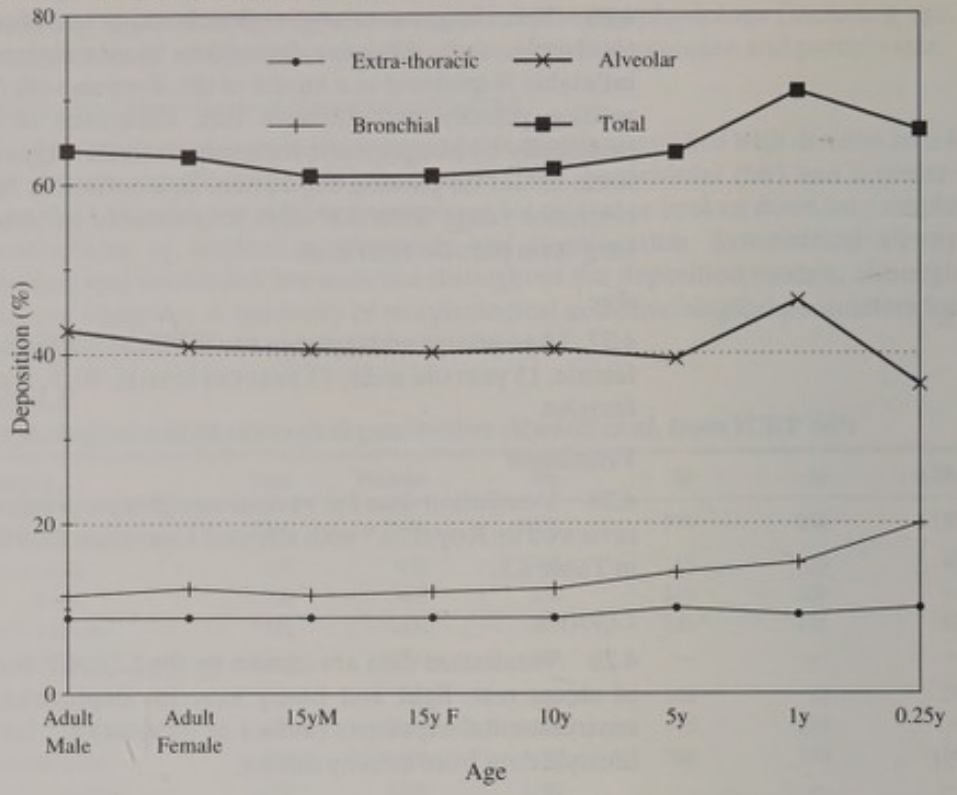


Figure 4.4 **Lung deposition v age (0.20 μm)**

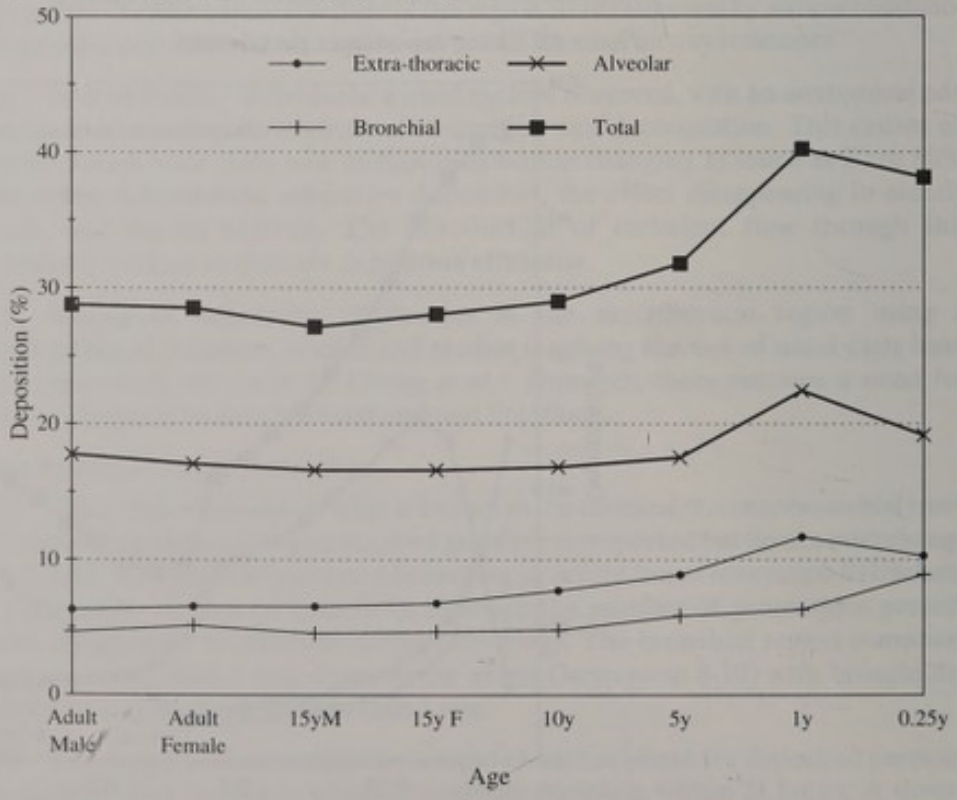


Figure 4.5 **Lung deposition v age (0.70 μm)**

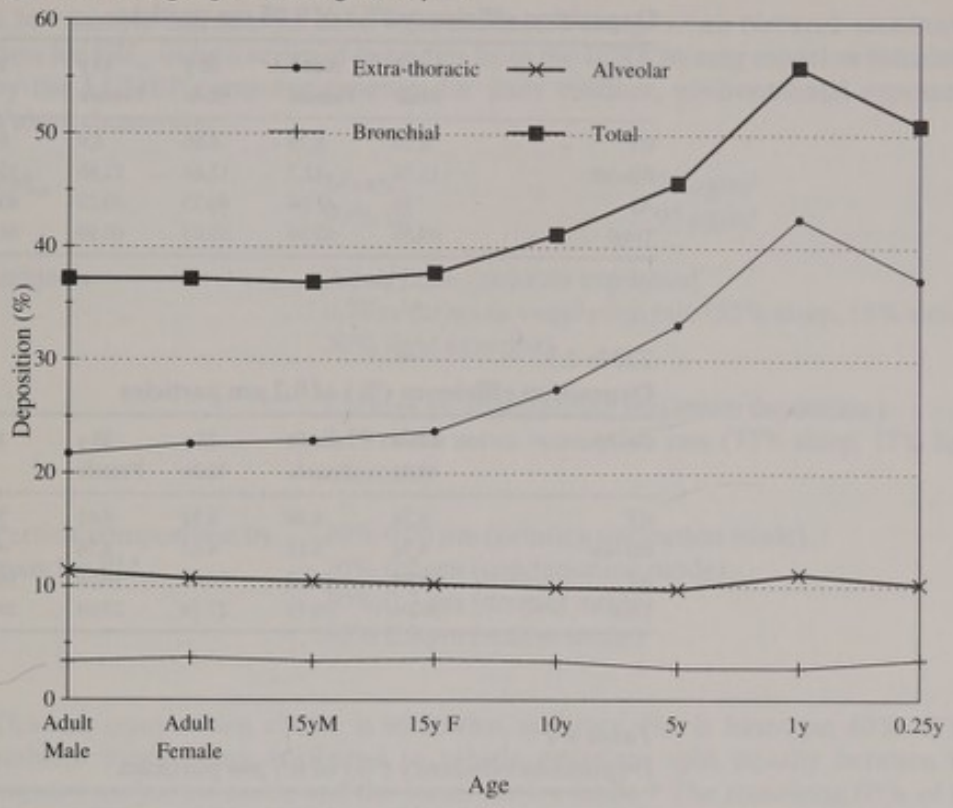


Figure 4.6 **Lung deposition v age (2.0 μm)**

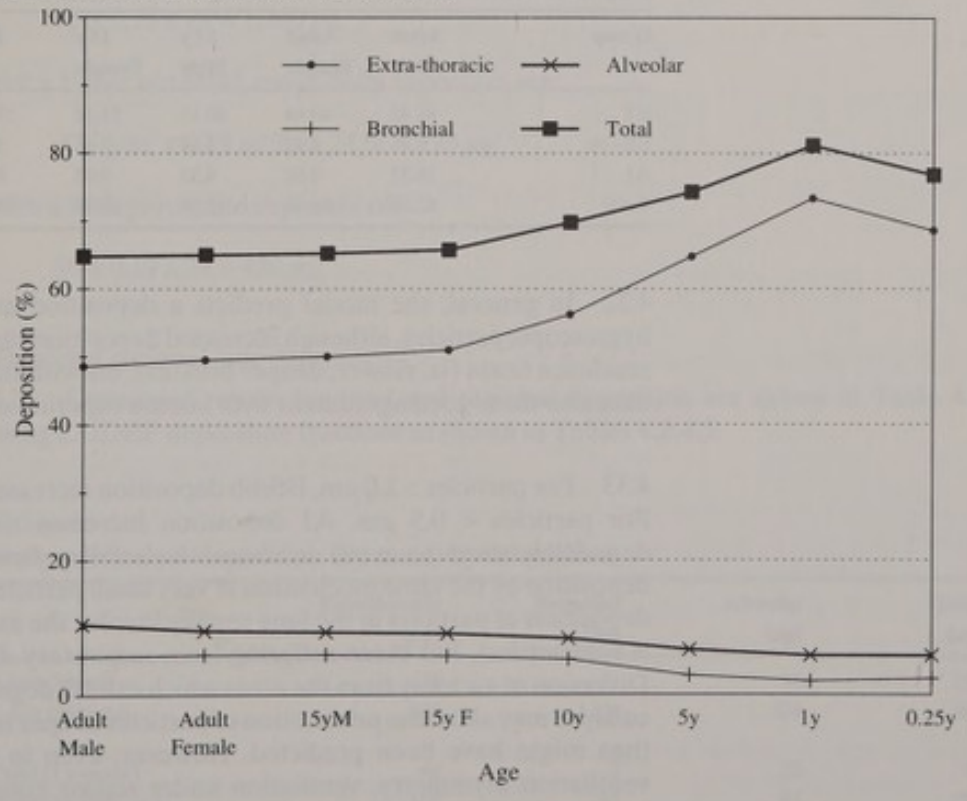


Table 4.2
Deposition efficiency (%) of 0.05 μm particles

Group	Adult Male	Adult Female	15 y Male	15 y Female	10 y	5 y	1 y	0.25 y
ET	8.76	8.79	8.86	8.9	8.96	9.71	9.21	9.79
BB+bb	11.76	12.7	11.64	11.86	12.12	14.24	15.16	20.26
AI	43	41.08	40.53	40.22	40.46	39.51	45.92	35.66
Total	63.53	62.56	61.03	60.99	61.54	63.46	70.29	65.72

Table 4.3
Deposition efficiency (%) of 0.2 μm particles

Group	Adult Male	Adult Female	15 y Male	15 y Female	10 y	5 y	1 y	0.25 y
ET	6.24	6.39	6.39	6.61	7.54	8.78	11.6	10.04
BB+bb	4.74	5.12	4.67	4.76	4.86	5.74	6.22	8.65
AI	18.06	17.2	16.68	16.58	16.76	17.4	22.55	19.24
Total	29.04	28.71	27.74	27.94	29.17	31.92	40.37	37.93

Table 4.4
Deposition efficiency (%) of 0.7 μm particles

Group	Adult Male	Adult Female	15 y Male	15 y Female	10 y	5 y	1 y	0.25 y
ET	22.71	23.16	23.24	24.09	27.9	33.36	42.47	37.12
BB+bb	3.62	3.85	3.64	3.62	3.54	2.86	2.88	3.76
AI	11.52	10.86	10.46	10.27	9.89	9.71	10.9	10.04
Total	37.85	37.87	37.34	37.98	41.33	45.93	56.25	50.92

Table 4.5
Deposition efficiency (%) of 2.0 μm particles

Group	Adult Male	Adult Female	15 y Male	15 y Female	10 y	5 y	1 y	0.25 y
ET	49.43	49.84	50.11	51.14	55.91	64.28	72.78	67.73
BB+bb	5.76	5.97	5.84	5.66	5.17	2.54	2.04	2.31
AI	10.37	9.68	9.33	9.02	8.09	6.98	6.01	6.1
Total	65.56	65.49	65.28	65.82	69.17	73.8	80.83	76.14

4.32 In general, the model predicts a deposition minimum at 0.5 μm for non-hygroscopic particles, although increased deposition can be shown for increased lung residence times (ie, slower, deeper breaths), outwith the adopted model values. The data also show good agreement with human experimental data.

4.33 For particles > 2.0 μm, BB/bb deposition increases as AI deposition decreases. For particles < 0.5 μm, AI deposition increases then decreases as diffusional deposition starts to move up from the smaller airways; thus increasing BB/bb deposition by the same mechanism at very small particle sizes. Models used to predict deposition of particles in the lung usually involve the assumption that the ventilation is symmetrical. For those suffering from respiratory diseases this may not be true. Diversion of air away from the areas which exhibit degrees of bronchoconstriction or collapse may allow the penetration of particles deeper to functioning parts of the lung than might have been predicted. However, even in normal lungs there is some ventilation asymmetry, ventilation under resting conditions being greatest at the bases and declining to the apices.

Sample calculations of deposition of the UK ambient particulate aerosol in the respiratory system

Criteria

4.34 Sample calculations have been conducted using Urban Network monitoring data for PM_{10} using a series of examples from the ICRP 66 lung model as calculated by the LUDEP computer program for daily outdoor, environmental exposures. Values chosen are:

PM_{10}	Mean	27 $\mu g/m^3$
	99% ile	95 $\mu g/m^3$
Subjects	Adult male (outdoor exposure) 0.78 m^3/hr mean ventilation rate (55% sleep, 15% sitting, 30% light exercise)	
	Child (1 yr, representing maximum deposition) 0.19 m^3/hr mean ventilation rate (73% sleep, 17% light exercise)	
Particle composition by mass for PM_{10}	20% 0.05 μm (primary nucleation mode) 20% 0.2 μm (condensation mode) 30% 0.7 μm (droplet mode) 30% 2.0 μm (coarse mode)	

The size composition choice is somewhat arbitrary, but is based on 40% of the ambient mode being attributed to vehicle emissions split equally between the primary nucleation mode and the condensation mode.[16] The remaining 60% of the urban particle mass is split equally between the droplet (sulphate-rich) and weathering modes.

Total exposures

4.35 Mean daily exposures for an adult, therefore, are:

$$27\ \mu g/m^3 \times 0.78\ m^3/hr \times 24\ hr = 505\ \mu g$$

with a 99th percentile exposure of

$$95 \times 0.78 \times 24 = 1{,}780\ \mu g.$$

For a 1 year old child, mean daily exposures are:

$$27\ \mu g/m^3 \times 0.19\ m^3/hr \times 24\ hr = 123\ \mu g$$

with a 99th percentile exposure of:

$$95 \times 0.19 \times 24 = 430\ \mu g.$$

Total and regional lung deposition

4.36 Calculated results for total and regional deposition are shown in Table 4.6 using LUDEP deposition fractions as shown in Tables 4.2-4.5.

Table 4.6
Daily particulate deposition (by mass) by calculation

	Extrathoracic (μg)	Bronchial (μg)	Alveolar (μg)	Total (μg)
Adult (Mean)	125	31	95	251
Adult (99% ile)	438	109	334	881
Child (1 y-mean)	48	7	23	78
Child (1 y-99% ile)	168	25	81	274

Daily particle retention in the adult averages 250 μg, approximately half of which penetrates into the thoracic region of the lung. For the 1 year old child, retention averages 78 μg, such that total deposition efficiency is greater than in the adult, but penetration to the thoracic region is reduced.

4.37 One further area of interest is whether overloading of particles may occur in alveolar macrophages and estimates of daily penetration can be made. However, this assumes that all alveoli are ventilated equally.

4.38 If a particle concentration for 0.05 μm particles of 1,000 particles/cm^3 is assumed (see Birmingham data presented in Chapter 2), adult daily intake can be calculated as follows:

No. of particles = 1,000 x 780,000 x 24 x 0.43

= 8.06×10^{10} particles/day.

= 296×10^6, then number of particles per alveolus = 270 per day.

Crapo *et al*[17] estimate 2.16×10^{10} macrophages in the human alveolar region, implying 73 macrophages per alveolus. Uptake of particles by macrophages on this scale is not likely to lead to "overloading". Morrow[18] has estimated that macrophage overloading begins when the total volume of particles ingested by a macrophage reaches 60 μm^3. The volume of a macrophage has been estimated as 1,000 μm^3. Overload of a macrophage is said to be complete, ie, mobility of the macrophage is reduced to zero, when the total volume of the ingested particles reaches 600 μm^3, ie, 60% of macrophage volume. The volume of a particle of diameter 0.05 μm is 0.000065 μm^3. A macrophage would therefore need to ingest 917,431 such particles before beginning to be overloaded. Oberdörster[19] has demonstrated macrophage overloading on ingestion by macrophages of single 10.3 μm diameter polystyrene spheres. The volume of one such sphere is 572.2 μm^3.

Retention

4.39 Table 4.6 shows that approximately 95 μg particle per day penetrates to the alveolar region in the adult using the assumptions detailed in paragraph 4.34. Material penetrating to the alveolar region generally demonstrates multi-phase clearance which will be size and composition dependent to some extent. If clearance is simplified by assuming first order clearance kinetics, and the worst case situation is chosen (all clearance is in the slower phases) estimates of equilibrium lung burden can be calculated.

4.40 For example, at equilibrium, (Ao) particle retention = particle clearance = 95 μg/day. For first order kinetics:

$$A/Ao = e^{-kt}$$

$\ln (A/Ao) = -kt$ (where $A/Ao = 0.5$ (half-time of clearance), and $t = 365$d is assumed)

Thus: $k = 0.0019\ d^{-1}$

Then, for $t = 1$ (ie, clearance in 1 day):

$A/Ao = 0.9981$ (where $A = Ao-95$)

therefore: $(Ao-95)/Ao = 0.9981$

$Ao = 50{,}000\ \mu g$.

Thus, assuming a half-time clearance of one year, the lung burden of particles at equilibrium will be approximately 50 mg; for a half-time of 10 years, the equilibrium burden would be 500 mg. Using the same assumptions and calculation for particle number a half-time of one year would give an equilibrium particle number of 143,000 particles per alveolus, equivalent to 1,950 particles per macrophage.

Confounders

4.41 The above calculations generally assume an ideal case as predicted by the deposition models for standard humans, in an outdoor environment. However, a series of additional factors apply which must be taken into account in overall risk assessment.

Indoor aerosol exposure

4.42 The importance of indoor air quality is increasing in developed countries, particularly where seasonal climate extremes occur, and where energy efficient building codes are in operation, effectively "sealing" buildings. Consideration of indoor air is important as:

— lifestyle diaries indicate that up to 85% of time can be spend indoors;

— the outdoor ambient aerosol can penetrate indoors, submicron particle transfer is particularly efficient;

— indoor combustion aerosols from gas cooking and heating, from wood burning and from environmental tobacco smoke can typically double particle exposure;

— indoor exposure to specific allergens may give rise to specific health effects.

Hygroscopicity

4.43 As discussed previously, changes in regional lung deposition may arise from the hygroscopic nature of the UK ambient particle due to its salt and sulphate components. It should be noted that this effect will generally move deposition upwards in the respiratory tract decreasing penetration to the alveolar region. For example, Martonen demonstrated sulphate growth from 0.5 μm to 2.2 μm by G10 of the bronchial region, enhancing upper airway deposition.[20] The effects of hygroscopic growth on deposition are dealt with in greater depth in Appendix 3 of the second MAAPE report.[5]

Enhanced toxicity of submicron particles

4.44 A meeting of inhalation toxicologists in Irvine, California,[21] considered the hypothesis that for equivalent mass, submicron particle exhibited increased toxicity relative to larger particles. The group concluded that the following observations were of relevance:

— submicron particles show increased penetration indoors;

— submicron particles exhibit increased penetration into the respiratory tract with more efficient deposition;

— relative dose is higher in humans than in animal studies where large doses to the turbinates are observed;

— that ultrafine (20 nm) particles exhibited enhanced toxicity in animal studies (see discussion of the studies of Oberdörster *et al* in Chapter 5);

— that further personal monitoring data and size selective sampling data were required for human exposures before conclusions could be drawn.

Ventilation asymmetry

4.45 The data presented from the deposition models assumes symmetrical and equal ventilation to all regions of the lung without considering factors which may enhance asymmetrical ventilation (the normal condition in humans) such as disease (eg, chronic obstructive pulmonary disease, COPD), or turbulent flows introduced by the larynx/pharynx or at cartilaginous rings and carinal ridges at the airway bifurcations in the upper bronchial region.

4.46 These issues are being addressed in more complex supercomputer models being developed by Martonen and coworkers,[22] in which effects such as bronchoconstriction and ventilation asymmetry can be quantified.

Inter-subject variation

4.47 Caution should be exercised in the interpretation of the calculated data as they represent idealised conditions, whereas in real life, substantial inter-subject variability is likely to arise principally due to physiological and anatomical differences. For example, in a series of four experiments described by Evans *et al*,[23] the proportion of the lung deposit in the bronchial region showed consistent differences between five subjects ranging from 40-80%, although intra-subject data were consistent.

Personal exposures

4.48 There is limited personal exposure data available from the US,[24] suggesting that personal exposures often exceed estimates of exposure from static samplers by a significant factor (as a person's activity often generates a "personal dust cloud"). This may be significant with respect to calculated doses.

Uncertainties

4.49 There remains a lack of UK data related to key areas of assessment of PM_{10} dosimetry, and these include:

— UK personal monitoring data versus static EUN samplers;

— size-selective monitoring of ambient aerosol including variation of particle number concentration;

— evaluation of the significance of hygroscopic particle growth in ambient and indoor aerosols, particularly with respect to children;

— evaluation of VOC's associated with ambient particles pre- and post-inhalation to assess the importance of particles as carriers of VOCs, thus affecting their dosimetry;

— a lack of advanced lung diagnostic techniques.

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Chapter 5

The Toxicology of Inhaled Particles and Gases

Introduction

5.1 When particles are inhaled they may exert a toxicological response, the extent of which will depend upon the following factors:

a. The particles themselves:
   i. Size
   ii. Number
   iii. Concentration
   iv. Chemical and physical characteristics

b. Anatomy of the respiratory tract:
   i. Airway structure
   ii. Cell distribution
   iii. Age and species differences

c. Differences in respiratory physiology:
   i. Breathing rate
   ii. Tidal volume
   iii. Respiratory manoeuvres including breath holding.

All of these factors will influence the dose of particles delivered to the tissues lining the respiratory tract and, if absorbed, the rest of the body. Most of these factors have been considered in detail elsewhere [1,2] and in Chapter 4 of this report.

5.2 In assessing the possible mechanisms underlying any relationship between the concentration of inhaled particles and any toxicological effects, it is essential to establish the physico-chemical nature of the particles, their surface characteristics and electrostatic charge, their internal structure, their size, whether they carry any associated chemicals (solid, liquid or gas), their site of deposition, their fate after retention within the lung and whether there is evidence that they initiate any toxicological response.

5.3 The dose of a chemical to the respiratory tract, whether it be a gas or particulate aerosol, is normally estimated from a knowledge of the inhaled concentration (C), the time (t) for which it is inhaled, the volume of the air inhaled and the amount retained within the respiratory tract. The product of the concentration and time (Ct) is a measure of the total amount of chemical to which the animal or man has been exposed. It is not a measure of dose since it is the volume of air inhaled that determines the amount to which the animal or man is exposed and, of this, only a fraction may be retained. Hence, a person at rest breathing 10 l/min will inhale 5 times less than a person who is exercising and breathing 50 l/min. The effect of exercise on the toxicity of several environmental pollutants is well documented.[3,4,5]

5.4 Knowledge of the amount of a toxic substance inhaled is insufficient to determine the dose since a large proportion may be exhaled. It is necessary to measure both the inhaled and exhaled concentrations to determine the amount retained. For technical reasons, these measurements are difficult, and in most studies have not been undertaken.

5.5 The factors which determine gaseous or particulate retention within the respiratory tract are fundamentally different.

5.6 For gases, the amount retained is, in large part, a function of water solubility, vapour pressure and chemical reactivity. If there is no reaction between the gas and the liquid phase lining the airways, then the amount of gas in the liquid phase can be expressed as a ratio equal to the Henry's law constant, H. This is conveniently written:

$$H = \frac{C_g}{C_l}$$

or

$$C_g = HC_l$$

where C_g is the concentration of the gas in the gas phase and C_l is the concentration in the liquid phase. H is the ratio at equilibrium and is constant for a given temperature.

5.7 The smaller the value of H, the more soluble the gas in the liquid phase and, in general, the site of absorption of an inhaled gas appears to be related, to a significant degree, to the value of H. The less water soluble the gas, the further down the respiratory tree it will penetrate to be absorbed or to exert a toxic effect (see Table 5.1).

Table 5.1
Henry's Constant: moles/L (air)/moles/L (water) at 37°C. Data after Miller *et al*[6]

Gas	Henry's Constant H	Major site of absorption or toxicity
Nitrogen	77	Pulmonary
Oxygen	42	Pulmonary
Nitrogen dioxide	8.8	Tracheobronchial and pulmonary
Ozone	6.4	Tracheobronchial and pulmonary
Formaldehyde	0.56	Upper respiratory tract
Sulphur dioxide	0.05	Upper respiratory tract and bronchi
Ammonia	0.0011	Upper respiratory tract

5.8 The uptake, ie, percentage of inhaled gas removed, by the respiratory tract of four common atmospheric pollutant gases, ozone, nitrogen dioxide (NO_2), sulphur dioxide (SO_2) and formaldehyde differs. That of ozone differs between species, but in humans, the total respiratory uptake is 87% with the upper respiratory tract (URT) having an uptake efficiency of around 40%, and the lower respiratory tract (LRT) of about 68%.[7]

5.9 Nitrogen dioxide retention in humans has not been measured, but in rhesus monkeys, 60% of the inhaled gas was absorbed by the entire respiratory tract.[8] The site of absorption was not established, but in rabbits and dogs, 42% was absorbed in the URT.[9]

5.10 Unlike ozone and NO_2, the absorption of SO_2 is believed to be complete in the conducting airways with little inspired gas penetrating to the alveolar level.[10]

5.11 The absorption of formaldehyde, a common gaseous pollutant inside buildings, has only been studied in lower species. In rats, 93% is absorbed within the nose,[11] and Engle[12] has shown 95-100% is absorbed in the URT of dogs.

5.12 Both inhaled gases and particles independently may induce adverse reactions within the respiratory tract, the extent of which will depend on the factors described above. When inhaled together, their combined effects may be less than, greater than or the same as the sum of their individual toxicities. The aim of this Chapter is to consider those factors that may result in an increase in toxicity when the concentration of particles present in the inhaled mixture of gases, ie, the surrounding atmosphere, increases.

Mechanisms by which increased inhaled concentrations of particles might result in an increased toxic response

5.13 Two mechanisms may be proposed to explain why an increase in the concentration of particles in the environment might lead to increased adverse effects in the population exposed:

a. The particles themselves, or soluble compounds released from them, induce an adverse response.

b. The particles act as carriers for other atmospheric chemicals which might otherwise not reach regions of the respiratory tract where their effects will be manifest.

These possibilities will be considered and evidence to support these hypotheses examined.

The particles

5.14 The inhalation of large concentrations of particles as dusts and smokes is well documented in industrial situations. Many induce well known disease conditions including, for example, pneumoconiosis (coal dust), silicosis (silica), asbestosis (asbestos) and berylliosis (beryllium). These conditions are generally characterised by chronic exposure to high concentrations (by ambient standards) of dust which may lead to pulmonary fibrosis, reduced pulmonary function, chronic bronchitis, and, in some cases, cancer.[1] Levels of dust in UK coal mines are controlled in terms of the mass concentration of particles 1-7 μm in diameter and expressed as mg/m^3. In the UK, the maximum allowable level of such dust in return roadways is 7 mg/m^3.[13] Exposure to high concentrations of allergenic particles such as pollen, pollen fragments, fungal spores and other organic and inorganic dusts may lead to hypersensitivity reactions which may be manifested as pneumonitis, allergic rhinitis or asthma.[14]

5.15 In rural and urban environments, however, the concentration of particles is considerably lower than has been seen in the industrial setting and ranges between 10 and 45 μg/m^3 with short-term peaks exceeding 60 μg/m^3 in 1992 for sites in London and Birmingham.[15] The moving average for London is fairly stable at 30 μg/m^3 as measured by PM_{10} determination. However, there can be large variations in PM_{10} from one day to the next, and since the variation in road traffic is small, this variation is most likely due to the influence of meteorological factors, in particular, wind speed and rainfall. [For details see Chapter 2.]

5.16 The composition and concentration of these atmospheric aerosols is notoriously variable from one location to another and the extent of this variation has been comprehensively described in a previous report,[15] and has been described in Chapter 2.

5.17 PM_{10} is the present measure, in most developed countries, of respirable aerosol. However, PM_{10} is a mass determination of aerosol concentration and from a toxicological point of view, an inadequate measure upon which to base an assessment of the dosage of atmospheric particles to the respiratory tract. (See paragraph 5.44.) This has been recognised with the introduction of dichotomous samplers where $PM_{2.5}$ is also measured. In early studies (1982) in Yorkshire, it was shown that the average total mass concentration at an urban site was 35.5 μg/m^3 and at a rural site, 26.9 μg/m^3. Of the total mass sampled in either a rural or urban environment, 63% was less than 2.5 μm in size.[16] Eighty five percent of the sulphate was associated with the fine fraction and it was the largest single component of this fine fraction (27-29%) in both the rural and urban samples. Nitrates accounted for around 8% of the total fine fraction.

5.18 A major pollution peak occurred in September of 1982 in which the mass particulate levels increased by 2-3-fold to 192 and 97 $\mu g/m^3$ at the urban and rural sites. At the same time, sulphur dioxide levels rose to 136 and 110 $\mu g/m^3$ (47.5 and 37.5 ppb).[16] During this peak period, however, the proportion of fine aerosol increased to 76-78% of the total mass and on a lower peak day in August it reached 81% of the total aerosol mass. Unfortunately, a full particulate size distribution was not made.

5.19 The mass of a 1 μm particle of unit density is equivalent to the mass of one thousand, 0.1 μm particles. However, the surface area of one thousand, 0.1 μm particles is 10 times greater than the single 1 μm particle. Consequently, a 10% increase in PM_{10} could represent a very large percentage increase of both the number of particles and the surface area of particles, and hence toxicant, presented to the bronchial, pulmonary and alveolar regions of the lung. The increased surface area would also greatly facilitate the rapid dissolution of any sorbed or soluble material. With the increased surface area to volume ratio of submicron particles and their known entry into and retention within the pulmonary region of the human lung,[17] they present a potential and, as yet, undefined toxicological hazard.

5.20 The change in the number of particles in the air during pollution incidents may be a critical factor in the initiation of toxicological responses. Recent dynamic measurement of changes in the entire spectrum of particle sizes (0.01-25 μm) over 24 hr periods using modern instruments, has been completed in Germany.[18] When the wind direction changed from a major highway to that from a rural area, there was an 8-fold fall in the number of particles, but only a 2-fold fall in mass concentration. This fall was well correlated with a fall in nitrogen monoxide (NO) concentration. Whilst the change in particle number above 2,000 nm was small, below this size, the changes in particle number reached around 100-fold at the lowest size measured (10 nm).

5.21 An additional series of measurements in the same study[18] showed marked peaks in particle numbers between 06.00-12.00 h and 16.00-21.00 h, which corresponded with much smaller fluctuations in particle mass concentrations.

5.22 Recently, attention has been directed to the fate of ultrafine (< 50 nm) particles within the lung. Oberdörster's group has shown that after instillation of ultrafine titanium dioxide particles (60-1,000 μg in 200 μl saline) into the rat lungs a significant number are absorbed into the interstitium or taken up by the epithelial cells lining the airways.[19] This increased interstitialization was accompanied by an acute inflammatory response as indicated by increased numbers of polymorphonucleocytes (PMN) amongst lavaged cells.[20] Oberdörster's group have also shown that prior exposure to NO_2 (5 ppm, 9.4 mg/m^3; 1 hr) will reduce the rate of the slow phase of pulmonary clearance of aerosols of DPTA (0.7 μm) from 3.1% per minute to 1.7% per minute.[21]

5.23 Carbon black particles also induce an inflammatory response, but the mechanism appears to be different since carbon black particles are known to induce chemotactic serum factors such as C5a, whilst this is not true for titanium dioxide.[22] It might be expected from such effects that continued exposure to ultrafine aerosols, regardless of their chemical or physical character, could induce a prolonged inflammatory state within the interstitium, the severity of which would depend on the dosage rate and frequency of exposure.

5.24 Several authors have established that there is an increasing concentration of many toxic elements such as arsenic, beryllium, cadmium, chromium, manganese, nickel, lead, tin, selenium, titanium, vanadium and zinc in atmospheric and ultrafine particles with decrease in particle size in fly ash.[23-25] By implication, this means that the small particles which remain suspended in the atmosphere for the longest periods, and which deposit in the pulmonary regions of the lung, contain the highest concentrations of toxic elements. Linton *et al*[25] have confirmed by Auger and ion microprobe and mass spectroscopy that a number of elements exhibit significant

increases in concentration near particle surfaces. The authors emphasise that conventional bulk analyses of particles provide a poor measure of the actual concentrations of many toxic trace elements that are in effective contact with the external environment of the particle. For a particle of an aerodynamic diameter of 1 μm, as much as 80% of the trace elemental mass is within the surface extractable layer. This would be equally true of adsorbed gases and water soluble salts and acids.

5.25 The presence of high concentrations of metal ions and other adsorbed/condensed chemicals on the surface of particles deposited in the pulmonary region will clearly have a major influence upon the toxicological response induced. Adsorbed gases may be catalytically converted to other products which may, or may not, be more toxic than the parent compound, this is discussed in more detail below. The adsorbed species itself may, of course, elicit its own response. Realistic measures of dose, however, do not appear to have been made, although some attempts have been made to calculate from theoretical considerations the amount of metal ions delivered to the pulmonary regions of the lung after inhalation of environmental particulates.[26]

5.26 That the metal ion composition of aerosols is critical to their biological effect was demonstrated in a comparison of the irritant potencies of sulphate salts.[27] The order of irritant potency of aerosols of particles size range (MMD: 0.1-0.8 μm; salt concentration: 0.13-0.77 mg/m^3; sulphate concentration 0.43-10.98 μg/m^3) was ammonium sulphate > ammonium bisulphate > cupric sulphate. Significantly, however, only the copper sulphate aerosol potentiated the response to SO_2 (0.36 ppm, 1.03 mg/m^3 SO_2 and 0.4 mg/m^3 $CuSO_4$) as measured by an increase in airways resistance and a decrease in compliance. In conjunction with earlier studies, the authors were able to rank the irritant potency of sulphates (see Table 5.2).

Table 5.2
Relative irritant potency of sulphates. Data after Amdur *et al*

Compound	Relative potency
Sulphuric acid	100
Zinc ammonium sulphate	33
Ferric sulphate	26
Zinc sulphate	19
Ammonium sulphate	10
Ammonium bisulphate	3
Cupric sulphate	2
Sodium sulphate	0.7

5.27 The salts of manganese, vanadium and ferrous iron have been shown to potentiate the response to SO_2,[28] and at concentrations of 14-18 μmol of metal/m^3, they increased the response by 3-4-fold. These metals are known to catalyse the oxidation of SO_2 to sulphuric acid (see below) and Chang *et al*[29] have shown that copper sulphate also promotes this catalysis. Of the metals studied, copper appears to be the most powerful potentiator of this oxidation in aerosols.

5.28 Two other parameters need to be considered if serious attempts are to be made to predict the amount of retained gases and chemicals upon atmospheric particles:

a. The morphology and structure of the particle surface which will affect the adsorption characteristics for a given material.

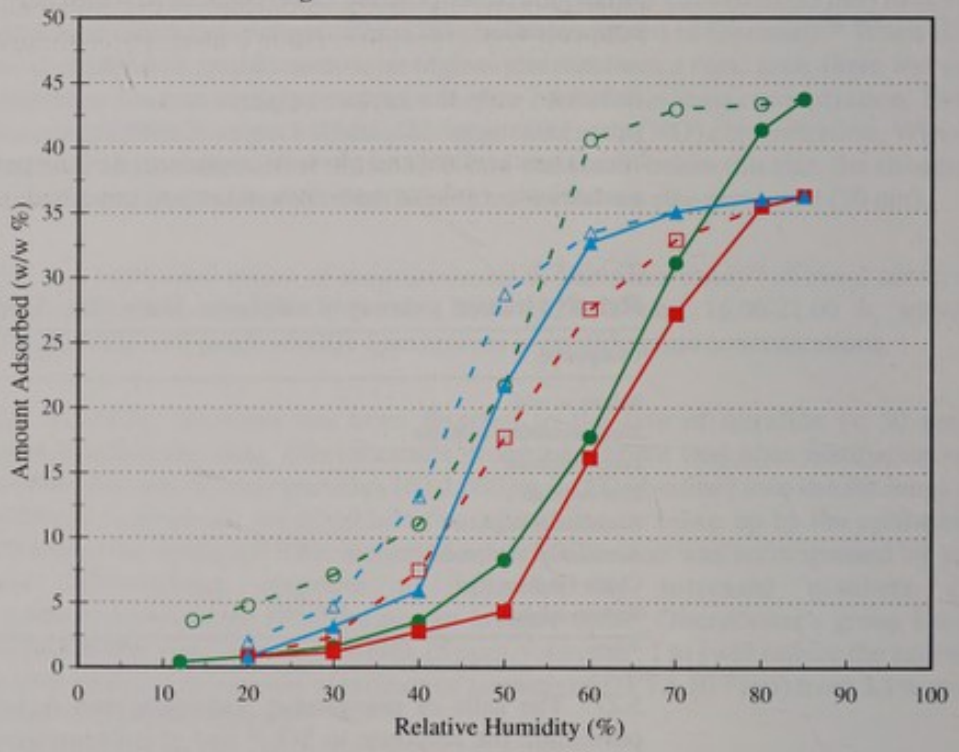
b. The effects of other adsorbates (mainly water).

5.29 The surface and internal structure of aerosol particles is highly variable and dependent upon the source of the particles. Schure *et al*[30] have described in detail the

surface area and porosity of coal fly ash and shown that small ash particles (< 5 μm) are predominantly nonporous spheres with irregular surface morphology due to very small embedded particles of porous carbon. The latter have a major influence on the surface area of the ash. Any vapour deposited on this ash is likely to be available for direct interaction with biological tissue, although the amount of organic and inorganic material adsorbed is highly dependent on power plant design.

5.30 The amount of material adsorbed onto a particle is usually defined in terms of its adsorption isotherm. The shape of this isotherm only applies for a given set of conditions which include temperature, relative humidity (RH), pretreatment of the adsorbate (chemical or drying, for example). Figure 5.1 shows the absorption isotherms for two different types of charcoal; that in red is for a coal based BPL carbon as received from the supplier, and that in blue is the same carbon aged in a humid atmosphere for several months. The water content of the carbon at 50% humidity is 22% (w/w) and 30% (w/w) of the absorption and desorption parts of the hysteresis loop; however, these data change to 5% and 18%, respectively, after ageing. The green lines are for a totally different type of charcoal measured as received.

Figure 5.1: Water Isotherms on Carbon



5.31 By deduction, the water uptake of 1 g of BPL charcoal at 50% RH (a typical ambient value in the UK), would be expected to be 90 mg. The aged sample, however, would absorb 240 mg (2.7 times as much) and the nutshell charcoal (characterised by the green curve in Figure 5.1) would have a significantly different saturation adsorption of some 70 mg higher than the BPL charcoal. Adsorption phenomena are competitive in nature and the presence of water may have a major influence on the adsorption of hydrophobic materials and upon the available surface area in porous materials. Such variations are difficult to predict for "well characterised" materials such as charcoal. There is extreme difficulty in deriving such information for complex and highly variable materials such as atmospheric particles. Sampling and storage may be other significant experimental variables.[31]

5.32 For environmental gases such as SO_x and NO_x, adsorption would be expected to be as variable as that of water. Davini[32] has shown that the adsorption of SO_2 on a substrate such as carbon is very dependent on the way the surface is treated. For a

series of carbons, the sulphur dioxide content can vary by a factor of three, from 49 mg/g to 146 mg/g. There is evidence that silica based adsorbents are just as variable and very dependent on the type of silica.[33] In all cases, adsorption is a competition between the gas of interest and the ever present water vapour. It is difficult to define an adsorption characteristic without reference to humidity conditions at the time adsorption and desorption occur.

5.33 The complexity of these adsorption processes is illustrated by the studies of Gray and Do,[34] and Rothenburg *et al.*[35] The former authors developed a theoretical model of adsorption and desorption based upon a single large (2 mm) particle of activated carbon, whilst the latter authors, using diesel exhaust particles, concluded that such particles have a considerable capacity for absorbing materials from ambient air and for catalysing atmospheric reactions. Similar studies by Rothenburg[36] on coal fly ash showed it to have a large surface area (1 m^2/g) and to be completely covered by a monolayer of water under most conditions of environmental interest. This layer may inhibit the adsorption of PAH compounds but may facilitate that of SO_2.

5.34 The problem of adsorption/desorption isotherms and the associated chemical reactions with the particle surface is central to an understanding of the epidemiological studies upon the effects of particles on human disease. None of the key studies contain any measures which would permit an estimate of the dose of inhaled materials to the bronchiolar and pulmonary regions of the lung. The following important information is absent from these investigations:

a. The particle size distributions.

b. The chemical and physical composition of the particles and hence the extent to which each aerosol has adsorbed/desorbed chemicals and water in the environment.

c. The surface chemistry and the extent of chemical reactions with these surfaces.

d. The nature of interactions between the surface of particles and the complex molecules, eg, proteins, of biological fluids.

5.35 The studies of Medalia *et al*[37] illustrate the complexities of the problem and point to potential difficulties in the interpretation of toxicological studies where carbon black has been used as a surrogate for environmental carbonaceous particles. The authors have shown that carbon black is composed of aggregates of colloidal carbon (< 1 μm in the longest dimension) with very small amounts of inorganic solids, tars and moisture; some are chemically oxidised after production. Soots, on the other hand, contain variable quantities of carbonaceous and inorganic solids together with adsorbed and occluded organic tars and resins, liquids and gases—especially water, sulphuric acid and nitrogen oxides. As might be expected, the authors demonstrated that soots possessed much higher levels of mutagenicity than carbon blacks. Great care should be taken in the extrapolation of any information obtained with one type of atmospheric particulate material to another.

5.36 To establish cause and effect relationships the following information is essential:

a. Precise identification of the particulate material including data on surface area and the hydrophobicity of the surface.

b. Information on the adsorption characteristics of the particles together with information on the effect of atmospheric pollutants and water vapour adsorption.

c. Information on the kinetics of the adsorption and desorption to predict effects, such as the age of the particle and moves from one area to another, and when it enters the respiratory tract.

d. A complete particle number and mass size distribution.

Experimental studies upon the effects of concurrent inhalation of particles and environmental pollutant gases

Introduction

5.37 The combination of particles with gases and their effect on toxicity was recognised by Dautrebande and Capps[38] who demonstrated that aerosols of carbon black, oil and sodium chloride (0.2-0.3 μm) accentuated the irritancy of SO_2 and sulphur trioxide (SO_3) (200-500 ppb) which of themselves were not irritant, and of formaldehyde, acrolein and 5 organic peroxides, which were. Later studies[39] assessed eye irritation only, but showed potentiation between formaldehyde, sulphuric acid, nitric acid, used motor oils and silica dust (0.1 μm).

5.38 Two important early studies which investigated the respiratory effects of combined gas and particulate exposure were those of La Belle *et al*[40] and Amdur.[41] Goetz[42] later used these in his theoretical treatment of the adsorption of gases upon inhaled particles and the factors which might control the synergy.

5.39 La Belle *et al*[40] examined the effects of co-exposure of mice to vapours of formaldehyde, acrolein or nitric acid in the presence of aerosols of four liquids: triethylene glycol, ethylene glycol, mineral oil or glycerin, a solution of sodium chloride or 4 solids: Dicalcite, Celite (both diatomaceous earths), attapulgus clay or silica gel. Experimental conditions were arranged such that the gaseous exposure would kill the exposed animals in around 100 minutes and then the time to death of other groups of mice were determined in the presence of particulate aerosol. This study might have been expected to provide a useful guide to the relationship between particulate concentration and morbidity. However, there are features of the study which seriously limit the value for extrapolation to the assessment of the effects of environmental pollutants:

a. Of the three vapours used only one concentration was specified (acrolein) and that was very high (15 mg/l). The others must be presumed to be very high as they killed within 100 minutes.

b. The aerosol concentrations were very high (0.31-2.21 mg/l for the formaldehyde study; 0.05-0.39 mg/l for acrolein and nitric acid).

c. The MMDs of the aerosols were between 1.8-3.3 μm which is too high for penetration into the bronchiolar region of the mouse (Raabe *et al*[43] have shown that only 10% and 6% of 1.1 μm particles reach the pulmonary and bronchial region, respectively, in this species).

d. The period of exposure of control mice to the aerosol itself was considerably shorter than that of the test species.

5.40 Despite these serious reservations, it is clear from the studies that there were distinct interactions between the vapours and the aerosols, but these were not uniform in their effects. In general, formaldehyde was more toxic in the presence of droplet aerosols and the diatomaceous earths, whereas nitric acid was less toxic. With acrolein, no consistent pattern emerged. On this basis, the authors proposed that whenever the penetration of the aerosols into the deep lung is greater than the penetration of the vapour, then toxicity is increased, but that when the penetration of the vapour exceeds that of the aerosol then there is either no effect or a lower toxicity.

5.41 As will be seen later, this is probably over-simplistic as it ignores the extent of adsorption and subsequent chemical reaction with the aerosol. Nevertheless, Goetz[42] used this study to develop a theoretical treatment of such interactions and proposed the following:

a. *In the absence of aerosols* the toxicological response should *increase with gas concentration.*

b. *In the presence of aerosols* the response should:

   i. *Increase with particle concentration (Cp) if the gas concentration (Cg) is constant.* (Assuming that the gas concentration, in the gas phase, is only a small proportion of the gas associated with the particles.)

ii. *Increase with Cg if Cp is held constant.*

iii. *Increase as particle size decreases* (if Cg and Cp remain constant). This is because as surface area increases, more gas is adsorbed and the dose to the parenchyma increases.

iv. *The degree of synergism, for a given Cg, should increase for small values of Cg until saturation of the particles occurs, after which there will be no synergism.*

5.42 These conclusions may be interpreted in the following way: at low gas concentrations, as the gas concentration increases, more is adsorbed onto the particles so that the difference between response in the presence and in the absence of aerosol is greater (if the effect is to carry more gas into the target area). However, there comes a time when the particles are saturated and their effect on the total response will diminish as the gas concentration rises. This presumes that on arrival at the parenchyma the adsorbed gas then desorbs; if it does not then the effect of the aerosol is to reduce the effects of the gas.

5.43 The conclusions from Goetz's[42] proposals may be expressed simply as follows:

a. *Synergy is greatest at low gas concentrations.* At high concentrations of gas, particle concentration is less important unless *most* of the gas is normally absorbed in the URT. It all depends on the total amount of gas molecules adsorbed onto the particles and whether they can be desorbed or solubilised.

b. *If particle mass stays constant, but particle size decreases (more particles and no aggregation) then synergy will increase.* (In toxicological terms the dose-response curve, for pulmonary effects, shifts to the left for gases that are scrubbed out in the URT.)

5.44 If these conclusions are true then the conditions normally experienced in atmospheric pollution incidents meet the criteria established by Goetz (*viz*: low gas concentrations and increasing particle numbers). One would predict that as the number of small particles increased then the degree of synergy would increase for a fixed concentration of gas. As discussed above (paragraph 5.19) a relatively small increase in the mass of particles collected by a PM_{10} sampler could mean a large increase in the number of ultrafine particles. This would result in a greater degree of synergy than might be expected from the small fractional increase in aerosol mass as the amount of adsorbed gaseous phase would increase as a squared function of particle size in line with the increase in surface area of the particles. With the present state of knowledge upon particle size distribution, chemical composition and lack of knowledge of the adsorption isotherms for complex, highly varied atmospheric pollutants, it is currently impossible to make realistic calculations of the adsorbed material. Measurement of the full particle size distribution of atmospheric aerosols in urban and rural environments would allow first approximations of these effects to be made.

Sulphur dioxide and sulphuric acid

5.45 The respiratory effects of SO_2 and sulphuric acid have been comprehensively reviewed elsewhere[10] and will not be considered in detail here. This section will consider the experimental evidence that when inhaled in the presence of particulate aerosols, they are more hazardous.

5.46 Some of the most well designed and controlled animals studies upon the effects of particles and gases inhaled simultaneously have carried out by Amdur's group.[44-59] Early studies by Amdur[50] examined the interaction between sodium chloride aerosols and formaldehyde, and were used by Goetz[42] in his theoretical assessment of such interactions. Subsequently, Amdur and colleagues, using SO_2 and sodium chloride aerosols, established three characteristic features of such interactions:

a. Particles of less than 1 μm diameter potentiate the SO_2 response to a greater degree than those above 1 μm.[51]

b. The animal response to a given concentration of SO_2 increases with aerosol concentration.[52,53]

c. The increased effects result from chemical events on the particle producing a more irritant aerosol.[52,53]

5.47 In humans, Koenig *et al*[54] have shown that in a group of eight atopic, but nonasthmatic adolescents, who had signs of hyperactive airways, there was an increased sensitivity to 1 ppm (2.86 mg/m³) SO_2 over that in normal adolescents. This effect was between 3-22 times greater than that in normal subjects, but was not further enhanced when they were exposed to 1 ppm (2.86 mg/m³) SO_2 in the presence of a 1 mg/m³ aerosol (MMD 0.9 μm; σg 2.0) of sodium chloride droplets at 75% RH. Earlier work in this laboratory had demonstrated that a combined sodium chloride droplet aerosol/SO_2 exposure of this type reduced pulmonary airflow in the guinea pig, whereas a crystalline sodium chloride aerosol with SO_2 did not. It was hypothesised that the SO_2/sodium chloride droplet was irritant and contained sulphite and bisulphite ions that penetrated beyond the URT[55] and more closely simulated the aerosols present in the environment.

5.48 In the earlier animal studies, there were reservations about the nature of the aerosol used and the high concentrations necessary to demonstrate effects. Based upon evidence that aerosols produced by smelters and the combustion of coal contained increased concentrations of metals in the submicron fraction, later studies used furnace generated zinc oxide aerosols in the 0.05-0.1 μm range.[56,57] There is evidence that urban aerosols have a 100-1,000 fold enrichment of elements such as lead, antimony, selenium, arsenic, nickel, chromium, zinc and sulphur and these increase markedly in concentration with decreasing particle size in fly ash from coal fired power plants.[58]

5.49 Guinea pigs were exposed, in atmospheres of either low relative humidity (30% RH) or high relative humidity (80% RH), to zinc oxide (ZnO) aerosols generated in a high temperature furnace. When exposed to ZnO aerosols (2.42 mg/m³) of 0.05 μm generated in the presence of 1 ppm (2.86 mg/m³) SO_2 for 1 hour, there was a statistically significant reduction in airways resistance of the airways only when the relative humidity was high. At low relative humidity, the response could be completely accounted for by the responses expected from the ZnO and SO_2 alone. At high relative humidity, there was a rapid increase in airways resistance to 29% above the control which was rapidly reversed at the end of the exposure.[46]

5.50 Electron Spectroscopy for Chemical Analysis (ESCA) and Atomic Absorption Spectroscopy (AAS) indicated that at low relative humidity there was no evidence of association of sulphur with the particles,[46] whereas when water vapour was added downstream from the generator, there was evidence for the presence of sulphite. When water vapour was added during the generation process, ESCA showed that sulphate predominated with sulphite and sulphur trioxide in the surface layer and was removed by the sputtering of the ion beam. Addition of these aerosols to water produced a rapid decrease in pH, indicating the ready availability of surface acid.

5.51 If there is a catalytic conversion of SO_2 by the metal ions, then the number of reaction sites which is directly proportional to the number of particles and not the SO_2 concentration, will control the amount of sulphuric acid formed. This would predict that when the number of particles increase for a given concentration of SO_2, the measured effects should increase. Within narrow limits (1 ppm, 2.86 mg/m³ SO_2 and 1.3 and 6 mg/m³ ZnO) a dose-response relationship of this type was established.[44]

5.52 More recent studies, by this same group, using ultrafine aerosols of ZnO generated at 500°C in the presence of SO_2 and water vapour, have confirmed the presence of oxidised sulphur (S^{VI}) on the particle surface.[48] This is thought to be predominantly sulphuric acid and zinc sulphate. Exposure of guinea pigs to these aerosols, carrying the equivalent of 20 μg/m³ sulphuric acid, produced an increased

hypersensitivity to subsequent exposure to acetylcholine. Such effects could only be reproduced by a pure sulphuric acid aerosol of 10 times the concentration (200 $\mu g/m^3$).[48, 49] There was also a dose-dependent reduction in the lung diffusing capacity for carbon monoxide (DL_{CO}) which became statistically significant at the equivalent of 10 $\mu g/m^3$ sulphuric acid. From a study of the biochemistry and histopathology, there was also evidence of increases in the permeability of the endothelial and epithelial cells of the air-blood interface.[45]

5.53 Particles which contain metal ions in their surface layers are not a necessary prerequisite to the catalytic conversion of SO_2 to sulphuric acid. Novakov *et al*[59] have shown that 20 μm carbon particles produced in a laboratory furnace in the presence of SO_2 contain sulphate on their surface. Oxygen was shown to be necessary, and although water molecules enhanced the sulphate concentration, they were not essential. It was shown that at initial SO_2 concentrations of 5.5 and 9.9 ppm (15.7 and 28.3 mg/m^3), the amount of SO_2 converted to sulphate was independent of the SO_2 concentration. This was attributed, as in the studies of Natusch *et al*,[58] to the saturation of the available active sites on the soot particles. It did increase, however, with an increase in the number of very small, high-surface area particles produced in oxygen rich flames.

5.54 It is difficult to extrapolate these results to the human situation. The levels of SO_2 examined in these studies were considerably in excess of current levels of environmental SO_2, though not of those serious pollution episodes of the past. It is known that guinea pig bronchi and peripheral airways have a thicker smooth muscle layer than those of humans which results in an increased sensitivity to irritants. However, increases in airways resistance of humans after inhalation of SO_2 are well documented[60] and these effects are rapid, dose-dependent and tend to reach a peak after about 10 min. Mouth breathing and exercise cause greater changes in pulmonary resistance as would be expected from a gas that was largely absorbed in the upper respiratory tract.

5.55 What is clearly established is that in complex combustion processes a significant number of submicron particles are generated which have a high concentration of metal ions or, in the case of carbon, reaction sites in their surface layers. These catalyse the oxidation of sulphur to sulphuric acid, sulphate and sulphite which also reside within the surface layers of these particles. The studies upon the fate of ultrafine particles within the lung (see above) show that such particles penetrate readily to the deep lung. The 10-fold increase in potency of this acidic aerosol, demonstrates that the potential exists for irritant chemicals to be generated at the surface of ultrafine particles and be carried into the pulmonary region.

Oxidant gases: Ozone and nitrogen dioxide

5.56 The respiratory effects of the gases ozone and NO_2 have been reviewed recently,[61, 62] and will not be considered in detail here. This section will consider the experimental evidence that either gas when inhaled, in the presence of particulate material, is more hazardous.

5.57 An early study of the interaction of NO_2 with particles was that of Boren.[63] Using coconut shell charcoal, mice were exposed to either charcoal alone (I), NO_2 alone (II and III) or charcoal which had been saturated with NO_2(IV):

I. Carbon only, exposed for 6 h per day for total times between 6-640 h in a year.

Nitrogen dioxide alone:

II. A single 30 min exposure (LD50: 250-500 ppm, 470-940 mg/m^3).

III. 30 min per day (25 ppm, 47 mg/m^3), 5 days per week for 4.5 months.

IV. Carbon/NO_2 group. The carbon had been pre-saturated with NO_2 (552 mg NO_2/g carbon) 6 h/day, 5 days/week for 3 months. In this group the amount of NO_2 in gas phase during exposure was measured at 25 ppm (47 mg/m^3).

5.58 Exposure to charcoal alone resulted in large amounts being distributed to all parts of the lung which cleared slowly in the next 18 months but which did not produce any evidence of tissue damage, pulmonary oedema, accumulation of inflammatory cells or damage to alveolar walls. Acute exposure to high levels of NO_2 produced deaths within 24 hours mainly from a permeability type pulmonary oedema with bronchiolar inflammation. Surviving animals recovered within 7 days. Chronic exposure to 25 ppm (47 mg/m^3) NO_2 had no measured effect on any mice; however, of the mice exposed to the charcoal/NO_2 mix, 13 out of 20 died. Those that survived appeared normal and were gaining weight; however, on histological examination, there was focal loss of alveolar walls which were covered by charcoal particles. In some cases, the lesions extended all the way to the pleural surface. There was little evidence of inflammatory cell infiltration and no fibrosis or pulmonary oedema.

5.59 As the experimental protocol for each exposure group was different, comparisons are difficult, furthermore, in the charcoal/NO_2 exposure, significant amounts of the adsorbed NO_2 had desorbed into the gas phase. This study is useful in that it illustrates the difficulties of calculating the dose of NO_2 carried into the pulmonary region of the lung even when the apparent conditions of exposure are known. The mixture was prepared by repeatedly adding NO_2 gas to 20-30 g of carbon in a 5 l flask until no more NO_2 was adsorbed. Chemical and physical analysis showed 553 $\pm$ 25 mg NO_2 absorbed per gram of carbon. All but 25 mg of this could be recovered by heating the carbon, and, if allowed to stand in the open air, the amount of NO_2 decreased slowly. During exposure, a concentration of 25 ppm (47 mg/m^3) of NO_2 was achieved in the gas phase.

5.60 To calculate the dose of NO_2 present on the charcoal in the deep lung, the following information is provided in the paper:

a. Of 16,000 particles of carbon per one cm^3 of inhaled air, 6,080 were less than 2 μm in diameter. The particle size distribution is not given.

b. The charcoal carries 552 mg NO_2 per gram.

However, the following information has to be assumed:

a. That all of the particles below 2 μm enter the deep lung of mice (but see paragraph 5.39(c)).

b. The minute volume of mice (approximately 20 ml/min).

c. The surface area and density of the particles.

d. That all of the carbon entering the pulmonary region desorbs all of its gas.

e. There has been no chemical reaction between the nitrogen dioxide and the carbon surface.

Clearly, these variables introduce a very large degree of uncertainty into any calculation, and suggest that for polymorphous aerosols, extrapolation is not feasible with the current level of knowledge.

5.61 Gardner *et al*[64] showed that female mice exposed to ozone (100 ppb, 200 μg/m^3) for 3 hours followed by sulphuric acid aerosols (900 μg/m^3) for 2 hours were significantly more susceptible to the effects of inhaled *Staphylococcus pyogenes*. Exposures to gas or acid alone, or if the acid preceded the ozone, were without effect. It was speculated that the changes may have resulted from:

a. Altered frequency and depth of respiration.

b. Ozone induced biochemical and physiological changes which increase sensitivity to sulphuric acid.

c. As a consequence of b, there may have been increased deposition of sulphuric acid resulting in a greater dose to sensitive tissue or deeper penetration into the respiratory tract.

5.62 Sequential exposure of healthy human volunteers to ozone (300 ppb, 600 $\mu g/m^3$) followed by sulphuric acid aerosols (0.1 mg/m^3; 0.13 μm MMD) induced a small change in bronchial hyperreactivity which was regarded to be of no apparent risk.[65] Combined exposures of 370 ppb (740 $\mu g/m^3$) ozone, 370 ppb (1058 $\mu g/m^3$) SO_2 and 100 $\mu g/m^3$ sulphuric acid (0.5 μm MMD) for 2 hours including two, 15 min periods of exercise, only induced a small decrease in FEV over that which would have been induced by the ozone alone.[66]

5.63 Direct measures of the effect on the respiratory tract, of combined exposures to ozone and sulphuric acid or ammonium sulphate aerosols have been made by Last and his co-workers.[67-71] In the earlier studies,[67] rats were exposed to ozone concentrations of 400-500 ppb (800-1,000 $\mu g/m^3$) and 11- 3000 $\mu g/m^3$ of sulphuric acid aerosols (MMAD 0.38 μm). Exposure for 3 or 14 days, to 500 ppb (1,000 $\mu g/m^3$) ozone at the same time as 1 mg/m^3 sulphuric acid produced highly significant increases of 127% (3 days) and 132% (14 days) in glycoprotein secretion in tracheal explants from the rats. Sulphuric acid alone was without effect, and ozone alone decreased secretion. Lowering the sulphuric acid concentration to 11 $\mu g/m^3$ produced similar results.

5.64 Exposure of rats for 7 days to ozone (0.5-2 ppm, 1-4 $\mu g/m^3$) or NO_2 (5-20 ppm, 9.4-37.6 mg/m^3) produced clear dose-response relationships between the rate of collagen synthesis and the exposure concentration of the gases.[68] On this basis, ozone is some 15-20 times more toxic to rat lungs than NO_2. Simultaneous exposure to an ammonium sulphate aerosol (5 mg/m^3; MMAD 0.8-1.0 μm) increased collagen synthesis induced by ozone by 180%, although the ammonium sulphate itself was without effect. Replacing the aerosol with sulphuric acid (1 mg/m^3) had similar effects. The interstitial thickening and influx of inflammatory cells, characteristic of ozone exposure, was accentuated in the presence of ammonium sulphate aerosol and there was an almost 3-fold increase in fibroblasts to account for almost 33% of the total cell content. This was associated with an increased deposition of collagen fibres. Similar studies with NO_2 (5-25 ppm, 9.4-37 mg/m^3) and ammonium sulphate aerosols (5 mg/m^3) produced a 190% increase in collagen synthesis over that seen in the absence of aerosol.

5.65 Subsequent studies have indicated that neutral aerosols (sodium sulphate or chloride) are without effect and it is the acidity of the aerosol and not the sulphate content that is responsible for the synergy.[69] By comparing two different particle sizes, the authors claimed that synergy could be demonstrated with 0.5 μm, 1 $\mu g/m^3$ sulphuric acid aerosol, but not with a 0.02 μm aerosol. However, the 0.5 μm size cited was a MMAD and the 0.02 μm a CMD and were thus not strictly comparable.

5.66 On the basis of these and other studies,[70,71] Last[72] has proposed that the lowering of pH at the site of impaction of acid aerosols extends the life of free radicals generated by interaction of ozone with lung cells or the lung lining layer. The increased efficacy of 0.5 μm aerosols is claimed to support this observation as it would deposit in the same pulmonary zone as that of ozone. However, this may also be explained by the increased mass of acid deposited in the larger particles.

5.67 Others have investigated the synergistic effects of other types of aerosols with oxidant gases. Of special relevance is that of Kleinman *et al*[73] using diesel soot with admixtures of both ozone and NO_2. The soot was prepared from diesel exhaust, scrubbed free of SO_2 and carbon monoxide (less than 10% of the particles were lost by scrubbing though the size of these particles was not determined). The particles were shown to have a chain agglomerate structure typical of diesel soot aerosols with a primary particle size of about 0.04 μm. Exposure of the rats to the soot (250 or 500 $\mu g/m^3$) together with 400 or 600 ppb (800 or 1,200 $\mu g/m^3$) ozone, together with nitrogen dioxide 1.5 and 2.5 ppm (2.82 or 4.7 mg/m^3) and 110- 260 $\mu g/m^3$ nitric acid changed the lung histology, alveolar macrophage function and mucosal permeability.

At the highest concentrations used there were significant adverse changes in all measured parameters after 1 day and macrophage and permeability after 5 days. However, none of these differences was any greater in the presence of soot than in its absence, and there was a suggestion that the soot attenuated the response of the gases in a 20 day exposure. The authors concluded that diesel soot/oxidant gas mixtures are not more toxic than the gases alone.

5.68 Using carbon black instead of soot, Jakab and Hemenway[74] investigated the effect of combined exposure to ozone (800-3,000 ppb, 1,600-6,000 $\mu g/m^3$) and carbon black (10 mg/m^3; MMAD 2.4 μm; σg 2.75) in mice. Exposure to carbon black was without effect though ozone alone produced a pronounced inflammation and suppression of alveolar macrophage phagocytosis. Exposure to carbon black, either before or after the ozone, did not accentuate these effects; however, simultaneous exposure produced a further doubling in the levels of PMNs, indicating a significant inflammatory response over that induced by ozone alone, 24 hours later.

5.69 In all of these animal studies the observed pathology and histopathology is the same for the mixture of gas and particles as for the gas alone. What appears to have happened is that the dose-response curve has moved to the left and the presence of particles, which in themselves appear without effect, increased the potency of the gas itself. The simplest explanation for this phenomenon is that the particles have carried increased amounts of the gas into, and/or further into, the respiratory region of the lung, although in the case of both ozone and NO_2 all evidence indicates that they penetrate to this region of the lung quite effectively anyway.[6]

5.70 It would, however, be wrong to assume that this is the only reason for the apparent synergy as the substances used as aerosols are diverse and it is unlikely that the interaction between the gases and the substrates are identical. In addition, pulmonary responses to injury are limited and inflammatory cell invasion, permeability oedema and evidence of early fibrotic events is common to a diverse range of chemical insults. Of more serious concern is that the concentrations of both gases and particles studied are 1-2 orders of magnitude higher than measured in the epidemiological studies reported elsewhere in this report. The limited studies in humans, which in themselves use relatively high concentrations of gases and particles, suggest only marginal changes in measured parameters and hence the significance of the animal studies to humans remains contentious.

5.71 Recent studies have shown that inhalation of ozone at 3 ppm (6 mg/m^3) for 15-20 min, by guinea pigs induces a marked bronchial hyperreactivity (BHR) to a range of inhaled but not injected broncho-constrictors.[75] The degree of BHR was a function of the duration of ozone exposure and reached a 180-fold increased reactivity to inhaled substance P aerosol. The authors propose that the enzyme neutral endopeptidase (NEP) is probably the first and most important target for the oxidative effects of ozone in inducing BHR. Since this enzyme resides in the cell membrane of airways lining epithelium, it is a primary target for either the direct or indirect effects of ozone. This proposal is supported by the observation that aerosolised NEP reverses, in some degree, an increase in responsiveness to intravenous substance P after ozone exposure in the guinea pig.[76] Tepper *et al*,[77] using guinea pigs depleted of tachykinins with capsaicin, have added further support to these proposals.

5.72 Other authors have confirmed these effects in humans with exposure to ozone[78] or nitric acid or ozone/nitric acid combinations.[79] Exposure of 2 healthy young women and 5 men to 250 ppb (500 $\mu g/m^3$) ozone for 1 h exercising, followed by bronchoscopy with airways and bronchoalveolar lavage showed that levels of both substance P and $PGF_{2\alpha}$ (a marker for oxidative free radical reaction) were significantly higher after exposure than before. FEV_1 declined by 12.4%. The levels of both these components were significantly correlated one with the other and indicate that ozone decreased NEP activity with subsequent increase in concentration and activity of substance P.[78] Any mechanism that might increase the delivery of ozone to the surface of these epithelial cells such as adsorption on fine particles might be expected to increase the effects and hence the BHR.

5.73 In contrast, in another study[79], 10 healthy athletic men were exposed to 500 $\mu g/m^3$ nitric acid vapour with 200 ppb (400 $\mu g/m^3$) ozone or ozone alone for 4 hours. Measures of SRaw, FEV_1, FVC and bronchoalveolar lavage components were made. No differences were found in pulmonary function tests or in cellular or biochemical constituents (total and differential cell counts, LDH, fibronectin and total protein) in BAL with nitric acid exposure. There were also no differences between nitric acid/ozone or ozone only exposure experiments, or between the bronchial biopsy specimens in all exposures.

5.74 In summary, there is evidence that exposure to ozone or other oxidants with particulate aerosols of diverse character will increase the effects induced by gases alone. Furthermore, increases in reactivity of airways after exposure to ozone have been recognised, although whether these effects are potentiated by aerosols has not yet been determined. However, caution must be exercised in extrapolation of responses in guinea pigs to humans since this species responds more dramatically than humans (see also paragraph 5.54) and the concentrations of both gases and particles used in all studies are greatly in excess of measured environmental levels.

Formaldehyde and acrolein

5.75 Both formaldehyde and acrolein are formed during the combustion of organic material, including fuel, and both are produced in the photochemical oxidation of hydrocarbons in the atmosphere. It has been estimated that some 50% of the total aldehydes in the urban atmosphere is formaldehyde and 5% is acrolein. Formaldehyde has also been of recent concern inside buildings with improperly installed urea-formaldehyde foam insulation.[80]

5.76 Unlike ozone and NO_2, most of the inhaled dose of formaldehyde is scrubbed out in the nose and URT, where it is a primary irritant, with concentrations in the 0.5-1 ppm range detectable and in the 2-3 ppm range, irritant. Risby *et al*[81] have made one of the few systematic studies to assess the amount of a gaseous pollutant that is adsorbed on and released from inhaled particles. A thermodynamic model, based on measurable physicochemical properties, was derived to predict behaviour and this was then validated using a nose only exposure system for mice with two oxidised and two unoxidised carbon blacks and formaldehyde. Interestingly, the oxidised carbon blacks were prepared commercially by oxidation with either ozone, nitric acid or nitrogen oxides. It was predicted that with a formaldehyde concentration of 6 ppm only 200 μg of formaldehyde is adsorbed onto 1 gram of charcoal. This is equivalent to only 2 ppb of the formaldehyde being adsorbed on to the carbon with most of the formaldehyde being in the gas phase. The formaldehyde associated with the carbon would be expected to be released immediately on deposition in the alveolar liquid lining of the distal lung.

5.77 Risby *et al*[81] drew attention to a major problem of all studies with particulate aerosols in that most authors have not quantified release as a function of the physicochemical properties of the particulate complex and, therefore, the results cannot be used for general prediction of the release of sorbed agents from the surfaces of particles of different environmental origins.

5.78 Analogous studies by Rothenburg *et al*[82] used collected house dust. They showed marked hysteresis in the adsorption/desorption isotherms which indicated adsorption of formaldehyde in the micropores and/or chemical reaction of vapour with the dust surface. Using suitable assumptions the authors estimated that there would only be around 10 μg of formaldehyde per g of house dust at 1 ppm (1.2 mg/m^3) of gaseous formaldehyde (a concentration at the upper end of what might be expected in mobile homes). This would imply that a person living in a mobile home with a formaldehyde concentration of 1 ppm would inhale 1 mg/h if breathing at 15 l/min. In a very dusty home (1 mg/m^3), and with 20% of the particles deposited in the pulmonary region, only 2 ng/h would be delivered on the particles. In the context of outdoor pollution, these amounts appear insignificant.

5.79 Jakab[83] using "regal GR" (2.45 μm MMAD) (a carbon black characterised by Risby *et al*[81] and comparable to diesel particles) showed that co-exposure of female mice to 3.5 or 10 mg/m^3 of carbon black and 2.5 or 5 ppm formaldehyde had no effect upon either the alveolar macrophage dependent intrapulmonary killing of *Staphylococcus aureus,* or the Fc-receptor mediated phagocytosis, a day after exposure. However, from the 3rd to the 25th day after exposure, the alveolar macrophage Fc-receptor mediated phagocytosis was progressively impaired and did not fully recover until the 40th day. Neither the carbon black or the formaldehyde alone had this effect. This implies that such effects may be delayed, and that repeated or continuous exposures may have a cumulative effect on the ability of the lung to defend itself against respiratory infection.

5.80 Acrolein is extremely irritant to the respiratory tract and is produced in significant quantities during the pyrolysis of organic matter such as in tobacco smoke and car exhausts. Jakab and Hemenway[84] used similar techniques to those described above and showed that in mice exposed to 10 mg/m^3 carbon black and 2.5 ppm acrolein for 4 hours per day for 4 days, alveolar macrophage phagocytosis was suppressed for 11 days after the start of the exposure and did not recover until day 20. Exposure to higher concentrations resulted in an adaptive response as phagocytosis was re-established. In line with the work of Rothenberg *et al*,[82] it is reasonable to assume that formaldehyde and acrolein are adsorbed and absorbed onto the carbon and liquid layer on the carbon which has the potential to transport acrolein into the pulmonary regions of the lung. Although the ratio of gas phase aldehyde to solid phase is of the order of 100:1, clearly the effects would be greater for the pulmonary region when particulate matter was present. The larger the surface area, ie, the greater the number of small particles, the greater would be the effect. Nevertheless, the concentrations of particles and gases used in these studies was, in pollutant terms, extremely high.

Conclusions

5.81 With few exceptions, studies in animals have suggested that inhalation of mixtures of gases and particulate aerosols produces effects which are greater than those produced by exposure to either the aerosol and gas alone. In general, the measured response is that normally elicited by the gases themselves, ie, there appear to be no changes in the nature of the histopathology, biochemistry, pharmacology or toxicology. In the presence of particles the same response is elicited at a lower Ct of gas, or is intensified at the same challenge Ct; there is little evidence that different responses from those to the gases alone have been identified.

5.82 In most experimental studies in humans and animals, the concentrations of both gases and particles used have been in considerable excess of those levels which occur in the urban or rural environment. That there is synergism between gases and particles is proven; that this occurs at ambient levels of these components is not.

5.83 Measures of PM_{10} or even $PM_{2.5}$ are inadequate measures upon which to base the assessment of the toxicological hazard of inhaled particulate pollutants to the respiratory tract. The measures are those of mass and do not indicate the change in particle size and number distribution within the atmosphere. There is evidence to indicate that the number of submicron particles increases significantly in pollution incidents and these will have the significant bearing on the surface area available for the sorption of other gaseous pollutants and condensates. This may provide a mechanism for the increased delivery of vapours and gases, normally removed in the URT, to the deep lung.

5.84 In the epidemiological studies reported elsewhere in this report, the level of particles was the only factor which correlated significantly with mortality. In many cases, there were no correlations with other gaseous pollutants such as SO_2 and ozone, though in a large number of cases SO_2 levels were correlated with particulate levels. In all cases, however, correlations were made with the mass of measured particles. No determinations of particle size distributions, or changes in the particle number distribution as pollution indices increased, were reported. Of major interest

is whether periodic daily or seasonal rises in pollution levels were associated with a shift in the size distribution of the aerosol. For a given particle mass, a 10-fold decrease in the mean particle size would result in a 10-fold increase in available surface area for the same mass of particulate material collected. It is of considerable importance to know whether, in pollution incidents, the morbidity and/or mortality incidents are better correlated with particle size distributions rather than mass distribution.

5.85 Currently, it is extremely difficult to predict the amount of any gaseous pollutants upon a well characterised adsorbent such as charcoal without defining very precisely the conditions under which the measurements are made and the conditions under which the charcoal has been stored. In a heterogeneous aerosol, such as would be found in a rural and urban environment, it is currently not feasible to calculate the sorbed mass of other pollutants which would be inhaled and deposited within the lung. There is at present, insufficient knowledge of particle size distribution, particle morphology, surface characteristics, chemical composition and physical properties and how these vary temporally and geographically upon which to base realistic estimates.

5.86 The possible toxicological role of ultrafine atmospheric particles is of growing concern. It has long been established that the greater part of the mass of metal ions formed in combustion processes is associated with ultrafine particles. Furthermore, the greater proportion of the condensed metal constituents are associated with the surface layers of these particles and would be readily available for chemical interactions with sorbed materials and for rapid dissolution when deposited upon the liquid lining of the respiratory surfaces. Toxicological assessment of the significance of these possibilities is urgently required.

5.87 Ultrafine aerosols themselves have been shown to induce inflammatory responses in the pulmonary interstitium which may, or may not, be initiated by alveolar macrophages. As the clearance times of these particles is considerably prolonged compared with larger particles, the possibility exists that if exposure is prolonged a chronic, low grade inflammatory response may be induced within the lung. Further investigation of the consequences of these interactions is merited.

Recommendations

5.88 The particle number distributions of atmospheric aerosols, between 10 nm and 25 μm, should be measured dynamically at relevant sites (roadsides, urban centres, rural sites) throughout the working day. Correlations need to be established between the particle number distribution, particle mass distribution and indices of gaseous pollutants.

5.89 The dynamic changes in the concentration and numbers of submicron particles during periods of high pollution incidents should be determined. Evidence for rapid, short changes in both these parameters should be sought.

5.90 Correlations should be sought between particle number changes and morbidity and mortality in the UK population.

5.91 Research is required upon the effects of ultrafine particles (of various compositions) on pulmonary toxicology and in particular upon lung inflammatory responses.

5.92 The role of metals in the surface layers of ultrafine particles must be defined. There is a need to know whether they catalyse chemical reactions, interact with tissues and induce toxicological sequelae.

5.93 Atmospheric particles are highly variable in physical and chemical composition and size. Furthermore, the environment in which they are formed is also highly variable in composition and time. Studies of the loading of contaminants upon such particles will necessitate stringent definition and control of these variables to be of value in the assessment of their toxicological effects in humans.

5.94 There is a need to re-assess and repeat the studies of Goetz[42] using environmentally relevant particle sizes, numbers and concentrations of particles and gases. If the predictions are correct, they will have significant value for predictive purposes and for the understanding of the mechanism by which particles may influence the pulmonary toxicity of gases.

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Chapter 6

Effects of Particulate Challenge in Volunteers

Introduction

6.1 Challenge studies involve the exposure of volunteers to individual pollutants either alone or in combination. Exposures take place under carefully controlled conditions either in a challenge chamber or via a closed circuit system. There have been relatively few challenge studies of particulate pollutants: but the pollutant most studied has been sulphuric acid. The data from these studies are somewhat conflicting and a clear picture does not emerge from the results. For a number of reasons, it has not proved possible to carry out controlled human inhalation studies: it is difficult to simulate in the laboratory the mixture that is present in the outside air, and if such material is collected in bulk, it cannot be redispersed with appropriate size distribution. If subjects are exposed to emissions from specific sources, such as coal fires, petrol or diesel engines, effects of accompanying gaseous components tend to dominate. Studies have, however, been reported on some selected components of the suspended particulate matter, notably acid aerosols. These have irritant properties that may contribute to effects of the particles as a whole, though concentrations of acid in the air (as H_2SO_4) are, in general, very small. Studies on the irritant rather than the airway effects of particles have been described in Chapter 5.

6.2 Challenge by low concentrations of sulphuric acid in exercising adolescent asthmatic patients showed small decrements in spirometry in one study,[1] but this has not been reproduced in other work and is in contrast to negative studies at much higher exposures. Ammonium bisulphate challenge has suggested changes in patients with asthma at high dose. Solid particle (eg carbon) challenge has only rarely been performed with respect to changes in lung function, as opposed to assessment of regional distribution of particles being deposited within the lung.

6.3 There is a need for such studies to be performed, not only with respect to particulate challenge on its own, but also in combination challenges to assess potentiating or permissive effects, and may be the best way to determine the mechanisms of such effects.

Methodology

6.4 Sulphur dioxide (SO_2) challenge studies will not be considered here as they represent a gaseous exposure rather than an effect of particles. For an assessment of the effects of SO_2 challenge, the reader is referred to the Second MAAPE report.[2] We will consider studies of sulphuric acid, nitric acid, ammonium sulphate and bisulphate, hydrochloric acid, ferric sulphate and solid particulate matter.

6.5 The methodology of acid aerosol challenge studies has been much discussed because of conflicting results obtained using apparently identical methodology in early experiments. A number of factors have been thought to be important when assessing these experiments.

6.6 One factor which was identified as a possible explanation for such differences was variation in levels of oral ammonia (from undigested food residues) which might have neutralised inhaled acid.[3] Only the later studies employed a pre-challenge acid mouthwash to remove this source of ammonia which at least opens to question the validity of earlier studies.

6.7 Droplet (or particle)/size will also be variable in such challenges as the size and hygroscopic growth of the particles will vary depending on such factors as temperature and relative humidity.[2] Most challenges have used particulate aerosols of MMAD 0.1 to 1.0 μm. This may well not be an appropriate size when considering ambient acid exposures and results from such studies need to be considered bearing this fact in mind as the proportion of the inspired particles reaching the lower airways may differ between different studies despite apparently similar generated particle size. Hygroscopic growth of acid droplets was also not considered in many reported studies.

6.8 The osmolarity of the aerosol may have a bearing on response as hypo-osmolarity may enhance any bronchoconstrictor response which may be seen.[4] It is unclear how this may relate to ambient exposures, however.

6.9 The lung is capable of considerable buffering capacity which can ameliorate the effect of acid. However, more important may be the presence of a buffer in the challenge solution, as Fine and colleagues have shown that airway responses to sulphites may be enhanced in the presence of buffer.[5] The significance of this finding is far from clear when considering challenge by sulphuric acid or sulphates.

Effects in normal subjects

Sulphuric acid

6.10 One effect of sulphuric acid challenge demonstrated in a group of normal subjects by Amdur and colleagues, at a concentration range of 350 to 5,000 $\mu g/m^3$ over 5 to 15 minute exposure times, was a small reduction in minute ventilation and increase in respiratory rate.[6] This effect has not consistently been considered in subsequent acid challenge studies but may be of relevance in terms of the delivered dose of pollutant to the lung (concentration x time) for each challenge.

6.11 At concentrations of 1,000 $\mu g/m^3$, small changes in FEV_1[7] and MMEF[8] have been shown, but other studies have failed to show any changes in airway calibre at the same dose.[9-11] At lower concentrations (100 to 300 $\mu g/m^3$) no effects have been demonstrated and exercise seems not to have any modifying effect.[7,10-14]

6.12 Two studies have attempted to examine the effect of sulphuric acid on bronchial responsiveness to methacholine.[10,11] Utell *et al* showed an increase in bronchial responsiveness to methacholine after a 16 minute exposure to 1,000 $\mu g/m^3$ of sulphuric acid at rest, sGaw falling by 23% compared to 10% with methacholine alone ($p < 0.05$). There was also a smaller, but still significant change in MMEF (-10% compared to -7%). In contrast, Avol *et al* found no effect on bronchial responsiveness at 1,000 $\mu g/m^3$.

Nitric acid

6.13 In challenges with doses of nitric acid gas of 500 $\mu g/m^3$, healthy volunteers showed no changes in lung function, inflammatory markers from lavage samples or bronchial biopsies.[15]

Ammonium sulphate, ammonium bisulphate and sodium nitrate

6.14 No effects on FEV_1 or FVC have been shown in normal individuals over a range of concentrations (100 to 1,000 $\mu g/m^3$).[10, 12]

6.15 However, exposure to 1,000 $\mu g/m^3$ of ammonium bisulphate has been shown to significantly increase methacholine responsiveness in terms of sGaw (-7% compared to -10%) and, to a lesser extent, MMEF.[10]

6.16 Sodium nitrate, at a challenge concentration of 1,000 $\mu g/m^3$ was shown, in one study, to have no effect on either symptoms or lung function in normal subjects.[16]

Ferric sulphate

6.17 In a series of 20 normal subjects,[17] exposed to 75$\mu g/m^3$ ferric sulphate aerosol, 2 hour exposure, no changes were seen in many indices of lung function. No measures of bronchial reactivity or respiratory rate were made in this study. See also para 6.29.

Diesel exhaust

6.18 Rudell and colleagues exposed eight normal subjects to diesel exhaust, generating exposures of 1.6 ppm (3.12 $\mu g/m^3$) NO_2 and 43 million particles/cm^3 of exhaust. Lung function was not measured but bronchoalveolar lavage 18 hours post-exposure showed a significant increase in neutrophil numbers and reductions in intact mast cells and alveolar macrophages.[18] The significance of these high exposures in relation to more usual ambient exposures is difficult to assess.

Effects in subjects with asthma

Sulphuric acid

6.19 The study showing the greatest sensitivity of asthmatic patients to sulphuric acid is that of Koenig *et al.*[1] No changes in indices of lung function was found after exposure of asthmatic adolescents, at rest, to 100 $\mu g/m^3$ for 30 mins; there was however a fall in $\dot{V}$ max and FEV_1 (0.17 l), and an increase in respiratory resistance (30%) after further exposure to sulphuric acid for 10 minutes with moderate exercise. No attempt appears to have been made with sulphuric acid to determine whether individual patients are particularly sensitive.

6.20 The results of sulphuric acid challenge on airway calibre in asthma are conflicting. Sackner and colleagues[9] showed no effect of breathing 3,000 $\mu g/m^3$ on resting lung function, while exposure to 1,000 $\mu g/m^3$ with exercise also had no effect.[19] Avol and colleagues[11] exposed subjects with asthma to a range of concentrations up to 1,500 $\mu g/m^3$ while exercising and showed an increase in symptoms at the higher doses with a small reduction in FEV_1.

6.21 The possibility of a dose-related effect with respect to airway response was provided by Utell *et al.*[20] Asthmatic patients were exposed to 100, 450 and 1,000 $\mu g/m^3$ of sulphuric acid and significant changes in both sGaw and FEV_1 were seen at the highest dose, but only in sGaw at 450 $\mu g/m^3$. There were no changes at 100 $\mu g/m^3$. sGaw reflects large airway flow rather than small airway flow, and is often regarded as a very sensitive measure of airway gas flow. Further studies of exposure to 50 $\mu g/m^3$,[12] 100 $\mu g/m^3$,[10] and 400 $\mu g/m^3$ sulphuric acid[21] showed no effects.

6.22 However, the study by Koenig and colleagues,[1] which is of similar design to that of Aris *et al,*[19] showed an effect at 100 $\mu g/m^3$ in exercising adolescent asthmatic patients on both FEV_1 and $\dot{V}$ max. It is difficult to explain the differences in the results of these two studies. The size of the effects are substantially different and are unlikely to be due to differences in study design, although the subjects used by Koenig's group were younger (aged 12 to 17) than those used by Aris (aged 23 to 35).

6.23 Overall, any effects that might be seen after sulphuric acid challenge in subjects with asthma are small and generally only occur at high exposures. The possibility that sulphuric acid might act in a permissive way allowing other factors to act in a more potent way has not been tested except when given as a mixture with other pollutant gases (see below).

6.24 The study by Avol *et al*[11] which demonstrated an increase in symptoms and fall in FEV_1, failed to show any change in bronchial reactivity to methacholine (sulphuric acid concentrations 380-1,500 $\mu g/m^3$, with exercise). This is in contrast to the findings from Utell *et al,*[10] where exposure to both 450 and 100 $\mu g/m^3$ at rest increased methacholine responsiveness. The fall in specific airways conductance after methacholine preceded by the higher dose of sulphuric acid was 33% compared to 23% after methacholine alone, with smaller although significant differences in MMEF (-27% compared to -16%). At 450 $\mu g/m^3$ sulphuric acid there was a small enhancement of the effect of methacholine in terms of sGaw (-35% compared to -23%) but the difference in MMEF was not significant, although the scatter of results was wide.

Hydrochloric acid

6.25 A study of hydrochloric acid challenge at high dose (0.8 to 1.8 ppm) showed no effect on lung function in a group of patients with asthma.[22]

Ammonium sulphate, ammonium bisulphate and sodium nitrate

6.26 The study by Avol *et al*[12] showed that exposure to low concentrations of both ammonium sulphate and bisulphate (50 $\mu g/m^3$) had no effect on lung function. The elegant series of studies by Utell *et al*[20] showed that ammonium sulphate challenge at a dose of 1,000 $\mu g/m^3$ had no effect on either FEV_1 or specific airways conductance (sGaw). Sodium bisulphate had no effect on either parameter at a range of doses. Ammonium bisulphate showed a significant reduction in specific airways conductance (-10%), but not FEV_1, after exposure to 1,000 $\mu g/m^3$, but not at the lower concentrations of 100 and 450 $\mu g/m^3$.

6.27 Utell and colleagues[10] showed no change in methacholine responsiveness by prior exposure to 450 and 1,000 $\mu g/m^3$ of either ammonium bisulphate or sodium bisulphate.

6.28 Exposure of patients with mild asthma to sodium nitrate at levels of 1,000 $\mu g/m^3$ gave no rise to changes in either symptoms or lung function in one study.[16]

Ferric sulphate

6.29 A study of 18 patients with asthma exposed to 75 $\mu g/m^3$ ferric sulphate aerosol, 2 hour exposure showed no significant overall changes in any lung function parameter,[17] although at an individual level, some subjects did seem to show more

marked responses. This might suggest the existence of susceptible groups, but more data are needed in this area. The exposure level is high (equivalent to 20 $\mu g/m^3$ of iron) and simulated worst case ambient conditions.

Combination effects

6.30 Five studies on the effects of combinations of particles with other pollutants have been performed, four in normal subjects.

6.31 Kleinman *et al*[17a] exposed subjects to combinations of sulphuric acid (100 $\mu g/m^3$) with ozone (379 ppb, 758 $\mu g/m^3$) and SO_2 (370 ppb, 1,058 $\mu g/m^3$) while exercising over a 2 hour period. Small changes in lung function were seen. Stacy *et al*,[23] in a series of exposures of varying combinations of SO_2 (750 ppb, 2,145 $\mu g/m^3$), NO_2 (500 ppb, 940 $\mu g/m^3$), O3 (400 ppb, 800 $\mu g/m^3$) with sulphuric acid (100 $\mu g/m^3$) over 8 hour periods, including spells of exercise, showed that the combination of O_3 and sulphuric acid resulted in an 11% fall in FEV_1, compared to the 8% fall seen with O_3 alone. In contrast, Horvath *et al*,[24] using 250 ppb (500 $\mu g/m^3$) O_3 with a range of sulphuric acid concentrations up to 1,600 $\mu g/m^3$, showed no effect on FEV_1, although the exposure was shorter (2 hours).

6.32 In a group of patients with asthma,[25] prior exposure to sulphuric acid at low dose (100 $\mu g/m^3$) enhanced the response to 80 and 180 ppb (160 and 360 $\mu g/m^3$) but not 120 ppb (240 $\mu g/m^3$) ozone. Healthy subjects were not affected.

6.33 A study of the repeatability of the interactive responses to ozone with sulphuric acid[26] suggests that sulphuric acid does enhance the effect of ozone and exercise and this was repeatable when those with the greater response were restudied. Whether these effects are additive or synergistic cannot be assessed when considering single concentrations.

6.34 The one study that has assessed bronchial reactivity,[27] suggested that sulphuric acid alone, but not when co-delivered with ozone, showed a small enhancement of non-specific responsiveness.

6.35 Nitric acid given as a fog appeared to protect ozone sensitive subjects with asthma from ozone challenge.[15] This might be a reflection of fog as a vehicle rather than nitric acid *per se*.

6.36 Sulphur dioxide plus vanadium coated plastic microspheres (SO_2: 13mg/m³, microspheres: 10mg/m³) had no effect on normal subjects,[28] with a similar negative result being seen with activated carbon.[29]

6.37 A more recent series of experiments in normal subjects, published as an abstract[30] showed that airway resistance increased more significantly following a combination of carbon (0.5 μm diameter at 250 mg/m³) and acid than with acid alone. However, symptoms appeared to be less when exposed to the combination than with acid alone.

6.38 The effects of combination exposures are, therefore, somewhat confusing with contradictory effects seen in both normal subjects and those with asthma. There have as yet been no studies on interactions between acid and allergens. This needs to be investigated in view of the interaction between ozone and grass pollen[31] and nitrogen dioxide and house dust mite allergen.[32]

Conclusions

6.39 The reported effects of sulphates and sulphuric acid in both the normal and asthmatic lung are variable, although the results perhaps suggest that an effect may be more likely to be seen in asthmatic patients. However, there is some lack of consistency amongst the results.

6.40 In normal subjects no changes in lung function have been seen following challenge by either acid or sulphates. At high dose (1,000 $\mu g/m^3$) sulphuric acid enhances non-specific bronchial reactivity as does ammonium sulphate. However, the changes were only seen in specific airways conductance (sGaw), a very sensitive measure of airway gas flow.

6.41 Subjects with asthma have shown changes in dynamic lung volumes (FEV_1/FVC), usually at higher dose, although one study in adolescents showed a response at low exposures. Whether this finding represents a sensitive subgroup is unclear and these findings should not be extrapolated to children. No such challenge studies have been performed in children who might be regarded as a particularly at risk group when considering the evidence from epidemiological studies. Adults with asthma also show a response in sGaw to ammonium bisulphate but not other sulphates.

6.42 Subjects with asthma show enhanced non-specific reactivity following sulphuric acid challenge, but not, apparently, following sulphate challenge. However, all these changes in either lung volumes or bronchial responsiveness are, in general, small. The reasons for this may be in part methodological, but the evidence suggests that there is unlikely to be a large effect of acid or sulphate challenge on human subjects.

6.43 There is no real evidence that any specific site of action within the lung of acid or sulphates can be determined from these results, although higher doses show an effect on smaller airways (if one takes MMEF as an indicator of smaller airway flow) than lower doses where sGaw may be the only parameter to show a change.

6.44 Studies of combinations of acidic particle exposures with pollutants such as SO_2 and ozone have suggested a possible enhancing or additive effect in normal subjects, although the findings are not consistent. Nevertheless, these findings coupled with those on non-specific responsiveness do suggest that more subtle, interactive effects of particles could occur during ambient exposures.

6.45 In particular, the possibility that combinations of acid/sulphates with allergens might have a health effect, similar to the effect of O_3 with grass pollen allergen and NO_2 with house dust mite allergen, needs to be explored.

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Chapter 7

Epidemiological Studies of Acute Health Effects: Summary Description of the Evidence

Introduction

7.1 The purpose of the following three Chapters is to assess the epidemiological evidence linking ambient suspended particulate matter (SPM) with adverse health effects. The assessment will focus on the reliability of that evidence; and on how it can help answer a number of questions relevant to health policy and to possible mechanisms of action. It is necessary to distinguish between acute and chronic effects.

Acute and chronic effects

7.2 Studies of acute health effects aim to identify and describe the relationships, if any, between day-to-day changes in mortality or morbidity and same-day or previous-day levels of air pollution. Studies in recent years have reported relationships between levels of air pollutants and acute health effects ranging in severity from death, through hospital usage, restricted activity days (RADs), and exacerbations of asthma, to occurrence of respiratory and other symptoms and minor changes in lung function.[1,2]

7.3 It is widely accepted that any acute mortality and hospital usage effects of very recent exposure to air pollution arise only against a background of existing ill-health,[3,4] possibly by helping trigger or by exacerbating an acute event such as pneumonia or heart attack. For less severe endpoints such as cough and shortness of breath, or lung function changes, the word "acute" also suggests transience of effect. These acute effects should be distinguished from the way in which long-term exposure to ambient levels of particles may help initiate or promote development of chronic disease. Such chronic effects may, in due course, lead to increased or earlier hospital usage or to premature death; irrespective of whether higher air pollution levels on preceding days had a role in triggering these acute adverse effects.

7.4 Because of these differences, chronic effects will be considered in Chapter 9. The present Chapter will indicate the scope and scale of the epidemiological evidence linking SPM ambient air pollution and acute health effects, with particular reference to papers which report exposure-response relationships and so form the cutting edge of the present debate. The reliability of these studies will be considered in Chapter 8.

Some design issues

7.5 Most studies of acute effects are either time-series studies of a defined population or longitudinal studies of a panel of subjects and have the following general design. A study group, whose composition is more-or-less unchanging, is followed up over time. Health effects in the study group are measured day-by-day, or over shorter periods. Measurements are also made of daily variations in the ambient levels of air pollutants to which the study group is exposed and of possible confounding factors. Then, same-day or previous-day pollution is examined in relation to health outcomes, taking account of the possible confounding factors.

7.6 Studies of acute mortality and hospital usage need large populations, possibly several million people studied over several years, to identify relationships if they exist. This is because the rate of daily occurrence of the events studied is low and air pollution explains, at most, a small proportion of the day-to-day variations in these events. In these large population studies, subjects are not tracked at the individual level. Instead, information about deaths, hospital admissions or emergency room visits in a well-defined geographical area is obtained from routine health records, giving a time-series of daily numbers of occurrences; or, possibly, several parallel time-series for, say, the various individual hospitals in a region.[5] Because the study population is considered as a unit, and because much the same population is at risk

throughout the study period, factors such as smoking habits and socio-economic status are taken to be more-or-less invariant day-by-day and so do not need to be considered explicitly as explanatory variables.

7.7 By contrast with these population-based studies, acute effects of air pollution on less severe endpoints such as asthma attacks, symptoms and lung function changes are typically based on groups or panels of identified individuals. A panel study takes a group of subjects, either with or without pre-existing lung disease, and follows them prospectively over a period of time, usually more than four weeks. Studies of patients with lung disease have usually concentrated on those suffering from asthma, and most studies have looked at children rather than adults. The subjects record symptoms and peak flow readings usually twice daily and each subject is effectively used as his or her own control. A different form of panel study is more opportunistic, taking advantage of the occurrence of a pollution event of unusual size and its effect on a group of subjects who were monitoring (or having monitored) their symptoms and/or lung function before and during the event. As before, use of much the same study group safeguards, by design, against confounding by smoking habits and other factors. It is, however, usual to classify individuals by age, smoking habits, early childhood illness or current chronic disease and other factors, to see whether and how these factors influence susceptibility to the effects of pollution.

The need for careful statistical analysis

7.8 As noted above, air pollution typically explains but a small percentage of the daily variations in measurements of ill health. Typically, there are long-term fluctuations (trends; seasonal or other cyclic patterns) in the long time-series on which mortality and hospital usage studies are based. Various aspects of the weather (temperature, humidity) may have a strong influence. Other factors such as influenza epidemics, which may or may not be important though not measured explicitly, may show an effect through correlations between numbers of occurrences in succeeding days. Sophisticated statistical methods are usually needed to identify pollution effects reliably.

7.9 Panel studies are typically over short periods of several weeks or months only, and so are much less affected by longer-term patterns than time-series studies. Also, weather is generally a less important influence in panel studies. However, powerful statistical methods are again necessary to study pollution effects day-by-day within and between subjects, in the presence of possibly unexplained correlations on succeeding days.

7.10 Use of advanced statistical methods can make the original papers reporting studies difficult to read for non-specialists. We begin, therefore, with a detailed description of one paper[6] which illustrates the approach adopted in several key population-based studies of mortality and hospital usage. The description focuses on methodological issues, to make these more transparent. (There are some comments on the reliability of methods used; these are considered more comprehensively in Chapter 8.) In the original paper, Schwartz writes clearly, but economically: in some instances the following description expands on points which he takes as understood. The paper by Schwartz has been chosen as a particularly well presented report of this type of study.

Example of a population-based hospital admissions study[6]

Population

7.11 The at-risk population was about 517,000 persons aged 65 yr or more (from a total population of 4,382,000: 1990 data) in the Detroit metropolitan statistical area ("Detroit"), USA. Study duration was four full years, from 1 January 1986 to 31 December 1989. The study is therefore, a typical time-series study and not a panel study.

Health effect measurement

7.12 Hospital admission data for all hospitals in Detroit were used to construct daily counts of admissions for pneumonia, for asthma, and for chronic obstructive pulmonary disease (COPD) other than asthma. The hospital admissions data are used to obtain reimbursement from Medicare, and are standardised and likely to be complete. Diagnosis is recorded at time of discharge (and so is likely to be more

accurate than diagnosis at time of admission) and was coded according to the current international standard, International Classification for Disease, ninth revision (ICD9).

Air pollution data

7.13 Daily air pollution data were obtained from the Environmental Protection Agency (EPA) database. Separately for PM_{10} and for ozone, daily data (24-hr averages) for the at-risk population were derived by averaging over all relevant monitoring stations in Detroit. The number of PM_{10} stations varied by year. Agreement between the stations is not reported, though based on other studies, we would expect that it was high.

7.14 Problems of missing data are described only cursorily. PM_{10} measurements were available for 82% of the study days. The pattern of, or reasons for, missing data are not described; nor does the paper report what was done, either for missing days or when results were unavailable for particular monitors. Presumably the 270 (18%) days affected were excluded. Ozone data were unavailable for 15% of days. If patterns of missing data for ozone and for PM_{10} were independent, and days with missing data for either variable excluded, then analyses will have been based on about 70% of possible days.

7.15 No detail is given on how missing days affected the investigation of lagged pollution effects or the construction of multiple-day averages. More information here would have been helpful. It is likely, however, that these issues will have been dealt with sensibly; and it is reasonable to assume that methods of handling missing pollution data will not have affected the study's conclusions.

Confounding factors

7.16 Data on daily mean temperature and dew point temperature (the latter being an index of humidity) were obtained from one site in Detroit. Daily measurements of these two characteristics were very highly correlated (correlation coefficient = 0.96). It is arguable that other characteristics of weather, for example, an index of night-time temperature changes, might usefully have been included.

Statistical methods

7.17 The author uses Poisson regression analysis, allowing for overdispersion, as the basic framework for statistical modelling. This provides a well-established, appropriate and flexible framework for investigating the effects of PM_{10} on hospital admissions, adjusting for confounding factors. The average or expected number of hospital admissions on any given day is represented as the product of effects associated with various measured explanatory variables. Unexplained differences (residuals) between observed and expected counts are assumed to follow a distribution similar to the Poisson distribution, except that the dispersion (variance) may be bigger than the mean by a constant factor to be estimated from the data. Such overdispersion is not uncommon when analysing data as counts.

7.18 As noted here by the author, and in many other papers also, there may be unexplained associations between observed numbers of hospital admissions on days that are near one another. Analyses which ignore such autocorrelation, when it is present in the residuals, may give spurious precision to the estimated relative risks, and so suggest as statistically significant some coefficients which, in reality, are not. The risk estimates themselves are less sensitive to autocorrelation than are their standard errors. Allowance for autocorrelation is made using generalised estimating equations (GEE), a relatively new and relatively complex methodology developed to take account of serial correlation in Poisson, logistic and other non-normal regression models. The GEE methodology is now well established;[7] Schwartz has collaborated with one of its key developers of applications in air pollution epidemiology.[8]

7.19 However, in the present study, no significant serial correlation was found in residuals from the principal Poisson regression models used. Thus, the reported results are based on the "simple" version of overdispersed Poisson modelling without need to use GEE methods to account for day-to-day carryover.

Modelling strategy

7.20 Analysing in the presence of confounders gives the following problem: although explanatory variables as a group may be related to hospital admissions, it is not straightforward to identify which variables are principally responsible. In this context, there is a danger of attributing to pollution some of the effects of the confounded variables, for example, weather. In this and in other studies, Schwartz safeguards against that danger with a unified modelling approach as follows.

7.21 First, he adopts a modelling strategy which is conservative in the sense that, where there is doubt about whether explanatory power should be attributed to air pollutants or to confounding factors, it is attributed to the confounders. Similarly, adjustments are made for long-term or seasonal patterns (even if these are in part attributable to pollution levels) before seeking to ascribe an effect to pollution. Pollution effects, if identified in this context, are less likely to be artefactual. Note that this is not the same as saying that they are less likely to be positive. Whether or not this is so depends on the complex patterns of association that may exist between, variously, long-term and short-term fluctuations in hospital admissions, weather and pollution. For example, in the present study, hospital admissions for pneumonia peak in winter, whereas PM_{10} and ozone peak in the summer. Without removal of long-term trends and temperature effects, the naive (unadjusted) association between admissions for pneumonia and PM_{10} or ozone is negative. Clearly, this negative association is artefactual and reflects seasonal patterns which must first be taken into account.

7.22 Secondly, at the level of implementing this strategy, the author develops a baseline model explaining variations in hospital usage or mortality in terms of long-term trends or seasonal variations and confounding factors, risking overfitting of these aspects. Then, residuals from this model are examined carefully to detect any remaining patterns suggesting longer-term fluctuations or association with confounders. If so, the model is adapted to take account of these. This iterative process of model fitting and model checking is continued until longer-term fluctuations and the identifiable effects of confounders have been modelled adequately. Only then are various indices of pollution included as potential explanatory variables. Finally, various sensitivity analyses are carried out to see if the estimated effects of pollution are robust to the precise formulation of the baseline model.

7.23 As a strategy and implementation approach to estimating pollution effects given time-related fluctuations and confounding, this is unarguably sound from the viewpoint of limiting the chances of false positive associations. Limitations, if any, arise in the details of model building. (It would not of course be a suitable basis for modelling if the principal interest were in the longer-term fluctuations or in the effects of weather; and indeed, in the present paper,[6] the author did not report regression coefficients for these characteristics.)

Constructing the baseline model

7.24 In implementing this approach, the author attempted to limit pre-judging the shape or structure of longer-term data fluctuations and of the effects of temperature. Rather, for longer-term fluctuations, the follow-up period was divided into 48 months and adjusted for month-by-month differences both in hospital admissions and in other, explanatory, factors using dummy or indicator variables[9] to denote to which of the 48 months each day belongs. (Typically, each dummy variable takes the value 1 if the day falls within the month in question, and the value 0 otherwise.) Thus, any associations between monthly average pollution levels and monthly average admissions are screened out of the analysis which is thereby restricted to pooled, within-month associations. This approach distinguishes absolutely between months, without presupposing any relationship between hospital admissions in adjacent months, or in the same month in different years. There is, on the other hand, no differentiation within months: exactly the same adjustment is made for all days within the same month and year. However, the fitting of linear and quadratic terms of time, to adjust further for any systematic longer-term trends, brings minor adjustments between days within months.

7.25 The shape of relationships with temperature is not well-established, but is likely to be non-linear. Consequently, in this study,[6] Schwartz again used a grouping and dummy variable approach to adjust for temperature effects. This was done separately for daily mean and for dew-point temperatures. The number of groups into which each variable was split was data-dependent but pre-defined to be at least seven. In practice, eight groups per variable were used, residual analyses then showing no remaining patterns linking hospital admissions with either characteristic. In principle, over-adjustment for weather might have implied fitting a separate dummy variable for each combination of mean daily and dew- point temperature. In practice, given the extremely high correlation between mean daily and dew-point temperatures, this would have been impractical and almost certainly of no real benefit.

7.26 Finally, various non-parametric smoothing methods were used, both to identify patterns in residuals from the fitted models, and as an alternative method of adjusting for longer-term fluctuations in, and for effects of confounders on, the daily hospital admission counts. As explained by Schwartz, these non-parametric smoothing methods are generalisations of weighted running means which highlight structure for descriptive purposes or remove it for purposes of adjustment, without presupposing what the shape of that structure may be. The running mean concept implies, however, that adjustments are smooth, rather than the jagged adjustment arising from using grouping and dummy variables.

7.27 In summary, in this paper Schwartz has made flexible use of a variety of complementary approaches towards eliminating longer-term fluctuations and the effects of confounders. Singly and together, these methods risk overfitting or over-compensating for confounders, in that the methods of adjustment are quite strongly data-driven and so may reflect and adjust for patterns associated with confounders only by chance; and so justify Schwartz's description of the modelling strategy as conservative with respect to identifying pollution effects.

7.28 Any limitations, therefore, lie in the choice of confounding factors studied, not in the thoroughness or correctness of the modelling done on those that have been examined. We have suggested that some measure of the range of night-time temperature may be related to hospital admissions, but this was not studied. Similarly, there is no evidence that lagged temperature effects were examined, and these may also be relevant. There may also have been systematic day-of-the-week patterns in the admission data. None of these is, of course, a true confounder unless related also to daily PM_{10} measurements.

Modelling the effects of PM_{10} and ozone

7.29 Both 24-hr average PM_{10} and 24-hr average ozone were added, separately and jointly, to a baseline model which used dummy variables to distinguish 48 months, eight ranges each of daily mean and of dew-point temperature and which included linear and quadratic terms in time. Both PM_{10} and ozone were included as linear terms in the Poisson regression model. This implies an assumption that the percentage increase (if any) in average daily admissions attributable to PM_{10} or to ozone is independent of background levels, over the range of ambient pollution implied by this study (10th percentile PM_{10} 22 $\mu g/m^3$; 90th percentile PM_{10} 82 $\mu g/m^3$).

7.30 Within this framework, positive and statistically significant relationships were found between PM_{10} and, respectively, pneumonia and COPD (excluding asthma), but not with asthma itself. Though described only cursorily, it is clear that the effects of pollution were examined using various lag periods; and that relationships were also investigated using average pollution levels over several previous days. Strongest relationships were found with same-day PM_{10} and previous-day ozone; these are the relationships that are reported.

7.31 The PM_{10} coefficient was similar whether or not ozone was included as an explanatory variable; implying that, having adjusted for longer-term fluctuations and temperature confounding, daily PM_{10} and previous-day ozone were effectively independent of one another. (Before adjustment, the correlation coefficient between

same-day PM_{10} and ozone was 0.35.) Taking pneumonia as an example, the estimated coefficient of PM_{10} was 0.00115 (standard error (SE), 0.00039; p-value, 0.0028). The associated percentage increase in daily hospital admissions for pneumonia in the elderly, per 10 $\mu g/m^3$ PM_{10} is 1.16%.

Checking the robustness of the estimated effect

7.32 The estimated percentage increase did not depend on whether adjustment for confounders was by dummy variables or by non-parametric smoothing. Also, it was insensitive to whether high-pollution days (defined as daily mean PM_{10} exceeding 150 $\mu g/m^3$, or 1-hr ozone exceeding 120 ppb; 240 $\mu g/m^3$) were excluded or not from the analysis. Thus, the effect was not attributable to "episodes" of high pollution, but rather reflected experience across a range of days when pollution levels lay below current US standards.

7.33 Finally, to check on the assumption that the percentage increase in expected daily hospital admissions was constant per unit exposure across the range of pollutant measurements studied, both same-day PM_{10} and previous-day ozone measurements were categorised into four groups, consisting of the four quartiles of the distribution. For each pollutant, dummy variables distinguishing the four quartile groups were added to the baseline Poisson regression model. Relative risks (RR) of the four quartile groups were then standardised by arbitrarily fixing the RR of the lowest quartile group as 1.0. Plots of the RR per quartile of PM_{10} against mean PM_{10} of that quartile showed no strong or suggestive evidence of a threshold. Moreover, the RRs between quartiles of PM_{10} were consistent with the assumption of constant percentage change per unit exposure; ie, assumptions of the earlier modelling are not contradicted by the data.

7.34 The agreement between the assumption of constant percentage increase, and the results of quartile modelling which make no assumption about shape between quartiles, is illustrated considering pneumonia and PM_{10}. The risk of admissions on days when PM_{10} was in the upper (fourth) quartile was about 1.077 that of days when PM_{10} was in the lowest (first) quartile, having adjusted as before for longer-term patterns and temperature. The mean PM_{10} of the first and fourth quartiles was about 21 $\mu g/m^3$ and 80 $\mu g/m^3$, respectively, a difference of 62 $\mu g/m^3$. The original log-linear model predicted a corresponding relative risk of $\exp(0.00115 \times 62) = 1.074$. This is equivalent, within rounding error to the quartile plot RR of 1.077.

7.35 A plot of pneumonia residuals versus PM_{10} with non-parametric smoothing, might have elegantly illustrated the shape of the relationship. This is done in some of the other papers which are considered later.

Example of a panel study[10]

7.36 Panel study methodology was reformed by Whittemore and Korn in their analysis of data from one of the CHESS studies.[10] Data were obtained from a total of 443 subjects with asthma, both children and adults, for 34 weeks spread over three years. Each subject provided daily data on symptoms and medication use but no objective measures, such as peak flow rates, were obtained.

7.37 The authors used an analytical strategy based on multiple logistic methods for each individual's attack probability, ie, a regression was obtained for each individual for each outcome measure in relation to specific pollutants. The individual coefficients from these subject-specific logistic regressions were then analysed across subjects to give summary estimates of the effects of the environmental variables.

7.38 In their paper, Whittemore and Korn identified a number of methodological shortcomings of panel studies up to that time and made a number of recommendations for future studies of this type.

7.39 Their analysis dealt with the possible bias that could be introduced by studying subjects with few symptoms or those with many who would show very little change in symptoms on a day to day basis. This apparent lack of response could potentially result in the missing of small, but important, health effects. Whittemore and Korn also recommended that objective measures of responses should be made rather than subjective assessments, (eg, "asthma attacks"), that longer time periods should be

used (in excess of 4 weeks) and that attempts should be made to measure personal exposures to pollutants rather than rely on data from a single sentinel monitoring site. Cofactors such as allergen exposure, viral infections, passive smoking and other factors such as emotional stress were identified as being important cofactors, while the type of heating used at each individual's home (clearly concerned with NO_2 exposure) and the presence or absence of central heating all needed to be allowed for. Season had a marked effect and needed to be adequately modelled either by month or season as dummy variables. The authors also showed that the most important risk factor for having an "attack" was having had one on the previous day, a factor which must be considered in panel studies.

7.40 These recommendations have been followed to a greater or lesser degree in subsequent studies, the most difficult area, largely for logistical reasons, being the development of adequate exposure data and assessment of co-exposure to viruses and allergens which are the most important exposures (apart from active cigarette smoking) when determining responses to environmental factors. Nevertheless, many studies have entirely failed to address important covariables which makes assessment of their results almost impossible.

Overview of acute mortality studies

Individual studies

7.41 There are now numerous studies reporting an association between day-to-day variations in mortality and day-to-day variations in particulate air pollution, having adjusted for the effects of other factors such as temperature, season, etc. Generally, these studies have examined deaths from non-accidental causes (ie, ICD 000-799). It appears that the excess deaths are principally from cardio-respiratory causes in older, ill people (see Chapter 8, paragraphs 100 onwards).

7.42 Studies reporting quantitative exposure-response relationships linking daily mortality with day-to-day variations in SPM air pollution include:

(i) Various re-analyses of mortality and air pollution in London winters, 1958/59 to 1971/72;[11-14]

(ii) A wide range of studies from the USA;[15-23]

(iii) Studies from various European cities;[24-26]

(iv) Studies from other cities internationally.[27-29]

7.43 Additional evidence from Europe is provided by recent studies of winter smog pollution episodes which, though markedly less severe than the London smog episodes of the 1950s, still show clear increases in mortality following increases in pollution mixtures including SPM.[30,31]

7.44 There are a few studies which have investigated acute mortality and air pollution including SPM, and reported relationships with other pollutants but not with SPM;[32,33] or with SPM in some seasons only but not in others.[23,24,27] These will be considered further in Chapter 8.

Reviews and meta-analyses

7.45 Several reviews of these acute effect mortality studies have been published in recent years,[1,2,34,35,36] The basic measurements of SPM pollution vary across studies (see also Chapter 2); and it is necessary to "translate" between various indices of SPM pollution in order to compare estimates of effects across studies. Ostro,[34] Dockery and Pope[2] and Pope *et al*[36] use PM_{10} as a common metric; Schwartz[35] translates to TSP. All these reviews/meta-analyses show strong agreement between results from studies conducted in different locations, with different sources of pollution, different mixtures of ambient pollutants, and different patterns of confounding between ambient pollution and weather. Consequently, the meta-analysis results are insensitive to inclusion or exclusion of particular groups of studies. In broad terms, these studies suggest overall that an increase of 1% in premature acute deaths is associated with a 10 $\mu g/m^3$ increase in PM_{10}.

Hospital admissions

7.46 Within the broad area of hospital service usage, it is usual and helpful to distinguish between hospital admission studies and studies of emergency room visits (ERVs). Exposure-response relationships from selected key studies linking day-to-

day changes in ambient SPM pollution with acute changes in both these hospital usage endpoints are summarised by Dockery and Pope.[2] Lipfert[37] gives a comprehensive and broad-based review of hospital usage studies up to about 1991; while some more recent studies are included in a review by Quenel *et al.*[38] Together, these reviews survey the situation well, though new papers continue to appear.

7.47 The key groups of studies reporting positive associations between day-to-day changes in hospital admissions for various respiratory causes and ambient PM pollution include the following:

(i) Studies in Southern Ontario;[39–42] in all Ontario;[5] and in Toronto specifically.[43] The earlier studies examined relationships between hospital admissions for asthma and 'summertime haze', including sulphates, acidity and ozone.[38–42] Recent studies have examined a wider range of respiratory conditions.[5,43] The Toronto study[43] set out to differentiate if possible between various measures of ambient SPM pollution, for example, pH, sulphate ion, and $PM_{2.5}$ and PM_{10}; and will be considered in more detail in Chapter 8.

(ii) Studies in New York State,[44] where pollution mixtures are similar to those in Southern Ontario.

(iii) Studies in the Utah Valley[45,46] where the principal source of particulate pollution was a steel mill. The hypothesis that these findings are artefactual, with increased childhood hospital admissions due rather to viral infection[47] will be discussed in Chapter 8, drawing on further analyses.[37]

(iv) Other recent US studies of hospital admissions in the elderly gave evidence of increased risks of hospitalisation for pneumonia and for COPD other than asthma; but not for asthma itself.[6,48,49]

(v) In Europe, recent studies have included positive findings from Birmingham[50] and negative findings from Helsinki.[51] The Birmingham study examined daily hospital admissions for asthma and acute respiratory conditions between 1988 and 1990 using routinely acquired data. Average daily levels of SO_2 and smoke were available, but levels of PM_{10} were not. Meteorological variables were allowed for, as were day-of-the-week and seasonal effects. The results suggested that during the winter, a 10 $\mu g/m^3$ rise in Black Smoke would result in an extra 0.5 asthma admissions and an extra 2.15 admissions for respiratory disease. A similar rise in SO_2 might result in 0.4 more asthma admissions and 1.55 more respiratory admissions from the Birmingham population of one million. These effects were seen at levels below EC Guidelines for smoke and SO_2 at the time. One problem with this study was that an influenza outbreak occurred during one of the years. Although influenza admissions were omitted from the analysis, a knock-on effect of influenza on other acute respiratory admissions could not be excluded. This might have exerted a significant attenuating effect on the associations with SO_2 and weakens the likelihood that these associations were causal. The effects in any case were relatively small, but the possibility that the effect was causal remains. The negative results from Helsinki are considered in Chapter 8.

Emergency room visits (ERVs)

7.48 The key studies reporting exposure-response relationships linking ambient SPM pollution with ERVs for various respiratory conditions include:

(i) An early paper reporting a relationship between ERVs for general respiratory conditions and SPM in Steubenville, Ohio.[52] (This paper does not clearly separate out an effect of SPM from a possible effect of SO_2.)

(ii) Emergency room visits for chronic obstructive pulmonary disease (COPD) in Barcelona.[53,54]

(iii) ERVs for asthma in Vancouver[55] and in Seattle.[56] The Seattle study, referring to older (aged > 65 yr) subjects, reports an exposure-response relationship. The Vancouver study gives evidence of an association which varied with season and age-group, but could not be clearly identified. Another study, in North-East USA, found relationships between ERVs for asthma and ozone, but not SPM.[57]

(iv) A study of childhood croup in Switerzland involving visits to paediatricians rather than ERVs as such.[58]

Restricted activity days (RADs)

7.49 Two papers using data from the US Health Interview Survey (HIS) report relationships linking various forms of restricted activity day with particulate air pollution;[59,60] a third paper describes relationships with ozone but not with SPM.[61] Here a 'restricted activity day' included a day spent ill in bed; a day off work or off school; or some lesser, minor restriction (MRAD). By contrast with all the other studies described here, these were cross-sectional and not longitudinal studies; and so they are subject to the difficulties of distinguishing the effects of pollution from those of smoking habit, socio-economic status etc. The endpoint under study was the number of RADs in the two weeks prior to interview, where the interview was with the subject or a close relative. In such studies there are greater possibilities of reporting biases, especially for MRADs which comprise the great majority of days reported, than in studies of mortality or hospital usage. A restricted activity day is also very subjective, as there are considerable intersubject variations in what constitutes restricted activity. However, intra-subject variability is much less variable and thus RADs may be more useful in following trends than in assessing effects cross-sectionally. These design limitations suggest that the RAD studies should be treated with caution, a viewpoint supported by some large differences in estimated effects between years within studies, and between papers from the same core database. On the other hand, these were large-scale studies from locations throughout the US; and they do add to the overall evidence linking SPM air pollution with acute adverse health effects.

Asthma attacks

7.50 The use of 'asthma attacks' as an endpoint presents difficulties as it is a very subjective index and will show wide interpersonal variation. There may be some merit in its use as at least each individual, being accustomed to their own disease and its control, is likely to be consistent in their assessment throughout the study. Whittemore and Korn, however, in their seminal paper on the conduct and analysis of panel studies, recommended that objective measures should be used.[10] Two of three studies where an effect on asthma attacks was reported showed increases of 1.4% and 11.5%, a wide variation which is likely to reflect differences in definition of an asthma attack.

Symptoms

7.51 Respiratory symptoms and use of bronchodilators are inevitably related amongst asthmatic patients, although not in a consistently predictable way. There have been more studies which have considered the effect of air pollution on symptoms than on treatment-use, highlighting that more of these studies have been performed in the "normal", ie, untreated, population. Of eleven panel studies, only two were in adults, the nine studies of children being more often of normal than asthmatic subjects.[58,62-70]

7.52 Lower respiratory symptoms are taken as wheeze, dyspnoea or chest tightness/ discomfort. Cough has been included in some studies while being separated out in others. Upper respiratory symptoms are limited to nasal symptoms and sore throat. Although the separation of productive from non-productive cough was commonplace in studies of the effects of sulphurous air pollution, this is not done as a routine in the studies we are considering here. One reason is that children do not usually report coughing up phlegm unless large quantities are being produced. Any they do produce they tend to swallow, so any attempts to differentiate types of cough in studies of children will be largely invalid.

7.53 The findings from published work are variable but are more consistent than some of the lung function studies with an estimated combined effect (per 10 $\mu g/m^3$ rise in PM_{10}) for lower respiratory symptoms of about +3%, bronchodilator use of +2.9% and for cough of +1.2%. The overall estimate of effect for upper respiratory symptoms of about +0.7% is effectively a non-effect as in 5 of the 6 studies where this was assessed, the effect was non-significant.

Lung function

7.54 The results of panel studies have shown a fairly consistent effect on lung function but many of these changes relate more to ozone than particles. Nevertheless, reductions in peak flow of the order of 5% have been shown when particulate exposures exceed 150 $\mu g/m^3$, while an attempt at quantification suggested that peak flow might fall by 0.8 to 1.6 l/min for a 20 $\mu g/m^3$ rise in PM_{10}. Most of these studies are in children. This suggests that particulate exposure at levels which may be experienced in the UK may have an effect on peak flow.

7.55 Changes in spirometric variables have been shown to relate to variations in levels of pollutants although there has been a wide range of reported responses. In two studies in children which have been reported from Holland, one showed no significant fall in FEV_1, while a later study showed a significant, 0.35% fall for a 10 $\mu g/m^3$ rise in PM_{10}.[62,71]

Summary

7.56 There are now a very substantial number of population-based epidemiological studies, principally, but by no means solely, from North America, giving quantitative exposure-response relationships linking mortality and hospital usage with same-day or previous day SPM pollution, having adjusted for seasonal and for other time-related factors, and for weather. There is also evidence from several panel studies that daily variations in exposure to particulate pollution may have an effect on lung function, and in some cases, on symptoms. Although asthmatic patients appear to be more sensitive to the less serious health effects examined in panel studies, it is not clear which subgroups may be particularly at risk from such effects nor what the significance of these effects may be in the long term. These and other aspects will be considered further in Chapter 8.

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Chapter 8

Epidemiological Studies of Acute Health Effects: Reliability of Reported Associations Between Levels of Particulate Matter and Acute Effects on Health

Introduction

8.1 In this Chapter, we assess the reliability of the reported associations between day-to-day changes in ambient SPM pollution and acute health effects, considering in turn the reliability of health effects endpoints, of ambient SPM measurements, of study design and statistical methods, and of adjustment for confounding factors uncontrolled in the design. Then we consider how the epidemiological studies of acute effects help answer a number of key questions relevant to public policy and scientific understanding:

(i) To what extent has it been established that acute health effects of air pollution are associated with particulate air pollution specifically, rather than with the gases (SO_2, NO_x, ozone) which typically are also present? (In this context we say little about complex questions of interactions between pollutants which is being addressed specifically by the fourth MAAPE report, currently in preparation.)

(ii) What is the shape of the exposure-response relationship? In particular, what is the epidemiological evidence regarding a threshold, or other non-linearities in the relationship?

(iii) What aspects of SPM air pollution may be responsible?

(iv) Who is adversely affected, and in what way?

Measurement of outcome

Reliability

8.2 The reliability of health effect assessment in air pollution epidemiology has been considered recently both by a Working Group of the EC COST 613/2 Concerted Action on Air Pollution Epidemiology[1] and by Samet and Speizer.[2] In general, reliable characterisation of health effects has been among the more straightforward of the issues to be resolved in conducting epidemiological studies of the acute effects of air pollution. For example, records of daily deaths, by defined geographical region, are good in the Western industrialised countries. Cause of death, though subject to error, is well established as an epidemiological endpoint.

8.3 There was some resistance initially to the acceptance of hospital or health service endpoints as valid indicators of morbidity in epidemiological studies, including because of perceived inadequacy in data reporting.[3] However, Lipfert,[4] in a comprehensive review of hospital usage studies to 1991, highlights some advantages: "Hospital data tend to be less subjective than symptom data and... unlike mortality, a trip to the hospital is not an inevitable outcome and thus, the degree of prematurity is not an issue." There is uncertainty in detailed diagnoses: for example, classification of an illness as "asthma" rather than as "bronchitis" is to some extent arbitrary.[5] Averaged over many hospitals in a large region, however, misclassification of diagnosis is unlikely to be systematic in any ways that are related to daily variations in air pollution levels over the same region; and so bias is unlikely. (Note that cross-sectional studies may not be safeguarded similarly; differences in diagnostic conventions may be correlated with exposure differences, for example, via regional differences.[6]) However there is some evidence[6] and understanding[7] that classification errors across the broad diagnostic categories used in many analyses of hospital admissions are likely to be unimportant in practice.

8.4 As noted earlier, the reporting of restricted activity days (RADs) in the US Health Interview Survey (HIS) is more suspect: assessment of restricted activity is inherently subjective, and that assessment was sometimes done by an informant other than the study subject.[8] However, the HIS data are but a small part of the overall picture.

8.5 Although there is little clear information on the reliability of the data acquired from panel or event studies, there are differences in reliability according to the outcome being measured. Whittemore and Korn[9] suggested that objective measures of responses should be made rather than less clearly defined subjective assessments such as "asthma attacks". Symptom reports or scores are also inherently subjective, though these constitute an important health endpoint of panel studies.

8.6 Peak flow readings are reliant on patients' honesty not only in providing a complete record but also in the accuracy both of measurement and timing. It is well recognised that in a clinical setting, compliance with peak flow measurement is at best variable, and may even be worse than compliance with therapy. However, there is some evidence from drug trials that patients involved in research studies are more reliable regarding peak flow readings and therapy because poor compliance would be letting others down rather than themselves. Logging peak flow meters will be a great advance in this regard once they have become more readily available. The mini peak flow meters used in panel studies have been shown to be non-linear with respect to true flow, although they are non-linear in a constant manner. They tend to over-read in the mid range (200 to 450 l/min) and under-read at higher values. It is not known what effect linearisation of values would have on the reported associations.

8.7 Finally, it is a well-established aspect of statistical theory that, in the presence of random misclassification errors of health effects, the estimated regression coefficients are unbiased; but the uncertainty (SE or CI) associated with these estimates is greater than if no misclassification of outcomes existed; and the statistical significance of the estimated effects is correspondingly reduced. (In the case of linear relationships, the underlying mathematics are summarised in one of Schwartz's hospital admissions studies.[10]) Thus, any random errors in assessing health effects tend to weaken the power of these studies to detect whatever real relationships exist, by reducing statistical significance; though the estimated effects, where identified, are not biased by the outcome measurement errors.

Similarity of endpoint definition across studies; and transferability of results

8.8 The mortality studies use the same principal endpoint of mortality from non-accidental causes (ie, ICD 100-799); and in this respect are comparable. Hospital usage studies show a greater variation in endpoint studied, and in detailed definition of those endpoints.[4,7] This variation complicates comparisons across studies.

8.9 Both the panel and event studies have used largely the same end points when assessing health effects. Symptom scores, usually on a twice daily basis, are invariably measured, usually with an assessment of bronchodilator use. Objective measures of lung function tend to have been used more in recent studies. Repeat (once or twice daily) measures of peak flow have been used more in panel studies than in event studies such as the Summer Camp studies, where variable numbers of repeat measures of FEV_1/FVC have often been employed. In the majority of these types of study, however, there is sufficient overlap of outcome measures between studies to allow at least for some comparisons to be made.

8.10 Even when the outcome measure is intended to be the same, there may be differences between studies, between regions, and between subgroups within studies, in how that endpoint is assessed. Such differences also complicate comparisons across studies, and transferability of findings. The importance will vary according to endpoint studied. Thus, the measurement of more-or-less objective characteristics such as cause-specific mortality or lung function should be reasonably independent of location and so be reliably transferable between populations and countries. Background rates will, of course, vary according to context. The measurement, as well as the true background levels, of respiratory symptoms may be more location-specific, given that symptoms are based on self-assessment. Background levels of hospital usage and of restricted activity days (RADs) are likely to be the most location-specific of the various health endpoints considered, because these depend on the organisation of, and access to, health care, work and education; ie, factors that

are likely to vary by location and by sub-population within location. Against this background, it seems likely that quantitative estimates of effects are more reliably transferable between locations if expressed as percentage change (per unit of SPM exposure) rather than as absolute numbers.

Measurement of exposures

8.11 The reliability of exposure estimates in air pollution epidemiology was considered in 1991 at a Workshop of the EC COST 613/2 Concerted Action on Air Pollution Epidemiology.[11] Almost all of the principal studies, both population-based and panel studies, considered in the present review use daily measurements of ambient concentrations from fixed-point monitors, rather than measurement of personal exposures. Four aspects in particular may be highlighted for the present review:

(i) Reliability of fixed-point monitoring.

(ii) Use of PM_{10} or TSP as a common metric across studies.

(iii) The relationship of fixed-point to personal exposures.

(iv) Unreliability of exposure estimates and attenuation of estimated risks.

Reliability of fixed-point monitoring

8.12 Modern measurements of PM_{10} are accurate and reliable. Of course, gravimetric techniques such as the measurement of PM_{10} using a TEOM device provides no information on the composition of particles: this may vary significantly from location to location. Automated techniques for measurement of concentrations of SO_2 and other gases are also reliable.

8.13 There are limited data to suggest that sentinel point monitoring will give a reasonable estimate of overall outdoor pollutant exposure. Amongst studies, those which are conducted in an area which is topographically relatively flat will give the best assessment of exposure from sentinel monitoring providing the area covered is not too wide. Although in such an area NO_2 levels will be relatively even, at significant distances from a central site there may be quite marked differences in levels of PM_{10} or other measures of particulate matter.

Use of PM_{10} or TSP as a common metric across studies

8.14 A major consideration in the determination of health effects of particulate matter is comparison of studies which have used different measures of particles, the difficulty being how to "translate" between different measures used in various locations. It is generally agreed now that size of effects should be equated to defined changes in levels of PM_{10} (eg, change in outcome measure per 10 $\mu g/m^3$ rise in PM_{10}),[12-14] though Schwartz[15] translates to TSP as a common metric. These comparisons require the use of conversion factors which are necessarily approximate and vary in reliability. For example, the convention that PM_{10} constitutes 0.55 TSP seems to have good support, at least for US conditions which form the basis of most studies to-date. On the other hand, the suggestion that British Smoke is comparable to PM_{10} is much less realistic. The relationship will vary by pollution sources and so, in the United Kingdom, varies not only between seasons, but also between cities[16] (see Chapter 2). Dependence of the Black Smoke/PM_{10} relationship on pollution source may show as a non-linear dependence on concentration; and so any simple conversion will, at best, be approximate.[17]

8.15 The issue is complicated by the fact that there is no good understanding of what is "really" the most biologically relevant index of SPM pollution and how to measure it; ie, while PM_{10} is perhaps the best choice of common metric given current knowledge, there is no assurance that it is fundamentally the most relevant characteristic to measure.

8.16 What is striking, therefore, is the similarity of effects across studies of the same endpoint, and the relative consistency of effects across different endpoints, when studies are converted to a common metric for purposes of comparison.[13,15] This similarity of findings suggests that the problems of variability in composition of SPM may not in practice be as great as might first appear; and supports the view that relationships expressed as PM_{10} are in some broad sense transferable between

locations, especially if attempts at transfer are informed by location-specific differences in SPM composition. It is accepted that this apparent transferability across different mixtures of SPM sits uneasily with a common toxicological explanation of the effects.

The relationship of fixed-point to personal exposures

8.17 As noted above, the studies reviewed generally use 24-hour measurements from fixed-point monitors, rather than estimates of personal exposures. The use of personal exposures is clearly impractical for large-scale population-based studies of mortality and hospital admissions. For panel studies, however, it has been recommended that personal exposures always be used,[9] though practical difficulties of sampling instruments, of logistics and of resources make this aim difficult to achieve in practice. For example, the available personal monitors for NO_2 are in the form of diffusion badges with long sampling times which cannot pick up short-lived peaks. Those that can do this are both heavy and expensive and are generally unusable in epidemiological studies at present.

8.18 There are no panel or event studies which attempt to measure personal exposures to particles because of the lack of adequate technology. Attempts at determining personal exposures using time activity analyses have been made for gaseous but not for particulate pollutants.

8.19 The question of whether to use personal exposures or ambient measurements may not, however, be as clear cut as has been suggested.[9] Clearly, personal exposures (if measured with sufficient accuracy and precision) are better at identifying any harmful effects of exposure to the particular substances or mixtures (SPM, SO_2 etc) with which studies of the effects of ambient air pollution are concerned. Indeed, if practicable, there are grounds for considering dose rather than exposure to these substances,[18] from the viewpoint of understanding underlying relationships and possible mechanisms. However, in practice, the policy-related issues such as compliance with standards, or "trigger" levels for the provision of advice to the public, are based on general ambient background concentrations of pollution, and not on personal exposures or on concentrations close to local sources. Thus, it is important to be able to estimate what changes in health effects may be associated with changes in ambient pollution, in the knowledge that these effects are mediated via the (unmeasured) personal exposures of individuals. In this context, there appears to be a legitimate role for direct modelling of relationships with ambient pollution, especially if the relationship between ambient concentrations and personal exposures is reasonably constant within the population studied.[19]

8.20 It is, however, important to have reliable information about the relationships between personal and ambient exposures under various circumstances. This might include knowledge of the relationships between ambient and indoor measurements of SPM and its constituent parts; and information about individual time-activity patterns in various micro-environments, and how these may vary with ambient pollution levels. There is at present limited information about these issues.

Unreliability of exposure estimates and attenuation of estimated risks

8.21 Epidemiological studies quantifying the risks of exposure to some pollutant usually put priority on avoiding bias, ie, systematic underestimation or overestimation, in the assessment of exposures because of the obvious impact on estimated risks. It is now well-known that risk estimates are also affected by imprecision in exposure estimates, and indeed in confounding factors also, even when bias has been avoided.[20] Arguably, the use of average ambient concentrations rather than personal exposures is the major source of exposure "measurement error" in air pollution epidemiology. The effect of measurement error in a single exposure variable, when other exposures and confounders are measured precisely, is to reduce (attenuate) the estimated risks associated with the mis-measured exposure; ie, to lead to underestimation both of risks and of their statistical significance. The direction of bias in estimated risks is not, in general, predictable when measurement

error affects several exposures which are simultaneously included in regression models. It is sometimes possible to adjust for these biases within the statistical analysis proper, but methods are well-developed for relatively simple situations only and are not in general use.[21] In particular, assessment, if any, of attenuation in studies of the acute effects of air pollution tends to be informal only.

8.22 The attenuation of risk estimates because of mis-measurement of exposure should be distinguished from the possible role of biological adaptation in attenuating the effects of repeated exposures in the short term. There is some evidence of biological adaptation for ozone. The issue has not been assessed in the case of SPM and so there is no direct evidence, though this could be studied in the context of panel studies or by challenge experiment. However see also the section on 'Shape of the exposure-response relationships' (para 8.75).

Design issues and statistical methods

Study design and validity

8.23 The various study designs used in air pollution epidemiology have been reviewed at a series of Workshops in 1992/93 of the EC COST 613/2 Concerted Action on Air Pollution Epidemiology.[22] This report also contains a useful assessment of study validity and potential biases and a brief review of methodological considerations for meta-analyses.

8.24 Almost all of the epidemiological studies of acute effects referenced in the present review are of time-series/longitudinal design which, by studying much the same population over time, safeguard against confounding by population characteristics (lifestyle, occupational exposures, smoking, diet, levels of chronic diseases, etc). This greatly simplifies the analysis. The only exceptions were the HIS studies of RADs which were cross-sectional in design and where, as noted earlier, the problems of confounding are consequently greater.

Statistical methods

8.25 Statistical regression modelling seeks to explain the average or expected value of an outcome variable by explicitly representing its dependence on one or more explanatory variables. For example, expected number of hospital admissions in a specified region on a given day might be represented in terms of effects of season, week-day, weather and air pollution characteristics. Expected lung function of a particular individual on a given day would additionally include personal characteristics, or the average of measurements for that individual over many days, as predictors. This is called the systematic part of the regression model.

8.26 Estimation of the dependence of outcome on specified possible explanatory variables depends also on the real and assumed pattern of "unexplained" variation between observed outcomes and what would be expected if we could specify that expectation correctly. This unexplained or random part of the regression model depends intimately on how the outcome variable is represented. Regression methodology was developed in the context of "normal" or Gaussian random error. These "ordinary" linear regression methods are often appropriate where the outcome variable is continuous (eg, lung function); and for counts, where daily numbers are large. Regression methods have, in the past 30 years or so, been extended to include such aspects as logistic regression of binary outcomes (eg, individuals' reports of presence/absence of a symptom on a given day) and to Poisson regression analyses of counts (eg, numbers of daily deaths or hospital admissions). These various approaches are all now well-established, and are particular instances of generalised linear modelling.[23]

8.27 It is usual, when the error distribution is Poisson, to model the expected counts (deaths, hospital admissions) as a product of exponential terms representing the combined effect of various explanatory variables; and this is common usage in the relevant air pollution studies also. This representation implies that the various explanatory variables affect the expected values (eg, expected deaths) as proportional or percentage changes rather than by a change in the number of events,

independently of background mortality or morbidity rates. This is intuitively satisfactory, and also appears to fit the data well in many applications. This combination of exponential systematic component and Poisson random component is what is known as "Poisson regression". It is possible, if the exponential form is considered inappropriate, to model other representations of expected mortality together with a Poisson distribution for errors, within the framework of generalised linear modelling.

8.28 Similarity of outcome on adjacent or proximate days is an issue in studying health effects over time. Such similarity or autocorrelation may, to some extent, be explained by similarities in explanatory variables such as season, weather and pollution. Unexplained or residual autocorrelation may remain however and, according to its severity, may distort risk estimates (specifically, may inflate estimates of their statistical significance) if unaccounted for in the analysis. Methods of handling residual autocorrelation in "ordinary" linear regression modelling have been well-established for many years. The Poisson regression air pollution analyses of Schwartz and colleagues use a more recent methodology of generalised estimating equations (GEE). The GEE approach extends conventional Poisson regression and other generalised linear modelling to take account of residual/unexplained autocorrelation between days.[24,25] Moolgavkar *et al* consider that the GEE approach of Liang and Zeger may be inappropriate in the population-based time-series analyses because of small sample size.[26] The appropriateness of the technique may best be considered as unresolved at present. Fortunately, however, it seems not to be of great practical importance: substantial residual autocorrelation between days in these studies is very rare, and advanced methods to take account of it may be unnecessary. Thus, sensitivity analyses estimating the effect of ambient SPM pollution with and without adjustment for autocorrelation give very similar answers in many of the papers of Schwartz and co-workers. In practice, therefore, conclusions are based on generalised linear models without use of the more recent GEE methodology.

8.29 An alternative means of adjusting for longer-term trends or cyclical fluctuations in the daily counts of deaths or hospital admissions is to explicitly remove such effects by subtracting a running mean, or similar moving average, prior to further modelling. One such filter, developed during analyses of London data,[27] uses a weighted mean over 19-day periods centred on the day in question, with the weights being progressively smaller for days nearer the endpoints of the 19-day period. The same filter has been used by other workers studying mortality[28] and hospital admissions.[5,29-31] Such filtering can be viewed as an example of non-parametric smoothing as employed by Schwartz in many of his papers (eg, Schwartz 1994,[32] see Chapter 7); the principal difference being that in the filtering studies, the smoothed mean is explicitly removed from the daily counts prior to further analysis, rather than retained as an aspect of the full model being developed. The adjusted data will usually appear to be "continuous" rather than counts (because the 19-day weighted average is no longer a whole number) and so it is usual to analyse using ordinary multiple linear regression methods, where methods of adjustment for autocorrelation have long been well-established.

8.30 In conclusion, therefore, the statistical methods used in the principal papers are reliable and appropriate; and there is no substantial basis in theory for considering that the many positive findings from studies using relatively advanced statistical methods are an artefact of the statistical methodology as such. This viewpoint is borne out by papers which directly examine the sensitivity of results to the use of various statistical approaches; and find that the results are robust to variations in detailed statistical methods. These include several analyses of Philadelphia mortality data;[15] of Detroit hospital admissions data;[32] and analyses of mortality data from Los Angeles.[33] For example, Kinney *et al* examined the role of SPM pollution within three different kinds of regression model: ordinary least squares; log-linear regression (ie, exponential form for expected mortality, with normally distributed errors proportional to level of mortality); and Poisson regression. They reported no difference in relative risks linking PM_{10} with acute mortality as estimated from the three models.[33]

Adjustment for (non-pollution) confounders

The broad framework

8.31 Thus, with regard to the main epidemiological studies considered here, it appears that there are no major and fundamental flaws in study design; in reliability of measures of health effect and of exposure; or in statistical methodology underlying the body of evidence provided by epidemiological studies of the acute health effects of air pollution. Limitations will, in general, tend to reduce the chances of finding positive and statistically significant relationships, rather than generating them artefactually. We therefore consider a number of issues about model adequacy within the general regression methodology used in these studies. First we examine whether the role of non-pollution confounding factors has been represented well enough to avoid distortion of the effects of pollution.

8.32 As noted earlier in terms of a specific example (Schwartz 1994,[32] see Chapter 7), the broad strategy which Schwartz and co-workers adopt to the modelling of confounders within a Poisson regression is as follows:

(i) First, develop a baseline model which seeks to explain as much as possible of the daily variations in mortality (or morbidity) in terms of those non-pollution characteristics which have been measured and so are available for study.

(ii) Then, establish whether this baseline model can be improved (ie, have better explanatory power) by also including measures of particles and other air pollutants.

(iii) Finally, examine whether the estimated effects of particles are sensitive to the exact representation of the non-pollution confounders; ie, whether changing the baseline model leads to changes in the estimated effects of pollution.

8.33 Also as noted in Chapter 7, this is a sound strategy in dealing with confounding factors, especially so when the baseline model is built within a strategy of overfitting, rather than under-representing, the effect of the non-pollution variables available for study. Furthermore, results of sensitivity analyses within studies generally show that the estimated effects of air pollution are insensitive to the specific representation of non-pollution confounders, giving support to the view that adjustment for them has been adequate.

8.34 Any limitations to the approach, therefore, do not lie with the modelling strategy as such; or even with representation of confounding factors that have been explicitly included. Rather, they lie in the possible effects of unmeasured confounders and how they are dealt with. Some of these, for example, flu episodes, may show as residual autocorrelation between days; and the main studies both examine for, and where appropriate adjust for, autocorrelation. Possibly more important is the question of whether effects of weather have been taken sufficiently into account. Indeed, there are several reasons why appropriate adjustment for weather effects is both difficult and important in epidemiological studies of acute effects of air pollution, and especially in studies of the more severe endpoints (mortality, hospital usage).

Weather effects: their possible complexity

8.35 Weather effects, typically, are much more important than pollution in terms of explaining day-to-day variations in mortality.[34]

8.36 Temperature effects on daily mortality are markedly non-linear, in the sense that adverse effects are found under extremes of heat and cold rather than under "normal" conditions.[35-37] In general, air pollution studies have taken due account of this non-linearity when adjusting for temperature effects.

8.37 The pattern of relevant lagged effects of temperature on mortality can be both complex and important. This is illustrated by a series of papers on mortality in The Netherlands 1979-87, where the climate is maritime and generally moderate. Adjusting for influenza incidence and season, direct and indirect effects of moderate "heat" and "cold" were examined, lagged over periods of up to one month, taking account also of possible effect modification by wind speed and relative humidity.[36]

The identified effects of moderate "heat" (increases above 16.5°C) were rapid, and within one week. The principal effects of moderate "cold" (decreases below 16.5°C) were also rapid, with some delayed effects mediated via influenza. The confounding of weather with air pollution was examined in some detail subsequently.[38] Same-day association between SO_2 and mortality in The Netherlands 1979-87 disappeared when examined in a baseline model that included complex lagged temperature effects, especially "cold" lagged 1-5 days. The pollution data in this study were, however, quite crude: no measures of SPM were examined, and a single set of daily SO_2 values was applied to The Netherlands as a whole.

8.38 The causal mechanisms linking weather with mortality and other health effects may be complex. For example, there is research and informed speculation suggesting that weather, particularly rainfall, may be influential in asthma episodes via the release of pollen and fungal spores.[39]

8.39 It may be that use of one or two measures of weather is insufficient to characterise the relevant effects of weather on mortality. For example, the Dutch studies reported interactions between temperature, wind speed and humidity in describing the effects of weather on mortality.[36] In addition, it has been suggested that oppressive night-time conditions following a very hot day may be more stressful than the maximum temperature as such.[40,41]

8.40 To take account of this sort of complexity, it has been proposed that the effects of weather on mortality be described using a "synoptic" approach.[40,41] This allows for the simultaneous evaluation of numerous weather elements by combining them into groups or categories that are representative of the variety of micro-climates in a given location; and examining mortality differences in terms of these synoptic categories or micro-climates. Kalkstein[40,41] considers that this approach may help distinguish between weather and pollution effects; and the associated methodologies may indeed prove important in future studies of air pollution and acute mortality.

8.41 Finally, these complex weather effects on mortality and, possibly, morbidity, are important in studies of air pollution and health only because weather and pollution are usually highly correlated within location and season. Thus, even in studies where weather effects have been modelled with care, residual effects of weather may remain, unadjusted. If these are also related to pollution, they might be a source of artefactual relationships between pollution and mortality or morbidity.[34,38,42]

8.42 It seems that confounding by weather is much less serious an issue for the relatively mild health effects examined in panel studies compared with the population-based studies of mortality and hospital usage; ie, the health effects being considered in panel studies are less affected by weather. It is also possible that where the climatic variation is wider, the effect of temperature may be more marked and that different degrees of allowance may need to be employed for differing meteorological conditions.

Weather effects: evidence across studies

8.43 Given the importance of possible confounding of air pollution and mortality effects with climate, it is useful to review the evidence across studies. Here, the most striking aspect is the variety of situations studied, and, in particular, the range of different dependencies between temperature and pollution covered by the major mortality studies. Thus, for example, the climatic conditions and their interactions with pollution encompassed by studies in London, Athens, Detroit, Birmingham (USA), Utah, Missouri and California, is diverse in terms of seasonal dependencies and humidity. Nevertheless, the estimated effects of SPM on acute mortality in these diverse situations are strikingly similar. The argument advanced by Schwartz and co-workers seems convincing: that whereas a case might be made for inadequate control for weather in a specific location, it is practically inconceivable that such mis-specification would consistently result in an apparently positive effect of SPM pollution, of broadly similar magnitude, across a range of different temperature/pollution conditions.

Confounding by weather/climate: conclusions

8.44 In summary, then, the principal population-based studies have adopted a fundamentally conservative strategy in attributing mortality or hospital usage effects to air pollution in the presence of weather and other confounders and this strategy has been implemented carefully. The effects of weather on mortality in particular are, however, sufficiently important, sufficiently complex, and sufficiently confounded with pollution that there is room for legitimate doubt that pollution effects might be distorted. However, mortality studies across a wide range of locations with differing climates and differing patterns of correlation between climate and pollution show similar relationships between daily ambient SPM and acute mortality. This similarity of effects across different conditions gives reassurance that the apparent effect of air pollution on mortality is not an artefact of incomplete adjustment for weather. Relationships of air pollution with other endpoints such as symptoms and lung function are less likely to have been affected by climate.

Has the role of particles been distinguished reliably from that of other pollutants?

Mixtures and interactions

8.45 Ambient air pollution is a mixture of aerosols and gases; and it is not straightforward to attribute the apparent diverse effects of ambient pollution to the individual constituents of the mixture. This is especially difficult when there is evidence that the appropriate constituents have not been measured and studied; that the mixture as a whole may have an effect not well represented by the sum of its constituent parts; or that some constituents may interact with other factors in influencing health. There is, for example, evidence that combinations of SO_2 and ozone; of ozone and grass pollen; and of NO_2 and house dust mite allergen, may be important. The effect of air pollution on summertime hospital admissions in Southern Ontario has been described as an effect of the acid haze mixture as a whole,[5] with later analyses suggesting a key role for ozone and acidity.[30] Both the Ontario results, and hospital admissions studies of similar summertime haze in New York State[29] suggested interactions between acidity and ozone. Possible interactions between SO_2 and SPM have been examined in mortality analyses of London winter data[43] and of Philadelphia,[44] but the results did not support the idea of an interaction.

8.46 The nature of the analytical methodology used in most epidemiological studies of acute health effects of pollution attempts in the first instance to identify effects as if these are independent. (Note, however, that what may appear to be an independent effect and what may appear to be an interaction is to some extent model-dependent.[45]) Then, consistency of an effect of a particular pollutant over a range of studies carried out in different circumstances will lend weight to the existence of a specific health effect, although absence of an identified effect does not rule out the existence of some role, including via synergism/effect modification.

Particles and SO_2

8.47 Existing WHO Air Quality Guidelines for particles have been based principally on winter-time pollution episodes ("winter smog") where elevated levels of SPM are accompanied by high levels of SO_2 also.[46] These studies have been well reviewed previously[47] and have led to guidelines and standards jointly for SPM and SO_2. More recent European studies of pollution episodes, for example, that in Germany in 1985,[48] support the broad findings of earlier studies of winter smog but do not help in separating the effects of SO_2 and SPM.

8.48 Attempts at distinguishing the respective contributions of SPM and SO_2 using data from London winters 1958/9 to 1971/2 have, however, provided evidence implicating SPM (measured as Black Smoke) rather than SO_2. The results of the initial analyses[49] have been supported by later re-analyses.[17] These results were questioned on the grounds of biological plausibility.[50] However, further analyses by Schwartz[43] supported the associations with smoke rather than SO_2 and did not suggest that the SPM effect was modified noticeably by SO_2. However, preliminary findings from yet more analyses of London data, 1965-72, using a novel method of adjusting for season and weather, have pointed to acidity (H^+) and SO_2 rather than to SPM (Black Smoke) as being principally implicated.[51] See below for further discussion of the role of acidity.

8.49 The recent North American studies reporting relationships between SPM and acute mortality give further insight. Some were conducted in areas where SO_2 levels were uniformly low.[52,53] SO_2 was not examined directly in these studies which, nevertheless, show that presence of SO_2 is not a pre-condition of a SPM effect.

8.50 Some other studies, where particles and SO_2 were both examined, report relationships with SPM but not with SO_2. These include studies of mortality[54] and of hospital admissions.[30] Note that in both these studies, sulphates were measured as an aspect of SPM; and relationships with health were found for sulphates but not for SO_2 as a gas. It has been pointed out in Chapter 2 that a significant part of the UK aerosol is contributed by ammonium sulphate. The formation of this is dependent upon primary emissions of SO_2 both in the UK and in western Europe.

8.51 Other US studies report relationships linking acute mortality with both SPM (TSP) and SO_2 when each is included separately in baseline models which adjust for long-term fluctuations in daily deaths and for weather; but find that, when both TSP and SO_2 are jointly included in these analyses, the relationship of mortality with TSP is little changed, whereas that with SO_2 is seriously attenuated.[44,55] The authors, probably correctly, interpret this pattern as evidence that the role of SPM is more fundamental than that of SO_2 in these studies. The possibility of bias in risk estimates due to errors in exposures might lead to some caution in interpretation (see earlier paragraph 8.11). A relatively early paper on ERVs in Steubenville also reported relationships with TSP and SO_2 separately, but without distinguishing well the contribution of these pollutants.[56]

8.52 Recent re-analyses of the Steubenville mortality data[26] suggest that the original results are sensitive to which of two series of SO_2 measurements are used in the analysis; with the implication that the earlier findings pointing to TSP rather than SO_2 may not be well-founded in these data. (The re-analyses still find a relationship between mortality and TSP, but a weaker one than before.) The two series of SO_2 measurements are available for the early years of the study period only; it seems unusual that conclusions should be sensitive to which of the series is used. Clearly, however, there is an issue to be investigated further, possibly in other datasets also.

8.53 Many of the key European studies have used Black Smoke as the principal measure of particles. Results often show relationships with both Black Smoke and SO_2, when both are included in analyses adjusting for longer-term fluctuations and for weather.[37,57] Note that earlier analyses from these locations had pointed to SO_2 rather than to smoke.[58,59] The French two-cities study reported relationships of mortality with SO_2 but not with smoke.[60] On the other hand, the Birmingham (UK) hospital admissions study found relationships with both smoke and SO_2 examined separately, but principally with smoke when both pollutants were examined together.[61]

8.54 When comparing panel studies on a geographic basis, there are only two studies, both from Europe, which show an effect of SO_2.[62,63] The Manchester study did not measure particles, but did show an effect of ozone.[62] A study from part of the Czech Republic which suffers air pollution similar to that experienced in the UK before the Clean Air Acts (maximum daily SO_2 492 $\mu g/m^3$ (172 ppb); maximum daily PM_{10} 171 $\mu g/m^3$) showed no effect of PM_{10} in either adult or child asthmatics.[63] SO_2 did show a significant negative association with peak flow, but only in the children. In contrast, the Birmingham (UK) panel study showed no effect of SO_2 on either symptoms or peak flow in adult asthmatics, although during the summer a small effect of aerosol strong acid was seen on both peak flow and symptoms.[64]

8.55 Studies from Holland of normal children over winter periods of pollution, notably SO_2 and particles, showed decrements in lung function with persistent effects over two weeks. The effects were of similar size, around a 4% fall in FEV during and after the episode.[65-67] The only study of normal children which showed some effect of particles was during an SO_2 and particulate episode.[68] During this event, SO_2 levels

rose to an hourly maximum of 455 $\mu g/m^3$ (159 ppb) and TSP to 312 $\mu g/m^3$. Both FEV_1 and FVC were reduced by 1% during the event but the effect appeared to be prolonged since FVC was still 2% down two weeks later. This is in contrast to a similar event in 1976 where higher levels of both pollutants produced no effect on lung function.[69] An earlier study from Holland, not strictly an event/panel study, also confirmed similar differences in adult asthmatics during and after an air pollution episode of similar size.[70]

8.56 There have been only three event studies of asthmatic populations, two of adults in the UK and one of children from the United States.[71-73] In the earlier Birmingham (UK) study the authors were not able to measure levels of SPM.[71] In their second study,[72] of a winter air pollution episode (NO_2: up to 250 ppb, 470 $\mu g/m^3$; SO_2: up to 200 ppb, 572 $\mu g/m^3$; PM_{10}: up to 250 $\mu g/m^3$: all hourly averages) no effect of SO_2 could be demonstrated after increases in PM_{10} and NO_2 were allowed for. Levels of PM_{10} were, however, clearly related to decrements in peak flow and an increase in the use of bronchodilator inhalers. The effect was seen however, only in the group of severely asthmatic patients, the milder group showing no effect at all, suggesting that the more severely asthmatic patients may be most likely to be affected by short term pollution episodes. It should also be appreciated that identifying the separate effects of various pollutants and assessing synergism if any, may be difficult in event studies because the co-variation of pollutants may be particularly high during events. Although covariation has been adequately dealt with, the interactive effects of pollutants with each other or other environmental variables may be important and have not so far been dealt with in panel or event studies.

8.57 Two recent studies report results which appear to contradict the general evidence favouring SPM rather than SO_2 as an influence on mortality and hospital admissions. A study of daily mortality in Beijing showed relationships with SO_2 in both summer and winter; but with SPM measured as TSP in summer only.[74] Pollution, principally from domestic fires and industry, was generally very high by current UK standards with the median (5th and 95th percentiles) being, respectively, 336 $\mu g/m^3$ (155, 760) for TSP and 40 $\mu g/m^3$ (14 ppb) (6 $\mu g/m^3$, 391 $\mu g/m^3$; 2ppb, 137 ppb) for SO_2. The authors emphasise, however, that TSP concentrations were strongly influenced by natural soil dust, especially in winter and spring; and so daily SO_2 may more accurately reflect pollution from combustion sources, including SPM, than does daily TSP. As noted in Chapter 2, soil dust and other particulate material produced by attrition tend to fall into the coarse size range.

8.58 Similarly, a study of hospital admissions in Helsinki reported relationships with SO_2 and NO_x, but not with TSP or ozone.[75] Again, the TSP measurements were strongly influenced by dusts from natural sources. The authors ascribe the relatively high mean concentration of 76 $\mu g/m^3$ TSP to the "meteorologic conditions and the erosions of street surfaces caused by studded tyres during the winter, as well as the use of sand on the streets to treat icy surfaces". The principal sources of SO_2 and of NO_x were industry and traffic, respectively. It is again reasonable to look on SO_2 and NO_x, rather than TSP as markers of fine particulate pollution from these combustion sources. Thus, it is at least plausible, and arguably likely, that the observed relationships in these two studies reflect particulate pollution indicated by SO_2 and/or NO_x, rather than an effect of gases as such.

8.59 In summary, studies provide strong evidence that a principal role for particles can be identified across a wide range of situations where SO_2 is present in varying concentrations. Overall, the evidence supports a view that the role of SPM is more fundamental than that of SO_2; and that the joint presence of SO_2 is not a pre-condition of a SPM effect. It is unclear whether or not there is an independent but subsidiary SO_2 effect. The evidence favouring SO_2 seems strongest in studies where SPM is measured as Black Smoke. It is possible that, in these studies, SO_2 may be acting as a marker for aspects of particles not measured by Black Smoke.

Particles and NO_x

8.60 NO_x has been considered, and no real relationships reported, in several studies where relationships with particles have been found. Indeed, relatively few epidemiological studies report exposure-response relationships linking ambient NO_x

with mortality or morbidity. In those that do, SPM is generally also implicated, or NO_x is arguably a surrogate for unmeasured or inappropriately measured SPM. Thus, findings of increased daily mortality associated with daily NO_x[28] could very reasonably be ascribed rather to particulate matter represented as KM (a measure of particulate loading based on optical reflectance and similar to Black Smoke), with which NO_x was highly correlated in these data. Similarly, increased mortality during the December 1991 London pollution episode, which initially appeared as an episode of NO_x, could equally be attributed to SPM which was also elevated on those days.[76] The only mortality data apparently implicating NO_x, without strong evidence for SPM as an alternative explanation, are recent preliminary results of childhood mortality in São Paulo,[77] where further work is in progress to investigate the apparent absence of an effect of SPM.

8.61 As noted above, relationships of hospital admissions with NO_x in Helsinki[75] may reasonably be understood as an effect of traffic pollution generally, including combustion-generated SPM from traffic. Quantitative associations between NO_x and morbidity in a Norwegian panel study are clearly interpretated by the authors as representing an effect of general traffic pollution rather than an effect of NO_x as such.[78] (Other pollutants, including SPM, were not measured directly in that study.) Relatively recent re-analyses of the Los Angeles student nurses panel data also found relationships between NO_x and acute respiratory symptoms.[79] Though other pollutants were examined in this study, these did not include SPM; and so these results are not dependable evidence of an independent effect of NO_x on morbidity.

8.62 There remain occasional instances of what appears to be a small NO_x effect additional to that of SPM.[80,81] Overwhelmingly, however, the epidemiological studies show an effect of SPM independently of NO_x levels, whereas most of the relatively few positive findings associating NO_x with acute health effects may simply reflect a SPM effect.

Particles and ozone

8.63 In studies which examine mixtures of pollutants, the confounding of SPM with ozone is generally less serious than the confounding of SPM with SO_2 or NO_x. Several studies report exposure-response relationships linking daily variations in O_3 with variations in daily mortality;[28] hospital admissions;[29,30,32,82] ERVs;[83] restricted activity days (RADs);[8,84] asthma attacks;[85] respiratory symptoms[86] and lung function.[87] Most of these studies found relationships with SPM also, even in regression models which simultaneously included both SPM and ozone. It appears that in these studies, neither SPM nor O_3 is acting as a surrogate for the other.

8.64 Nine panel studies, out of a total of 26 we have assessed, show an effect of particulate matter on some health outcome, five in children (three of them involving asthmatic children), two in groups of adult asthmatics and two of mixed adult and paediatric populations. Two of the studies showed a co-existent effect of ozone in summer studies. However, the great majority of the summer panel studies showed no effect of particles but, more often than not, an effect of ozone. The remaining studies showed either an isolated association of morbidity with particles or an effect in combination with aerosol strong acid.

8.65 Of 15 event studies where a measure of particulate pollution was made, 11 were of populations of normal children, mostly attending Summer Camps. Almost without exception, the pollutant likely to be associated with an effect on lung function or symptoms was ozone. The only study of normal children which showed some effect of particles was during an SO_2 and particulate episode.[68] During this event SO_2 levels rose to an hourly maximum of 455 $\mu g/m^3$ (159 ppb) and TSP to 312 $\mu g/m^3$. Both FEV_1 and FVC were reduced by an average of 1% during the event but there appeared to be a prolonged after effect as FVC was still, on average, 2% less than normal at two weeks after the event. This is in contrast to a similar event from 1976 where higher levels of both pollutants produced no effect on lung function.[69]

Summary/Conclusions

8.66 General air pollution is a mixture involving SPM, SO_2, NO_x, ozone and other pollutants. Of these four, much the strongest and most consistent evidence of acute effects is that implicating PM_{10}. It appears that ozone is also related to a wide range of acute effects. There is no good evidence of an effect of NO_x as such. The question of an effect of SO_2 is unclear. What does seem to be well-established, however, is that the apparent effect of SPM cannot reasonably be attributed to the other non-particulate pollutants which have been examined in epidemiological studies.

8.67 This interpretation, that on current evidence SPM is the component of ambient pollution most clearly associated with adverse acute health effects, leaves open the question of interactions. On the one hand, findings from some studies suggest that the pollutant mixture, and perhaps the overall climate, may influence the effects of particles; with some evidence that the pollutant of principal importance may vary by season. On the other hand, aspects of the relationships between SPM and acute health effects seem quite robust to differences in circumstances, including background pollution mixtures and climate.

Is the (apparent) effect of PM_{10} independent of background levels of PM_{10}?

Acute effects of SPM: evidence of a threshold?

8.68 The following paragraphs review the epidemiological evidence about whether there is a threshold for the acute effects of SPM. By this we mean a threshold at the population level. As noted earlier and as discussed further below, there clearly is a threshold for individuals, in that only those whose health is already compromised are at increased risk of dying on high air pollution days.

8.69 As noted earlier, current air pollution guidelines, derived from high pollution winter smog episodes, embody a threshold concept at the population level for SPM and SO_2. Indeed, as recently as 1982, re-analyses of the London winter mortality data 1958/59 to 1971/72 were used to suggest a threshold of 300 $\mu g/m^3$ Black Smoke.[49] The authors recognised that this conclusion reflected strong preconceptions about that which they considered biologically plausible, rather than the best fit to the data as such. (They reported positive exposure-response relationships from three winters: 1968/69, 1970/71 and 1971/72 when smoke levels were always below 300 $\mu g/m^3$.)

8.70 The shape of the relationship between Black Smoke and mortality in these London winter data is well illustrated in Figures 8.1 and 8.2 from Schwartz and Marcus.[17]

Figure 8.1 **Daily mortality in London, by British Smoke level, for the winters of 1958–1972. Each point represents the mean total mortality and mean British Smoke (in $\mu g/m^3$) for 20 adjacent values of British Smoke, after sorting by British Smoke**

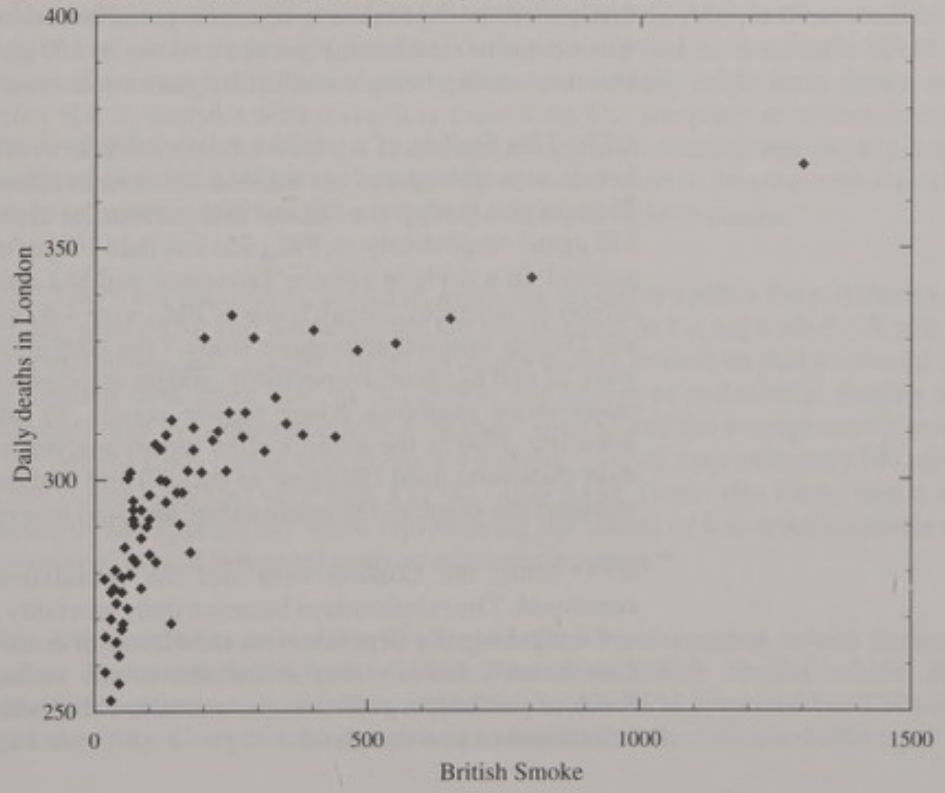

Figure 8.2 **Daily mortality in London, by British Smoke level, for the winter of 1963–1964. Each point represents the mean of total mortality and British Smoke (in $\mu g/m^3$) for 10 adjacent values of British Smoke, after sorting by British Smoke**

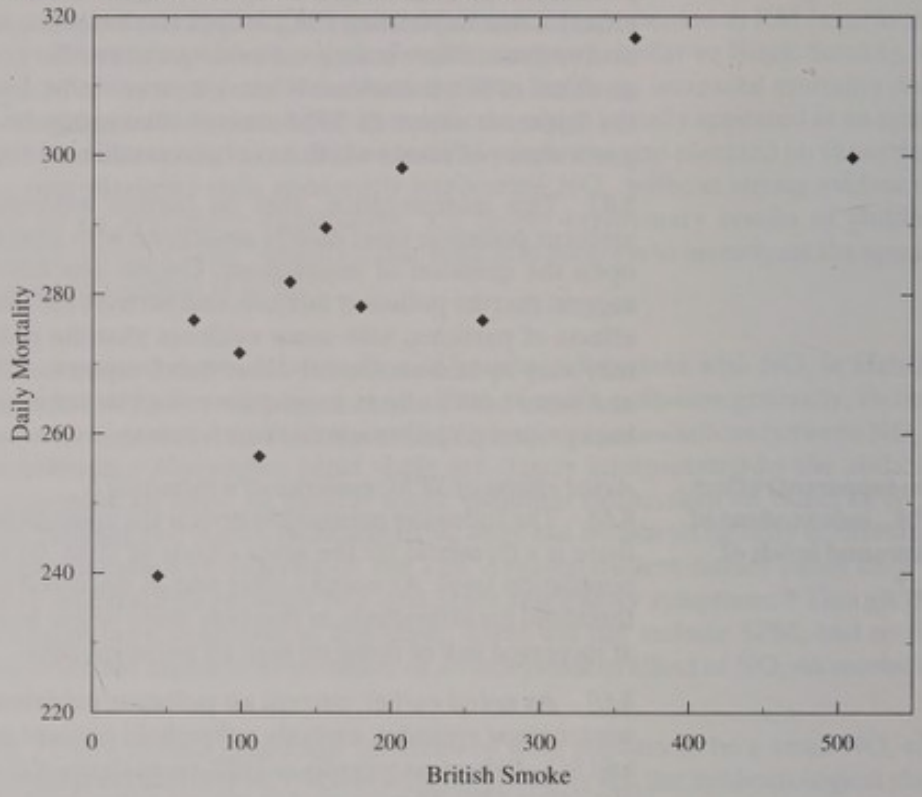

Figure 8.1 shows these average patterns for the data as a whole, while Figure 8.2 shows data for one particular winter, 1963/64, which various analyses of the London winter data suggest was not an untypical year. These graphs clearly provide no evidence of a threshold. On the contrary, they suggest more marked effects, per unit of smoke, when the background levels are low, compared with when they are high. (See below for further discussion of this aspect).

8.71 It is not surprising, therefore, that earlier regression analyses of these same data showed no evidence of a threshold.[88] Specifically, Ostro split the London winter data into two parts: days when smoke was less than 150 $\mu g/m^3$ and days when it was greater; and analysed data from each of the 14 winters separately. There were very few low smoke days in the two earliest years. In each of the remaining 12 years, there was a positive relationship between smoke at 150 $\mu g/m_3$ or less and daily mortality; that relationship being statistically significant in most years.

8.72 This finding, of a positive relationship even when the background levels are low, is now widespread across locations and health endpoints. For example, in the Philadelphia study,[44] the 5th and 95th percentiles of the TSP distribution were 37 and 132 $\mu g/m^3$, respectively; ie, PM_{10} was less than 100 $\mu g/m^3$ on most, possibly on all, days studied. In a study in eastern Tennessee and St Louis, Dockery *et al* demonstrated effects on mortality though levels of PM_{10} were 4-67 and 1-97 $\mu g/m^3$, respectively.[54] In the Detroit hospital admissions study,[32] the 10th and 90th percentiles of daily PM_{10} were 22 and 82 $\mu g/m^3$, respectively, and an association was demonstrated. There are many more examples giving similar results. In addition, within studies, (as in Schwartz, 1994[32]), the authors often report analyses excluding the highest pollution days (Schwartz used 150 $\mu g/m^3$ as cut-off) and find unchanged relationships; and/or examine the shape of the relationship, and find no evidence pointing to a threshold.

8.73 Thus, the London data and the cumulative evidence on this issue are consistent. The relationships between daily mortality and daily particulate pollution are not principally dependent on the effects of some especially high pollution days ("episodes"). Rather, they reflect day-to-day variations in pollution levels when levels of particulate pollution are well below that which previously might have been considered to be a threshold.

8.74 This cumulative evidence within and across studies does not, indeed cannot, prove that there is no threshold. There is at present a lack of direct information about whether severe adverse effects (mortality, hospital admissions) are associated with daily changes in SPM at very low background levels (say 10 or 15 $\mu g/m^3$), because of lack of studies of sufficient power to distinguish threshold and non-threshold models in these circumstances. But what is clear is that the evidence, as it has become available, has shown that various previously suggested thresholds all are untenable; and it seems prudent, on the epidemiological evidence, to consider that the relationship of SPM to acute effects has no threshold at the population level.

Shape of the relationship of SPM with acute effects

8.75 This viewpoint regarding threshold is supported by wider considerations of the shape of the exposure-response relationship. As noted above, graphical representation of the London winter data suggests a more marked effect, per unit of ambient smoke, when the background levels are low compared with when they are high. This suggests a relationship which might be better represented by the upper rather than the lower part of a sigmoid dose-response curve. This kind of shape suggests a log transform of the concentration data might be useful within the regression modelling framework used. In practice, Schwartz and Marcus examined the benefits of using a log transform, or any one of a range of power transforms (for power less than one). They found that a square root transform fitted the data best and they estimated a (non-threshold) relationship accordingly. (Mazumdar *et al* also considered a square root transform, but opted for a quadratic/threshold approach because they believed it reasonable to require a threshold.[49])

8.76 Clearly, a linear relationship with untransformed smoke data will approximate to the square-root transform relationship estimated by Schwartz and Marcus[17] over relatively short exposure ranges; with a steeper linear coefficient when daily concentrations are "low" than when they are "high". This indeed is what was found in year-by-year linear regression analyses of the London winter data, where the steepness of the curve was inversely related to the average background levels of pollution.[49]

8.77 In most other studies, the shape of the exposure-response relationship linking particles with acute mortality and morbidity is represented adequately by untransformed increases of SPM, within Poisson regression analyses where expected deaths are represented in exponential (log-linear) form. Several papers of Schwartz and co-workers present graphical evidence confirming this. Also, in these studies the exclusion of particularly high pollution days generally had no noticeable effect on estimated relative risks. (Non-linearity in the relationship might have shown as a higher RR in analyses with these data excluded.) The adequacy of untransformed indices of SPM may be because the range of pollution studied was usually much smaller than in the London data and so there would need to be gross non-linearity before transformations would be required over these smaller ranges.

8.78 There are exceptions, however, including mortality studies from Athens and Beijing, where TSP and Black Smoke are transformed to the log scale.[37,74] A plot of the transformed data against effects on health closely resembles that produced for the London data. Note that, as in London, the ranges of pollution in Beijing are extremely high by comparison with most other studies; and the average smoke levels in the Athens study (mean approximately 80 $\mu g/m^3$ overall, approximately 160 $\mu g/m_3$ in city centre) are also very high. On the other hand, Ostro also found that a log transform was appropriate when representing the effects of low-level sulphates on shortness of breath in a panel study of asthmatic patients.[89]

8.79 Evidence of non-linearity is also provided by comparing results between studies. For example, Schwartz[15] lists several mortality studies which give quantitative estimates of a relationship between daily SPM (expressed as TSP) and acute mortality. Comparison across studies suggests that the estimated effect, per 10

$\mu g/m^3$ difference in daily exposure, is negatively related to average background levels; ie, a pattern similar to that within the London, Beijing and Athens studies above.

8.80 Attempts have been made to interpret and explain the shape of the ambient concentration-response curve obtained by analysis of the London data. Among the ideas suggested are:

(a) that measurement error in the smoke measurements may be greater (in proportional terms) at higher levels of smoke, leading to greated attenuation of the true effect;

(b) that smoke may be a surrogate for some other characteristic(s) of particulate air pollution which influence mortality, and with which smoke is related non-linearly;

(c) that on high exposure days, individuals may adapt their behaviour to limit personal exposures;

(d) that the population truly at risk may become depleted (the harvesting theory) and not renew itself quickly enough, in the course of a series of high pollution days.

This last hypothesis has some wide currency anecdotally. It is interesting, therefore, that analyses of Schwartz and Marcus do not support it.[17] ("The essentially identical results in regressions where each series was prefiltered on its past makes this explanation less likely.") Also, in studying temperature/weather effects on acute mortality, Kalkstein[34] examined this same "depletion of those truly at risk" hypothesis, and found limited evidence for it. (See further discussion below).

8.81 In conclusion, there are now many studies reporting quantitative exposure-response relationships linking SPM with acute mortality and morbidity effects. These relationships reflect day-by-day changes in SPM pollution at background levels once considered safe, rather than the effect of pollution episodes. As a body of evidence, these studies do not support the view that there is a threshold at the population level; ie, that there are concentrations of ambient SPM pollution below which further reductions would be irrelevant to health. Rather, there is some evidence, though not compelling, that relative risks per unit exposure are greater when background levels of SPM are lower. However, most studies are not powerful enough to examine critically the issues of threshold or other non-linearity at very low pollution levels, say 20 $\mu g/m^3$ or less. Also, as noted earlier, relationships between health in the population and low ambient concentrations may reflect the experience of susceptible subgroups whose personal exposures are higher than average; so that an interpretation of these findings as no threshold at the individual level is not warranted. In terms of estimation of effects the simple representation, of constant percentage increase in effect per unit exposure, without threshold, appears to be the best representation of the relationship under normal background conditions. Simple extrapolation to very high background concentrations may over-estimate the effects.

If particles, then which ones?

8.82 Particles vary both by size and composition; and it is recognised that their effects upon health may vary accordingly. This section summarises the epidemiological evidence of how various indices of SPM pollution are associated with acute health effects. Underlying the review is the fact that the various indices are more or less highly correlated within individual situations, so that, when one index only is examined, it may be acting as a surrogate for other characterisations of SPM pollution; and when several indices are examined, it may be practically impossible to attribute effects independently.

Studies examining principally one index of SPM pollution

8.83 Many studies examine at most one measure of particulate air pollution. The choice of what measure of SPM is used is often pragmatic, dictated by what measurements have been made. Thus, UK studies and many studies elsewhere in

Europe have used Black Smoke only. Some US studies also use measures of visibility as a surrogate for levels of particles.[28,86]

8.84 Some recent European studies use TSP[75,80,81] which has also been widely used as the preferred measure in many studies in the USA[9,32,44,55,90] and in some other countries.[74] It is the common exposure metric to which Schwartz[15] converts various studies of acute mortality in comparing their relative risks.

8.85 Other recent reviews[12,13] have expressed the percentage increase in acute health effects in terms of PM_{10} concentrations; and PM_{10} is now the preferred measure in many recent studies, notably in the USA. These include both the population-based and panel studies by Pope and co-workers in Utah Valley;[53,91,92] other studies of acute mortality in the US and elsewhere;[54,77,93] studies of hospital service usage;[32,82,94] and panel studies by Brunekreef and colleagues in The Netherlands.[95-97]

8.86 There are also many studies which focus on the smaller size fractions and/or on particular components of the PM_{10} mixtures. These choices reflect the authors' views of biological plausibility as well as pragmatic considerations of data availability. Thus, the series of hospital admissions studies in Southern Ontario, Canada by Bates and co-workers[5,98,99] and the extension by Burnett *et al*[31] to all hospitals throughout Ontario, examine sulphates as the principal index of SPM; with some reference to acidity [H^+] also. The associated papers by Thurston *et al* [30,100] will be discussed in more detail below. Similarly, the hospital admissions studies carried out by Thurston and colleagues in North East USA[29,30] also use sulphates as a principal measure of SPM, though H^+ is examined also. Ostro *et al*,[89] in studying shortness of breath in asthmatics, also consider both SO_4 and H^+. Fine particles, ie, $PM_{2.5}$ was the measure of choice in analyses of the US Health Interview Study.[84,101]

8.87 As indicated in Chapter 7, most of the studies listed above show associations, in many instances expressible as statistically significant exposure-response relationships, between the particulate measure chosen and the acute health effect endpoint studied. Thus, they do not provide strong guidance about which aspects of SPM are the most relevant, biologically. Rather, a wide range of studies, in diverse locations, with differing measures of SPM, show relationships with a diversity of health or health-related effects. This finding should not be interpreted as proof that each index is biologically relevant. Rather, it may in practice reflect the high correlation between various measures.

Studies comparing different indices of SPM pollution

8.88 Despite the degree of correlation between the various indices, a few studies, with varying success, have attempted to separate out the effects of different indices of SPM pollution; or, more exactly have examined which of the various indices measured in that study is most strongly associated with acute health effects, having adjusted for confounders. Thus, Dockery, Schwartz and Spengler studied daily mortality and air pollution in St Louis, Missouri and Kingston/Harriman, Eastern Tennessee over a 12-month period 1985-86.[54] Their aim was specifically to "evaluate the relative importance of various measures of particles and gaseous air pollution as predictors of daily mortality". Having, as usual, developed a baseline regression model using non-pollution confounders, the authors found a statistically significant relationship between PM_{10} and daily mortality in St Louis (1.5% increase per 10 $\mu g/m^3$ PM_{10}) and a similar (1.6% per 10 $\mu g/m^3$) but not statistically significant relationship in Kingston/Harriman. In St Louis, both fine particles ($PM_{2.5}$) and coarse particles (PM_{10}-$PM_{2.5}$) were related to daily mortality ($p = 0.075$ and $p = 0.056$, respectively). Models including both components simultaneously did not help identify which was primary. The correlation between PM_{10}, $PM_{2.5}$ and (PM_{10}-$PM_{2.5}$) is not reported.

8.89 Both SO_4 and H^+ measurements were positively correlated with daily mortality, but were not statistically significant, when added to the baseline model separately and independently of PM_{10}. Both were positively correlated with PM_{10} ($r = 0.52$ and 0.76, respectively). Ranking the strength of association with daily mortality

in terms of statistical significance gave PM_{10} >$PM_{2.5}$ > SO_4 > H^+. In Kingston/Harriman, where none of the four measures was statistically significant, the corresponding ranking was $PM_{2.5}$ > PM_{10} > SO_4 > H^+. In both locations, each of a number of trace metals (aluminium, calcium, chromium, iron and silica) was positively but not significantly related to daily mortality, adjusting for non- pollution confounders. These metals were also positively correlated with PM_{10} concentration (r > 0.5 in St Louis; Kingston/Harriman values not given).

8.90 The short study period and the relatively small populations at risk (especially Kingston/Harriman) limit the power of this study to detect relationships between daily mortality and SPM pollution, as witnessed by the lack of statistical significance of the relationship with PM_{10} in Kingston/Harriman. The inter-correlation of the various measures of SPM pollution during the study period, and imprecision in measurement of H^+ at the low concentrations experienced on some days, further limited the study's ability to distinguish which aspect of particulate air pollution is principally related to acute mortality. The authors, aware of these considerations, nevertheless note the lack of evidence pointing towards any measured component of PM_{10} rather than to PM_{10} itself.

8.91 Thurston *et al* carried out re-analyses of London (winter) smog data to assess the role of acid aerosols.[101] The portion of the 1958-1972 winter mortality pollution record for which daily direct acid aerosol measurements were available (November 1 to February 29, 1963-1972) was analysed. The measurements of acid aerosol were made at St Bartholomew's Hospital (Medical Research Council Air Pollution Research Unit). It was found, in bivariate analyses, that the lag of the acid aerosol concentration was associated more strongly with raw total mortality than was Black Smoke or SO_2. It was felt that the nature of the relationship between mortality and acid aerosol concentration might imply a saturation model of pollution effects, possibly due to multiday pollution producing harvesting of a susceptible subpopulation.

8.92 Bates, Sizto and colleagues have focussed on sulphates as the principal measure of particulate air pollution in their studies of respiratory hospital admissions in Southern Ontario.[5,98,99] Bates and Sizto found relationships with air pollution in summer but not in winter.[5,99] There appeared to be an effect both of sulphates and of ozone. The authors were slow to attribute effects to any pollutant specifically, partly because of the correlation between the various pollutants measured. Rather, they speak of an "acid summer haze" effect of the mixture as a whole; and suggest that unmeasured characteristics (eg, H^+) may be most relevant to causality.

8.93 Thurston *et al* follow up this study with a study in Toronto,[30] Southern Ontario, over six-week periods during July and August, 1986-88. The initial paper described the pollution measurements taken. Acid aerosol episodes (defined as $H^+ \geq 100$ nmol/m^3) were found in these summertime periods. H^+ peaks were well correlated with sulphate peaks, complicating the task of distinguishing effects. The authors report that "virtually all of the H^+ was found to be present as ammonium bisulphate (NH_4HSO_4)". The acidity may be distinctive, in that Thurston *et al* trace its source to air pollution from the South-West (ie, inland USA) travelling over the Great Lakes, where the neutralisation of acid aerosols from ambient SO_2 was not as complete as it would have been with entirely overland transport. A wide range of particulate measurements were studied, including TSP, PM_{10}, FP ($PM_{2.5}$), coarse particles (CP: PM_{10}-$PM_{2.5}$), SO_4 and H^+. The inter- correlations between pollutants, de-trended and adjusted for day-of-the-week effects, are reported in detail. They include r(H^+, SO_4) = 0.82; r(SO_4, FP) = 0.84; and r(FP, PM_{10}) = 0.97, illustrating the difficulties of identifying effects separately.

8.94 Adjusting for non-pollution confounders, the clearest relationship with summertime respiratory admissions was found for ozone.[30] Adjusting for ozone also, and fitting the various particulate measures one at a time, the data showed a ranking of statistical significance (ie, the obverse of a ranking of "P-values") as H^+ > SO_4 > FP > PM_{10} > TSP, with only H^+ statistically significant at the 5% level. Thus, the

results support the earlier Bates/Sizto conjecture regarding acidity, and in this regard contrast with the mortality results above (para 8.89). The authors suggest a synergism between H^+ and O_3 in this summertime pollution mixture and include strong arguments for detailed characterisation of the size and composition of particulate air pollution.

8.95 In an earlier paper, Thurston *et al* examined respiratory hospital admissions in four locales in New York State in the summers of 1988 and 1989.[29] Statistically significant relationships were found both for SO_2 and for H^+, in 1988 only, in Buffalo and New York City. It again appears however, that in this study O_3 is the pollutant principally related to hospital admissions, with again an interaction suggested between O_3 and high levels of H^+. Thus, the results are consistent with the more recent findings from Toronto, which of course is geographically reasonably proximate. Indeed, Thurston *et al* consider that the distinctive summertime air pollution mixture of Toronto applies also to Buffalo, New York State. This similarity affects attempts to generalise the results.[30]

8.96 Against this background, some authors are in favour of PM_{10} as the index of particulate pollution most relevant to biological mechanism and/or to public health policy. Reasons for choice of PM_{10} include the diversity of situations and sources of particulate pollution, where quantitative exposure-response relationships have been identified; and the similarity of relative risks across those situations when expressed in terms of PM_{10}. Whatever the truth about causality, this relative consistency of effect, expressed as percentage change per unit PM_{10}, is helpful in any attempts to quantify effects.

8.97 Others, eg, Thurston *et al* , are less convinced.[100] They base their reasoning on the biological implausibility of similar effects of the various components of PM_{10}, expressed in mass terms; as well as on epidemiological and (limited) experimental evidence. They argue, surely correctly, for full characterisation of PM_{10} mixtures so that the issues can be investigated further. In principle, such characterisation should consider measures of particle count and surface area, as well as mass, on grounds of possible mechanism of effects.

8.98 In summary, the epidemiological evidence regarding the optimal measure of particulate matter is at present, inconclusive. Relationships with PM_{10} are well-established and appear convincing, statistically. The results of studies relating PM_{10} to changes in indices of health are presented in Annex 8A. Alternative measures, involving fine particles and acidity appear to be more plausible biologically, and have some support in epidemiology, but that support is by no means compelling. The answer may not be simple. It is possible, for example, that the true particulate "driver" of the relationship varies by location and/or by health effect; so that simple generalisations may not apply.

Who is at risk of what conditions on higher air pollution days?

8.99 Although the precise mechanisms of action are not well established, there is widespread agreement that the serious adverse health effects associated with increases in ambient SPM pollution are not due to those increases only. General considerations most strongly suggest that those at risk of premature death or of increased, earlier or more severe hospital usage on higher pollution days are those with pre-existing serious ill-health. A mechanism has been conjectured whereby, in people whose health is already compromised by chronic disease and/or by ageing, the severity of an acute event (eg, pneumonia, heart attack) may be increased on higher pollution days.[103] Similarly, when Lamm *et al* [104] proposed that increased childhood hospital admissions for respiratory conditions in Utah from April 1985,[91,92] were attributable to an episode of viral infections (respiratory synctial virus) rather than to air pollution, Lipfert[4] considered that these were false alternatives. In Lipfert's view, higher SPM air pollution might exacerbate conditions initiated by the viral infection; and he provides re- analyses of the Utah data to support this view.

Mortality

8.100 Characterisation of who is at risk is limited by the lack of information readily available in most routine databases of mortality and hospital usage, and by the difficulties of gathering new relevant information. The most thorough recent

examination of who is dying on higher pollution days, and from what conditions, is provided by analyses of the Philadelphia study data.[44] Differential effects were found by age-group, the relative risk (RR) of mortality from non-accidental causes per 100 $\mu g/m^3$ TSP being 1.027 in those aged < 65 yr, compared with the much higher corresponding RR of 1.095 in those aged ≥ 65; the overall RR being 1.068. Similarly, in Cincinnati, the RR per 100 $\mu g/m^3$ TSP overall was 1.06, whereas those aged 65 or more experienced the higher RR of 1.09.[90] The similarity of these results is striking. An early report of excess mortality from the London smog of 1952 also found higher risks among elderly people.[105] In this study, age may be a marker of increased likelihood of death.

8.101 Considering the cause of death, Schwartz and Dockery[44] showed that the excess occurred for COPD (RR per 100 $\mu g/m^3$ of 1.195, for pneumonia (RR 1.107) and for cardiovascular disease (RR 1.096), whereas the RR for cancer was substantially less than for "all causes". Results from other studies where cause-specific mortality has been examined are consistent with these findings. For example, deaths from pneumonia and from cardiovascular causes were particularly elevated in Cincinnati;[90] COPD and cardiovascular deaths were particularly elevated in Birmingham, Alabama;[93] the earlier Santa Clara study also highlighted respiratory and (to a lesser extent) circulatory causes[52] and cardio- respiratory causes were also found to be principally implicated in Athens.[37] Schwartz[103] reports further analyses of the Philadelphia data, contrasting those who died on high and on low pollution days (adjusted for weather, season etc). These analyses broadly confirmed the earlier findings of increased cardiorespiratory mortality as the primary or underlying cause of death; one difference being that death from lung cancer was also identified as higher on high pollution days. Moreover, they showed a substantial increase also in cases where respiratory disease, or vague respiratory cardiovascular symptoms, were reported as contributory causes.

8.102 The limited evidence on who is at risk of excess mortality, therefore, supports the general viewpoints and conjectures reported above: what is involved is a shortening of life in people whose life expectancy was, in any case, much lower than average. (This is sometimes colloquially described as an "harvesting" effect.[42]) There is, however, little information about the distribution of length of expected life lost. In particular, the conjecture that the excess deaths would all have occurred in any case within a few days does not appear to be well-founded. For example, the same question of "harvesting" has been investigated where excess deaths were weather-related.[34] There was some evidence of lower than expected deaths on days following excess weather-related mortality; but this subsequent drop accounted only for about 40% of the earlier weather-related excess. A mechanism like that suggested by Schwartz[103] seems more plausible. Irrespective of weather or pollution, acute events such as pneumonia or heart attack, against a background of already compromised health, will in many instances, lead to death on that occasion; the role, if any, of weather or pollution may then be to shorten life by at most a few days or weeks. In other instances, however, weather or pollution may precisely be what tips the balance between surviving this occasion or not; and the expected length of life lost may then be substantially greater. Thus, the distribution of length of life lost is likely to be heavily skewed to the right, with a median of perhaps a few weeks, but a mean of perhaps several months. This is consistent with Schwartz's findings that of a 22% increase in those dead-on-arrival at hospital on high relative to low pollution days, compared with an overall increase of 5% only. However, there is much conjecture in these remarks and reliable information is needed.

Hospital usage

8.103 Studies of hospital admissions have focussed on the effects of air pollution on daily admissions for respiratory conditions. Various other groups of conditions have been studied as control conditions and, as expected, have been found to be unrelated to daily variations in pollution levels. However, it appears that admissions for heart-related conditions have not specifically been examined for relationships with SPM pollution.

8.104 Within the broad framework of respiratory admissions, studies have variously looked at three broad groupings: (a) respiratory infections (or pneumonia); (b) asthma; and (c) other chronic obstructive pulmonary diseases (COPD). Evidence for an effect of SPM pollution on respiratory infections and on COPD is stronger than on asthma.[32] It is unclear whether this difference is informative about possible mechanisms, or simply reflects greater power of studies to identify relationships with infections and COPD.

8.105 There is ambiguous evidence on the extent, if any, to which relative risks vary by age-group within the population. In a large-scale study of hospital admissions for various respiratory conditions in Ontario, Canada 1983-88, similar pollution-related percentage increases were found across all three principal age-groups studied (2-34 y, 35-64 y and 65+), with an especially high percentage increase in the very young (0-1 y).[31] These effects were attributable to ozone more than SPM (measured as sulphates), though a relationship with sulphates was established also. Other recent papers, however, have examined ERVs[94] or hospital admissions[32,82] in the elderly (> 65yrs) only; presumably on the understanding that effects, if any, will be seen most clearly at these ages. This would be consistent with the mortality findings summarised earlier. It is unclear, however, what, if any, is the basis for this effect for hospital usage specifically.

8.106 There are some examples of SPM-related increased hospital usage among children specifically.[80,91,92,106] The paper by White *et al* [106] includes a summary of evidence that poverty may increase the effects of ambient air pollution.

Restricted Activity Days (RADs)

8.107 Design limitations of these studies have been noted earlier. In terms of results, it is noteworthy that relationships have been found not only with respiratory RADs,[84] but with RADs irrespective of specific condition.[102] Given the study limitations, it is unclear if this apparent non-specificity is real or artefactual. Note that the vast majority of RADs implicated were considered to be minor; ie, not requiring staying in bed, or staying off work.

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Annex 8A

Summary of studies of acute effects of particles *(adapted from Dockery DW and Pope CA. Acute respiratory effects of particulate air pollution. Annu Rev Public Health 1994; 15:107-132)*

Table 8A.1

Studies of acute effects of particles on daily mortality

Location and period	Particulate measure	Mean PM_{10} ($\mu g/m^3$)	% Change in daily mortality for each 10 $\mu g/m^3$ increase in PM^{10} (95% CI)	Reference
Total mortality				
St Louis, MO 1985-86	PM_{10} (previous day)	28	1.5% (0.1%, 2.9%)	1
Kingston, TN 1985-86	PM_{10} (previous day)	30	1.6% (–1.3%, 4.6%)	1
Utah Valley, UT 1985-89	PM_{10} (5-day mean)	47	1.5% (0.9%, 2.1%)	2
Birmingham, AL 1985-88	PM_{10} (3-day mean)	48	1.0% (0.2%, 1.9%)	3
Respiratory				
Utah Valley, UT 1985-89	PM_{10} (5-day mean)	47	3.7% (0.7%, 6.7%)	2
Birmingham, AL 1985-88	PM_{10} (3-day mean)	48	1.5% (–5.8%, 9.4%)	3
Cardiovascular				
Utah Valley, UT 1985-89	PM_{10} (5-day mean)	47	1.8% (0.4%, 3.3%)	2
Birmingham, AL 1985-88	PM_{10} (3-day mean)	48	1.6% (–0.5%, 3.7%)	3

Table 8A.2

Acute effects of particles on hospital usage

Measure of hospital usage	Location and period	Particulate measure	% Change in hospital usage for each 10 $\mu g/m^3$ increase in PM_{10}	Reference
Hospital admissions				
Asthma	New York City, NY	Daily mean SO_4	1.9% (0.4%, 3.4%)	4
	Buffalo, NY		2.1% (–0.6%, 5.0%)	4
	Toronto, ONT, Summer 86-88	Daily mean $PM_{2.5}$	2.1% (–0.8%, 5.1%)	5
All respiratory	New York City, NY	Daily mean SO_4	1.0% (0.2%, 1.8%)	4
	Buffalo, NY		2.2% (0.6%, 3.8%)	4
	Toronto, ONT, Summer 86–88	Daily mean $PM_{2.5}$	3.4% (0.4%, 6.4%)	5
	Southern Ontario, Summer 83–88	Daily mean SO_4	0.8% (0.4%, 1.1%)	6
Emergency department visits				
Asthma: >65 years	Seattle, WA 1989–90	Daily mean PM_{10}	3.4% (0.9%, 6.0%)	7

Table 8A.3

Studies of acute effects of particles on exacerbation of asthma

Measure of asthmatic response	Location and period	Particulate measure	Subjects	% Change in daily asthma response for each 10 $\mu g/m^3$ increase in PM_{10}	Reference
Bronchodilator use	Utah Valley, UT Winter 1989-90	Daily mean PM_{10}	School panel	11.2% (2.4%, 20.7%)	8
			Asthma panel	12.0% (4.7%, 19.7%)	8
	2 Dutch Cities, Winter 1990-91	Daily mean PM_{10}	School panel	2.3% (0.7%, 3.8%)	9
Asthmatic attacks	2 Dutch Cities, Winter 1990-91	Daily mean PM_{10}	School panel	1.1% (–3.5%, 5.9%)	9
	Denver CO, 1987-88	$PM_{2.5}$	Asthma panel	11.5% (8.9%, 14.3%)	10

Table 8A.4

Studies of acute effects of particles on lung function

Measure of lung function	Location and period	Particulate measure	% Decrease in daily lung function for each 10 $\mu g/m^3$ increase in PM_{10}	Reference
Forced Expired Volume				
FEV_1	4 Cities, NL Winter 1987-90	Daily mean PM_{10}	0.06% (–0.01%, 0.14%)	11
	Wageningen, NL Winter 1990–91	Daily mean PM_{10}	0.35% (0.23%, 0.48%)	12
	Salt Lake City, UT 1987–89	Daily mean PM_{10}	0.21% (0.05%, 0.37%)	13
Peak Expiratory Flow				
Daily (evening)	Utah Valley, UT 1989–90	Daily mean PM_{10}	0.25% (0.10%, 0.39%)	8
	Utah Valley, UT 1990–91	Daily mean PM_{10}	0.06% (–0.00%, 0.12%)	14
			0.04% (–0.02%, 0.09%)	14
	Wageningen, NL 1990–91	Daily mean PM_{10}	0.09% (–0.01%, 0.20%)	9
	Union Town, PA Summer 1990	Daily mean PM_{10}	0.19% (0.01%, 0.37%)	15
(≥ weekly)	4 Cities, NL Winter 1987–90	Daily mean PM_{10}	0.16% (0.05%, 0.28%)	11
	Wageningen, NL Winter 1990–91	Daily mean PM_{10}	0.16% (–0.03%, 0.36%)	12

Table 8A.5

Studies of acute effects of particles on respiratory symptom reports

Measure of respiratory symptoms	Location and period	Particulate measure	Sample	% Change in daily symptom reporting for each 10 $\mu g/m^3$ increase in PM_{10}	Reference
Lower respiratory symptoms	Utah Valley, UT Winter 1989–90	Daily mean PM_{10}	Children	5.1% (1.1%, 9.3%)	8
			Asthmatic patients	0.2% (–4.2%, 4.8%)	8
	Utah Valley, UT Winter 1990–91	Daily mean PM_{10}	Symptomatic children	4.8% (1.5%, 8.3%)	14
			Asymptomatic children	2.4% (–1.8%, 6.8%)	14
	Wageningen, NL Winter 1990–91	Daily mean PM_{10}	School children	1.2% (–3.1%, 5.7%)	12
	4 Dutch Cities Winters 1987–90	Previous day PM_{10}	School children	1.5% (–1.1%, 4.2%)	11
Upper respiratory symptoms	Utah Valley, UT Winter 1989–90	Daily mean PM_{10}	Children	3.7% (0.7%, 6.8%)	8
			Asthmatic patients	–0.2% (–4.2%, 4.0%)	8
	Utah Valley, UT Winter 1990–91	Daily mean PM_{10}	Symptomatic children	3.7% (0.6%, 6.9%)	14
			Asymptomatic children	–0.2% (–4.9%, 4.7%)	14
	Wageningen, NL Winter 1990–91	Daily mean PM_{10}	School children	2.6 (0.1%, 5.3%)	12
	4 Dutch Cities Winters 1987–90	Previous day PM_{10}	School children	–0.2% (–1.2%, 0.8%)	11
Cough symptoms	Utah Valley, UT Winter 1990–91	Daily mean PM_{10}	Symptomatic children	5.2% (2.3%, 8.2%)	14
			Asymptomatic children	3.4% (–0.1%, 7.06%)	14
	2 Dutch Cities Winter 1990–91	Previous day PM_{10}	Symptomatic children	0.1% (–0.8%, 1.1%)	9
	4 Dutch cities Winter 1987–90	Previous day PM_{10}	School children	1.3% (0.1%, 2.7%)	11
	Uniontown, PA Summer 1990	Daytime mean $PM_{2.5}$	Children	28.1% (4.5%, 57.1%)	15

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Chapter 9

Chronic Effects Related to Long-Term Exposures to Suspended Particulate Matter

Introduction

9.1 Preceding chapters have assessed the evidence linking exposure to suspended particulate matter (SPM) with acute health effects, ie, those occurring within a few days of increases in air pollution. These studies do not, however, show what, if any, is the role of exposure to air pollutants in the development of chronic disease or in increasing (annual) death rates in the community. Focussing on such slowly developing or delayed rather than immediate effects has several implications for epidemiological studies and the reliability of their conclusions.

9.2 It is important both to identify the biologically relevant indices of exposure and to assess their reliability. In terms of biological relevance, cumulative lifetime exposure, based on annual average concentrations through the years, may be appropriate. However, there are several problems in making such assessments: historic data are seldom available, substantial changes in concentrations and in composition of pollutants have occurred with time and people are liable to move between differently polluted areas in the course of their lives. It is also possible that exposure to specific episodes of high pollution may have long-term effects: there were reports following the disastrous London smog of 1952 of patients dating their onset of severe respiratory symptoms from that time. It is also biologically plausible that exposure at particular times of life, eg, in the early years, may be more important than those at other times, or that concentrations experienced in the later years are more relevant in respect of risks of premature death. Few of these aspects can be addressed adequately in epidemiological studies, and in general, the reliability of exposure estimates is poor.

9.3 Problems of confounding variables are also more difficult to handle than in studies of acute effects. Many other factors, including lifetime experience of acute illnesses, often linked with socio-economic conditions or the availability of medical services, and smoking habits affect the development of chronic disease, and these are often inadequately documented. However, many early studies indicated an important role of urban air pollution in the development of chronic, notably respiratory, disease and recent work has focussed increasingly on the particulate component.

Cross-sectional studies of mortality

9.4 Circumstantial evidence of the chronic effects of long-term exposures to the traditional urban air pollution complex of suspended particles together with sulphur dioxide (SO_2) and associated pollutants has come from cross-sectional studies of mortality in different areas of the United Kingdom (UK), the United States (US) and other countries.[1] In general, death-rates from all causes combined and from respiratory diseases in particular, have been shown to be higher in the more polluted localities than in others.

9.5 In an early study of death-rates in the County Boroughs of England and Wales for a period centred on the 1951 census, Daly[2] was able to show an association between death-rates and an index of pollution based on coal consumption in each locality, while Gardner *et al*[3] found associations of bronchitis and lung cancer death-rates with that index in a further study centred on 1961. When, however, this type of exercise was repeated by Chinn *et al*[4] around the 1971 census, no consistent associations between death-rates and pollution, either in terms of the concentrations of Black Smoke or SO_2 for that current period, or Daly's index of conditions some 20 years earlier, were found. The conclusion was that if there was a causal relationship with any of the pollutants, it had become weaker as concentrations declined over the decades as a result of control measures and changes in fuel usage.

9.6 Although in each of these studies various socio-economic or climatic factors that might have a bearing on differences in death-rates between towns had been taken into account, evaluation of the role of pollution remains difficult, since aspects such as smoking habits or selective migration over the years could not be considered directly. Further, any effects of pollution that could be demonstrated were related to the mixture of pollutants as a whole, then dominated by Black Smoke and SO_2.

Cohort studies of mortality

9.7 More definitive findings have emerged recently from long-term follow-up studies in which the characteristics of subjects, including their smoking habits, have been collected on an individual basis, subsequently examining their mortality experience in relation to measurements of air pollution in the towns in which they lived. The most detailed study of this type has formed part of the "Six Cities" study in the United States.[5] In this study, over 8000 adults living in six cities with differing levels of air pollution were followed for 14 to 16 years between 1974 and 1991. Mortality rates, for all causes combined, adjusted for sex, age, smoking habits, education level, occupation and body mass index were shown to be associated with levels of several of the pollutants that had been measured, most closely with fine particles (< 2.5 μm, with observations available from 1980 to 1985) or with sulphates. The ratio of the adjusted mortality rate in the most polluted city (Steubenville, Ohio, mean fine particle concentration 29.6 $\mu g/m^3$) to that in the least polluted (Portage, Wisconsin, mean fine particle concentration 11.0 $\mu g/m^3$) was 1.26, with the other cities occupying intermediate positions. As far as could be ascertained on the scale of this study, the excess mortality was confined to cardiopulmonary causes and lung cancer.

9.8 While this is the most carefully conducted study of links between long-term exposure to air pollution and mortality, some limitations remain. There were contrasts in the social characteristics between the cities, as illustrated by the higher proportion of people without high school education in the three most polluted cities compared with the other three, and the socio-economic indices included in the analysis may not adequately have represented such factors. To some extent adjusting for smoking, as included, covers some socio-economic aspects since at least in recent decades, the prevalence of smoking has shown a strong social class gradient. There could then be risks of either under- or over-adjustment for a range of lifestyle factors, in turn leading to over or under estimation of effects of air pollutants. Although ages of the subjects were widely spread (25 to 74 at the beginning of the study), no account was taken of the differences in duration of exposure that applied, nor of the higher levels of pollutants that they may have been exposed to much earlier in their lives. With what was essentially only six data-points in the final outcome, representing the six cities, the statistical power of the study was low, and trying to determine which of the measured pollutants was "driving" the relationship with mortality was not easy.

9.9 Some information is also available from the large cohort study carried out by the American Cancer Society, primarily in relation to smoking.[6] Subjects had been enrolled in 1982 and their vital status was ascertained up to the end of 1989. Some 552,000 lived in metropolitan areas for which data on particle concentrations, in 1980, were available. Mortality rates were adjusted for factors similar to those in the Six Cities study and the ratio of the adjusted all causes rate in the most polluted area (annual mean sulphate concentration 23.5 $\mu g/m^3$) to that in the least polluted area (annual mean sulphate concentration 3.6 $\mu g/m^3$) was 1.15. For fine particles (< 2.5 μm) less data were available and analyses were carried out for the 295,000 subjects living in 50 metropolitan areas where dichotomous samplers had been in use between 1979 and 1983. The ratio of adjusted all cause mortality rates, comparing the most polluted area (mean fine particle concentration 33.5 $\mu g/m^3$) with the least polluted (mean fine particle concentration 9.0 $\mu g/m^3$) was 1.17. There was careful control for smoking in this study and the associations with air pollution were seen both among smokers and among those who had never smoked. Relative risks were higher for cardiopulmonary causes than for others. The association with sulphate suggests a possible link with secondary pollutants derived from SO_2 emissions from non-nuclear power stations or other stationary sources, though the measurements may only be serving as proxies for other components of the pollution complex.

9.10 These cohort studies have allowed other relevant factors to be controlled more satisfactorily than in the earlier cross-sectional ones, strengthening the case for an adverse effect of long-term exposure to particles and associated air pollutants on death-rates. However, uncertainties such as the level of exposure to pollution in the earlier years of the populations remain, and the findings to-date are considered to provide a less secure basis for any quantitative risk assessment related to particulate air pollution than those on acute effects.

Morbidity (adults)

9.11 Much of the evidence of chronic effects on health resulting from long-term exposures to urban air pollutants in general has come from studies on the prevalence of respiratory symptoms among adults living in areas with contrasting levels of pollution. Bronchitis, characterised by symptoms of persistent cough and phlegm, has often been referred to as the "English disease", seen to be more common in the large UK cities that were heavily polluted by coal smoke. In some early studies carried out in both the UK and the US, a single occupational group, such as postal and telephone workers,[7] was used in order to control for specific occupational or socio-economic factors, and it has been found to be essential to control for smoking habits also.

9.12 Some recent evidence on the role of exposure to the particle/SO_2 complex of pollution in the UK has come from an analysis of data from a survey of 23 year olds, relating the prevalence of respiratory symptoms among them to pollution levels on a county of residence basis.[8] While the strongest associations were with smoking and social class, phlegm symptoms also showed a relationship to mean annual concentrations of Black Smoke within a relatively low range, as measured in 1981.

9.13 General population studies have been reported from Cracow, Poland,[9] where there was much pollution from coal-burning. A higher prevalence of respiratory symptoms and poorer lung function was found in areas where the annual mean concentrations of SO_2 and Black Smoke were 125 $\mu g/m^3$ (43.7 ppb) and 170 $\mu g/m^3$, respectively, than in those where they were 45 $\mu g/m^3$ (15.7 ppb) and 90 $\mu g/m^3$. Subsequent regression analyses of data from Cracow[10] confirmed the role of these pollutants in enhancing, along with smoking and occupational factors, the prevalence of chronic respiratory disease, with further support from a longitudinal follow-up in which comparisons were made between Cracow and Tucson, Arizona.[11]

9.14 An important series of studies has been carried out in The Netherlands, involving repeated surveys of respiratory symptoms and lung function in a polluted industrial area and a cleaner rural area over a period of 15 years.[12] Concentrations of SO_2 were high in the industrial area, ranging from 144-244 $\mu g/m^3$ (50-85 ppb) annual mean at the beginning of the series, but those of suspended particles were relatively low, 34-45 $\mu g/m^3$ annual mean as Black Smoke. There was a small persistent difference in lung function (FEV_1) between the two populations, considered to relate to the pollution complex as a whole, but interpretation of the large data set was difficult.

9.15 The conclusion reached by the World Health Organisation[13] on the basis of data available from the UK, the US and a number of other countries up to the mid 1980s in respect of increased respiratory symptoms among adults in areas polluted by particles together with SO_2 was that effects became discernible at mean annual concentrations of Black Smoke and SO_2 each above 100 $\mu g/m^3$. This did not imply specific thresholds, merely that the data were insufficient to determine exposure/effect relationships at low concentrations, nor was it clear what the respective roles of particles and SO_2 were: at that time they were considered jointly.

9.16 A retrospective analysis of data from a health survey (NHANES I) carried out across the US in the 1970s has been reported,[14] linking findings with measurements of total suspended particulates (TSP) in the areas concerned. Smoking habits had been recorded and after adjusting for these an association was found between the probability of self-reported or physician-diagnosed chronic bronchitis and TSP

levels. From the logistic regression analysis the increase in risk of having chronic bronchitis was about 7% for each 10 $\mu g/m^3$ increase in TSP annual mean (the values in each area ranging from about to 40 to 140 $\mu g/m^3$). An earlier analysis of lung function data (FEV_1 and FVC) in the same survey[15] has also shown significant relationships with TSP levels, and there appeared to be a threshold for these effects at about 60 $\mu g/m^3$ TSP as a quarterly average. Relationships between TSP and lung function were investigated further[16] among a sub-sample of children and youths examined in a second survey, NHANES II. Associations were demonstrated between both FEV_1 and FVC and annual mean concentrations of TSP, as well as with NO_2 and ozone, but not with SO_2.

9.17 Some information of possible effects of particles, in terms of TSP, with indirect estimates of PM_{10} and $PM_{2.5}$, on the development of chronic disease has been obtained from the prospective study among a wholly nonsmoking population of Seventh Day Adventists in California.[17] The authors express caution about the interpretation of the large range of relationships examined and about the possible weakness of the particulate pollution data, but associations were seen between the development of chronic respiratory symptoms and TSP concentration, but not with SO_2.

9.18 One of the problems to contend with now in trying to establish exposure/response relationships for SPM as a component of this "traditional" type of pollution complex is that concentrations have declined substantially in most areas of Western Europe and the US to the point where, even if contrasts in chronic respiratory disease were apparent, current pollution measurements would provide little guide to exposures experienced in earlier years.

9.19 The situation is, however, different in Eastern Europe, where until very recently pollution by SO_2/particles from coal-burning had remained high for some 40 years. In Erfurt (East Germany), for example, the mean annual concentration of suspended particles (gravimetric determination) in 1988 was 153 $\mu g/m^3$ with SO_2 217 $\mu g/m^3$ (75.8 ppb).[18] New studies of effects on health, including investigations of the prevalence of respiratory symptoms among adults are in progress, and comparisons with the situation in West Germany show a similar prevalence of chronic respiratory disease symptoms such as cough and phlegm, considered to be related to the SO_2/particulate pollution.

9.20 Even more extreme conditions linked with the continuing use of coal for industrial and domestic (heating and cooking) purposes are still found in China, and a number of studies on effects on health have been reported recently. Measurements of lung function (FEV_1 and FVC) have been made among adult non-smokers in three areas of Beijing,[19] in which annual mean concentrations of total suspended particles (TSP) were 389, 261 and 449 $\mu g/m^3$ with SO_2 concentrations 128, 15 and 57 $\mu g/m^3$ (45, 6.3 and 157 ppb), respectively. Lung function values were reduced among people who used coal for heating, and among others, an inverse association was found between lung function values and TSP or SO_2. The important role of indoor pollution, from the burning of coal is discussed in a later paper,[20] and it is clear that in these circumstances effects on health cannot simply be related to pollutant concentrations as measured outdoors.

9.21 An attempt has been made to assess possible effects of exposure to pollution from traffic in a series of studies among female adults in Tokyo.[21] The odds ratio for chronic cough and chronic phlegm was increased significantly in relation to distance of residence from busy roads. While measurements of SPM were made, greater emphasis was placed on concentrations of oxides of nitrogen, and it was considered that personal exposure monitoring would be required to obtain more definitive results.

Morbidity (children)

9.22 Many studies of longer-term effects on health of SO_2/particulate pollution have been undertaken among children, partly because other factors, such as occupational exposures to dusts or smoking do not feature or are of lesser importance than in adults, and also because they appear to be more sensitive. The

effects considered are not strictly "long-term" ones, as in the case of the development of chronic respiratory disease in adults over some tens of years, but related more to consequences of intermediate duration, such as an enhanced frequency of respiratory illnesses. In most cases, annual mean concentrations have been used as an index of exposure, though seasonal or other intermediate averaging times may be more relevant.

9.23 In a study in Sheffield in the 1960s, when concentrations of SO_2/particles were high but varied considerably in different parts of the city (annual mean Black Smoke 97-301 $\mu g/m^3$; SO_2 123-275 $\mu g/m^3$, 43-96 ppb) respiratory infections were more common in the more polluted areas.[22] Then, in a follow-up study 4 years later,[23] when pollution levels were lower (annual mean Black Smoke 48-169 $\mu g/m^3$; SO_2 94-253 $\mu g/m^3$, 33-88.5 ppb) contrasts in respiratory illness were no longer evident.

9.24 Another early study in the UK[24] was based on a cohort of children born in 1946 and followed to age 15. The frequency of lower respiratory infections among them throughout that period was shown to be related to an index of SO_2/particulate pollution in the areas where they lived, based on the amounts of domestic coal used.

9.25 Studies of effects of exposure of children to pollution in coal-burning areas have also been reported from Germany. In one study carried out in the 1960s,[25] lung function was compared among children in two areas with contrasting levels (6 month mean SO_2, 50 and 360 $\mu g/m^3$, (17.5 and 126 ppb) respectively, but no direct measurements of suspended particles), values being lower in the more highly polluted area. Also, in a more recent study in Eastern Germany,[26] still highly polluted, lung function and respiratory symptoms in children have been compared between polluted and control areas (annual mean SO_2 range 100-300 $\mu g/m^3$, 35-105 ppb, but suspended particles not reported): a higher prevalence of bronchitic symptoms was found in the more polluted area.

9.26 Comparisons have also been made between a highly polluted Eastern German city (Leipzig) and a clean region near Munich in respect of respiratory symptoms and lung function among children.[27] Annual mean concentrations of SO_2 were 310 and 11 $\mu g/m^3$ (108 and 3.8 ppb), respectively, with 24-hour mean suspended particles up to 1,070 $\mu g/m^3$ in Leipzig and 104 $\mu g/m^3$ in the Munich area. The prevalence of bronchitic symptoms was substantially higher in the more polluted area. Allergic disease as represented by hay fever was significantly more common in Munich. Asthma was also more common in Munich though the difference was less striking than in the case of hay fever.

9.27 Results reported recently[28] from a cohort study among school children in SW Germany, surveyed in 1977, 1979 and 1985, comparing the prevalence of respiratory symptoms between children in Mannheim and in a less polluted region near Freiburg with those in a rural Black Forest area, showed a relationship with SO_2 concentrations but not with suspended particles. One problem in interpretation is that suspended particle levels were no lower in the Black Forest area than in Mannheim, this finding being attributed to long distance transport of pollutants. Although quantitatively there was no contrast, there could have been qualitatively, with the rural particles probably being mainly secondary aerosols.

9.28 A recent study[29] comparing school children in a Polish town with those in urban and rural control areas in Sweden has shown a higher prevalence of respiratory symptoms in the former, though there was less atopic sensitisation. Concentrations of smoke and SO_2 were much higher in the Polish town than in either of the Swedish areas, and while these pollutants may well have played a role, the authors considered that differences in other lifestyle factors may also have been relevant.

9.29 Several studies among children have been reported from the Hamilton area of Canada. In one[30] related to emissions from two steel mills, the city was divided into 4 quadrants, among which total suspended particle concentrations during the study period ranged from 43-90 $\mu g/m^3$/(annual geometric mean); with corresponding

suspended particles less than 7 μm diameter, as measured during a prior period, being 70-62 $\mu g/m^3$ annual mean. The prevalence of symptoms was related to pollution levels and reductions in lung function more specifically to the fine fraction. In a longitudinal study carried out in Hamilton among children with asthma,[31] a reduced rate of growth of pulmonary function has been found in relation to exposure to SO_2/particulate pollution, with median values quoted as 27 $\mu g/m^3$ (9.4 ppb) for SO_2, 47 $\mu g/m^3$ for fine particles under 3.3 μm and 42 $\mu g/m^3$ for coarser particles, over 3.3 μm.

Conclusions

Effects of long-term exposures on morbidity in adults and children

9.30 It is not easy to come to firm conclusions in respect of these studies of long-term effects on morbidity. Collectively, they indicate a consistent adverse effect of exposure to air pollution, notably in the form of the SO_2/particle complex associated with coal-burning, and it is bronchitic symptoms (cough and phlegm) that have most often been associated with pollution rather than those of asthma. However, the types of studies, the adequacy of monitoring of particles and other pollutants and the extent to which confounding factors have been taken into account varies widely. Above all there remains doubt, as in the mortality studies, as to whether the current pollution levels that have usually been reported serve as a sufficient guide to those experienced earlier in life.

Carcinogenic effects

9.31 The possibility that exposure to SPM may play some role in the development of lung cancer arises from the observed higher incidence of that disease in urban as opposed to rural areas, and the presence of small quantities of compounds having carcinogenic properties adsorbed onto the particles. The most widely studied compound of this type is benzo(a)pyrene (BaP), with domestic coal fires its prime source in former years.

9.32 Assessing the magnitude of any impact on lung cancer has, however, proved to be a difficult task in the face of the overwhelming influence of smoking. An estimate made when this topic was reviewed in 1978 was that, in conjunction with smoking, air pollution may have caused some 10% of lung cancer cases in men in the 1950s, when coal smoke was still a major problem.[32]

9.33 Since that time, with coal fires having been eliminated in most major urban areas in the UK, concentrations of BaP have fallen dramatically, by a factor of 30 in London over a period of some 30 years,[33] now being in the region of 1 ng/m^3. The main urban sources of BaP now are emissions from motor vehicles, and particular attention has been paid to the potential carcinogenicity of diesel smoke.

9.34 In the late 1970s and early 1980s, extensive animal inhalation studies were undertaken in Europe,[34] the US and Japan, using both petrol and diesel engines. The main outcome was the development of lung tumours in rats subjected to massive exposures of diesel exhaust for near-lifetime periods.

9.35 To determine any link with lung cancer in man, epidemiological studies have been carried out, mainly among occupational groups having heavy exposures to diesel exhaust. The most critical of these has been a study of railroad workers in the US[35] exposed to fumes from locomotives during maintenance work and otherwise. In this group, an increased risk of lung cancer was detected, though not all studies on this topic have yielded positive results.

9.36 The findings from both the experimental and the epidemiological studies have been reviewed by an international group,[36] reaching the conclusions that there is sufficient evidence for the carcinogenicity in experimental animals of whole diesel engine exhaust and limited evidence in respect of humans.

9.37 The carcinogenic effect is associated with fine particles, but the lung cancer risk has only become perceptible at very high exposures and while there may be a detectable effect among some highly exposed occupational groups, at the concentrations of diesel smoke found in streets, any risk would appear to be exceedingly small. However, on grounds of prudence, it is a further reason for minimising concentrations of SPM in the general atmosphere.

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Chapter 10

Summary, Discussion and Conclusions

Summary

10.1 A detailed review of the possible effects of particulate air pollution on health has been presented in the foregoing chapters. These findings are summarised here and recommendations for further research made in Appendix 1 of the report. More detailed research recommendations can be found in the individual chapters of the report.

Terminology

10.2 This report is concerned with effects on health of "suspended particulate matter" (SPM), comprising solid (soluble or insoluble) or liquid material present in the air in particles small enough to remain in suspension for some hours or days and liable to travel considerable distances from the source. This corresponds approximately with the size range of particles, typically less than 10 μm diameter, capable of entering the respiratory tract and reaching the deeper parts of the lungs. Particles of biological origin are not considered.

Basic problems

10.3 SPM is not a defined entity: both chemical and physical characteristics vary widely with respect to source, location and time. There is no clear evidence as to whether effects on health are related to certain components or whether they represent non-specific effects of inhaled particles. Other pollutants or other factors in the environment, for example, changes in temperature, can affect the same health endpoints to a greater extent than particles. It has proved difficult to do representative studies of the effects of the ambient aerosol under controlled conditions because it is impossible to recreate the precise particle mixture found in outdoor air. Studies of the effects of well defined small particles could be done in humans and animals and they would contribute useful baseline data, but few such studies have been reported. Because of this, there is little evidence other than from epidemiological studies. Some insight into possible mechanisms of effect have come from animal studies though no completely plausible explanation for the findings of epidemiological studies has yet been produced.

Sources

10.4 Particulate pollution in the UK used to be dominated by smoke from the inefficient combustion of coal, notably in domestic fires. With that source now mainly eliminated the remaining, much lower, concentrations in the air are largely from motor vehicle emissions, non-nuclear power stations and from reactions between gases. Particles produced directly by combustion processes are referred to as primary; those produced by gas phase reactions are referred to as secondary or as the secondary aerosol. Primary particles are also produced by surface attrition.

Monitoring

10.5 To some extent SPM is characterised by the method of measurement. Traditionally a "Black Smoke" method has been used in the UK, based on soiling capacity, concentrations being expressed in terms of $\mu g/m^3$ of equivalent standard smoke. Methods based on mass are now being used increasingly, with sampling instruments having defined particle size responses. PM_{10} is the term now applied to particulate matter assessed by instruments having a high collection efficiency for inhalable particles of 10 μm diameter or less. Being based on different characteristics, there is no universal relationship between Black Smoke and PM_{10}. The traditional Black Smoke measurements, apart from being required still for regulatory control purposes, can add another dimension to the measurement of particles within epidemiological studies. Such measurements help to characterise pollution arising

mainly from incomplete combustion and now notably from diesel emissions. Such measurements also allow the continued use of the UK long-term database for epidemiological studies on Black Smoke.

Other indices of SPM

10.6 The mass concentrations of particles as measured routinely may not be the most relevant indicators of toxicity. Other useful indices might include the contributions made to the total mass by particles in different size ranges. Surface chemistry could be important, in which case surface area may be more relevant than mass. In addition, the number concentrations of particles could be important. Close to sources of particles, as amidst heavy traffic, there can be large, short term increases in number concentrations which have relatively little effect on the mass concentration.

Environmental concentrations

10.7 Annual mean concentrations of PM_{10}, in the UK, as determined from continuously recording instruments are mainly in the range 20 to 30 $\mu g/m^3$, with hourly mean peak values of up to about 150 $\mu g/m^3$ and occasionally higher. There is less variation between values at different sites across urban areas, or between urban and rural values, than is the case with Black Smoke. Where emissions from diesel vehicles are a major component, Black Smoke values are of the same order or greater than those of PM_{10}, but otherwise they tend to be lower. Black Smoke does not include the essentially colourless secondary aerosol.

Deposition in the respiratory tract

10.8 PM_{10} represents the size range of particles likely to pass the nose and mouth; $PM_{2.5}$ represents more closely the size range of particles able to reach the deeper parts of the respiratory tract. A significant proportion of the mass of material collected as PM_{10} is less than 2.5 μm in diameter. The deposition of particles in the respiratory tract varies with particle size and particles of about 0.5 μm diameter are least likely to be deposited. Exercise may have a variable effect on particle deposition depending on particle size and pattern of respiration. The estimated typical deposition of particles in adults in the PM_{10} range is about 250 μg/day: in terms of traditional studies of toxicity of inhaled particles this would be a small dose.

Experimental studies of mechanisms of action

10.9 Some experimental studies, mainly in animals and at high concentrations, show that mixtures of particles with pollutant gases such as SO_2, NO_2 or O_3 may have effects greater than those of the separate components, though it is not clear whether these results would apply at the low concentrations normally present in the environment. The adsorption of such gases, or of metals or acid-sulphates, on the surface of particles may be important. Animal studies also indicate a potentially important role for ultrafine particles (< 0.05 μm diameter). They are cleared only very slowly from the lung and they can penetrate the interstitial tissues of the lung inducing inflammatory responses. It has been suggested that allergenic material may be carried into the lung in association with particles though evidence is lacking.

10.10 Extensive studies of the effects of well characterised particles (eg, acid sulphates and sulphuric acid) have been carried out in volunteers. It has been demonstrated that at the concentrations likely to be experienced in the UK no effects would be expected in normal individuals. Subjects with asthma show enhanced non-specific bronchial reactivity following sulphuric acid challenge, and, perhaps, following sulphate challenge. However, all these changes in either lung function or bronchial responsiveness have been, in general, small. The reasons for this may be in part methodological, but the evidence suggests that there is unlikely to be a large acute effect of acid or sulphate challenge on human subjects. Studies of interactions between particles and other pollutants are lacking.

Epidemiological evidence

New studies

10.11 On the basis of findings from studies of pollution episodes in the 1950s to 1960s, when concentrations of SPM and SO_2 were very high, it was not anticipated that adverse effects on health would be demonstrable at the much reduced concentrations of more recent years. However, a series of intensive studies, mainly in

the United States, has demonstrated small changes in a wide range of health indicators, showing a more consistent association with concentrations of particles than with other pollutants.

Statistical techniques

10.12 To some extent, the new findings have been dependent on developments in advanced statistical computing techniques, handling large data sets covering many variables. Such methods have passed into general use during the past 10-15 years. These procedures have been examined carefully; they are considered to be appropriate and the results are robust to a variety of statistical methods. It is unlikely that the findings of recent epidemiological studies are an artefact of the statistical methods employed.

Indicators of acute effects on health

10.13 Those health indicators examined in relation to acute effects have included day-to-day variations in mortality, hospital admissions, emergency room visits, time off school or work, respiratory symptoms, exacerbations of asthma and changes in lung function. Of these various indices, the measurement of mortality is the most certain. In addition, effects on mortality have been particularly well studied and the results have been generally more consistent than those regarding the other indices. In most investigations, associations with SPM, expressed at least in the more recent studies as PM_{10}, have been observed, within a relatively low range of concentrations of similar magnitude to those found in the UK today. It does not necessarily follow that the same types or sizes or components of particles are involved in these diverse effects. The composition of particles monitored as PM_{10} can vary widely from area to area and with time. However, the size of the estimated effects, particularly as regards effects on mortality, does not vary greatly with location.

Confounders

10.14 Short-term variations in these health indicators have been demonstrated to be influenced by factors such as temperature and (even minor) epidemics of infections such as influenza, as well as possible effects of other pollutants, including SO_2 and ozone. Reported effects on health of day-to-day variations in concentrations of particles are small in comparison with those of these factors. Considerable efforts to control statistically for the effects of confounding factors have been made in recent epidemiological studies. For example, in the most recent studies in the United States, possible effects of air pollution have only been examined once all other identifiable variations in the health indicators have been accounted for. The likely success of the methods used inevitably depends on how well the confounding factors have been characterised and on this point there remains room for debate. Overall, control for confounding factors, in the more recent studies, is accepted as good. The possibility of some unmeasured confounding factor playing a role cannot be dismissed, but this is not considered likely.

Exposure/response relationship

10.15 Though the results of most epidemiological studies are described as providing exposure-response relationships, it should be remembered that, in general, they provide information on ambient concentration-response relationships across the population studied. In any population the range of personal exposure and consequently dose, is likely to be considerable and monitoring the ambient concentration of a pollutant will provide only an estimate of exposure.

10.16 There is no clear indication that effects on health are restricted to specific types of particles. Findings from epidemiological studies have demonstrated associations with particles in a wide range of circumstances, including those in which primary emissions from motor vehicles, industrial sources or coal fires or where secondary aerosols derived from gaseous emissions (SO_2 and NO_x from non-nuclear power stations and other stationary sources with further NO_x from traffic) are important. It is unlikely, however, that coarse, wind-blown particles have a significant effect upon health.

10.17 It is well established from the reported studies that people with pre-existing respiratory and/or cardiac disorders are at most risk of acute effects from exposure to particles. It has been suggested that these effects occur when air pollution aggravates an acute condition such as a respiratory infection or heart attack in people with pre-existing chronic disease. There is no evidence that healthy individuals are likely to experience acute effects on health as a result of exposure to concentrations of particles found in ambient air in the UK.

10.18 In most of the statistical analyses of epidemiological studies, relationships have been expressed as regression equations from which the magnitude of effects linked with changes in pollution can be judged. An example, from a study in Detroit, indicates that a 30 $\mu g/m^3$ increase in PM_{10}, as a 24 hour average, was associated with a 3.5% increase in hospital admissions for pneumonia. This, of course, does not imply that exposure to such pollution initiated the illness: if causal, this would be through predisposing to, or aggravating, the illness and precipitating the need for admission to hospital.

10.19 No evidence for thresholds of effect has been demonstrated in the studies so far reported, though it should be noted that several studies have not been sufficiently powerful to examine the issue critically at low concentrations.

Chronic health effects

10.20 In the UK, there has been a long-established association between the prevalence of, and mortality from, chronic respiratory disease (bronchitis) and exposure to the SO_2/particle complex associated with coal-burning. The role of the particulate component has remained uncertain and other factors, notably smoking, have been shown to be of major importance. Disentangling the roles of multiple factors operating throughout life has proved to be a difficult task, but in some recent US studies, it has been possible to follow selected population groups for a number of years, relating death-rates among them to local pollution levels. Associations have been found to be closer with concentrations of particles than with those of other pollutants, but in view of uncertainties about the possible relevance of (higher) exposures to pollution earlier in life and the difficulties in fully adjusting for confounding factors, quantitative assessments are in doubt. The lower prominence given to this aspect of the effects of particles on health in this report reflects the lack of data rather than the potential importance of possible effects on the public health.

Discussion

Acute health effects

Are associations causal?

10.21 The principal question to consider in reviewing the rapidly expanding literature on effects of SPM is whether the statistical associations demonstrated indicate a causal role. There is certainly a remarkable degree of consistency and coherence in the direction and magnitude of findings from a diversity of studies, carried out in different localities in the US and elsewhere, with a range of different health indicators and varying sources of pollution. The Committee considers the reported associations between concentrations of particles and effects on health principally reflect a real relationship and not some artefact of technique or the effect of some confounding factor. The indications that the association is likely to be causal are certainly strong.

Mechanisms

10.22 The only major difficulty in reaching any firmer conclusion about causality is the lack of established mechanisms of action. The mass of SPM associated with adverse effects is very small, and while there is evidence relating to acute effects of some components, the fact that in epidemiological studies similar effects have been reported in localities with different types of SPM suggests that there may be a non-specific effect of particles. The effects have not been explained in terms of the results of conventional inhalation toxicity studies but carriage of material on the surfaces of particles could play a role. It has been suggested, but by no means proven, that ultrafine particles (< 0.05 μm) may play a role. These have been shown in recent animal studies to be capable of producing inflammatory reactions in the lungs. Such particles would be more prominent close to sources, before they had time to coalesce

into the more stable accumulation mode, and they would represent only a small proportion of the mass of material measured as PM_{10}, though they would represent a high proportion of the number of particles present. Although reported studies indicate a range of effects, from small changes in ventilatory function or exacerbations of asthma through to increases in deaths among the elderly or chronic sick, it does not necessarily follow that the same components would be involved in each effect.

Implications for public health in the UK

10.23 We conclude that, in terms of protecting public health, it would be imprudent not to regard the associations as causal. We also believe that the findings of the epidemiological studies of the acute effects of particles, which have been conducted in the US and elsewhere, can be transferred to the UK at least in a qualitative sense. However, we consider that there are insufficient UK data available to allow direct extrapolation and reliable estimation of effects in the UK.

10.24 It would be possible, for any health effect of interest, to take a weighted average of the results of well-conducted published studies and apply this to conditions in the UK. [This would usually imply conversion across different measures of particles.] Thus, the relative risk calculated by Schwartz[1] with regard to effects of particles on mortality was 1.06 (CI: 1.05-1.07) for a 100 $\mu g/m^3$ change in total suspended particles, equivalent to some shortening of life in approximately 1% of daily deaths per 10 $\mu g/m^3$ increase in PM_{10}. Application to the UK of the results even of such structured meta-analyses does not formally take account of uncertainties in extrapolating to different air pollution mixtures (with generally lower concentrations of suspended particles), climate patterns and at-risk populations. Because of these uncertainties, we think it would be unwise to offer a single coefficient with regard to effects on mortality or any other index of ill health. The reader is referred to the tables in Annex 8A to Chapter 8, with the warning that the estimates based on studies reported in these tables are likely to provide only a first approximation to the actual effect. Studies should be undertaken urgently to allow better quantitative predictions to be made.

Measurement

10.25 Unless, or until, a clearer idea is obtained of the sizes or other characteristics of SPM that are most relevant to effects on health, we consider it appropriate to measure SPM in terms of PM_{10}, covering the whole range of material capable of being inhaled and reaching the deeper parts of the respiratory tract. However, there is also a pressing need for investigation of the particle size distribution, of subfractions such as $PM_{2.5}$ and for considering surface area and number concentrations as well as mass.

Averaging times

10.26 The epidemiological studies of acute effects have been related to PM_{10} values assessed over 24 hour periods, or sometimes over several days. It may be that number and mass concentration over shorter periods of time are important, but this aspect has not been investigated and it should be followed up. The hourly means available from continuous monitoring instruments do, however, help to characterise the pollution exposures. It has been suggested that the role of rate of change of concentrations of particles and other pollutants may also be important though this is seldom taken into account in monitoring strategies.

Chronic effects

10.27 Evidence regarding the effects of long term exposure to particles on health is less well developed than that regarding the acute effects. The possibility of confounding in such studies is considerable and it is difficult to estimate the exposures of individuals over relevant time periods. Here again the results of recent US studies are probably transferable to the UK in a qualitative sense though confidence in the accuracy of the predictions is lower than with regard to the acute effects of particles.

10.28 Though the evidence is limited we advise that it would be prudent to consider these associations as causal.

10.29 There is little evidence to show that exposure to atmospheric particles contributes significantly to the burden of cancer in the UK. The presence of genotoxic carcinogens in particles means that such a contribution cannot be ruled out, although it is likely to be very small.

Conclusions

10.30 The Committee considers that the reported associations between daily concentrations of particles and acute effects on health principally reflect a real relationship and not some artefact of technique or the effect of some confounding factor.

10.31 In terms of protecting public health it would be imprudent not to regard the demonstrated associations between daily concentrations of particles and acute effects on health as causal.

10.32 We find it difficult to reach a firmer conclusion about causality due to the lack of any established mechanism of action.

10.33 We believe that the findings of the epidemiological studies of the acute effects of particles, which have been conducted in the US and elsewhere, can be transferred to the UK, at least in a qualitative sense.

10.34 It is accepted that insufficient UK data are available to establish the reliability of quantitative predictions of the effects of particles upon health in the UK.

10.35 We consider that results of recent US studies of the effects of long-term exposure to particles are probably transferable to the UK, though confidence in the accuracy of the predictions is lower than with regard to the acute effects. Although the evidence is limited, we advise that it would be prudent to consider these associations as causal.

10.36 There is no evidence that healthy individuals are likely to experience acute effects on health as a result of exposure to concentrations of particles found in ambient air in the UK.

Reference

1. Schwartz J. Air pollution and daily mortality: a review and meta-analysis. Environ Res 1994; 64:36-52.

Appendix 1

Recommendations for Further Research

A1.1 Pending the outcome of further investigations, it is recommended that the monitoring network for suspended particulate matter should be expanded with further PM_{10} samplers, considering the introduction of some 24 hour equipment as well as continuous instruments. The need to determine the mass and number distributions of particles temporally and spatially is also stressed. Determination of $PM_{2.5}$ at selected sites would be valuable.

A1.2 At some selected sites, notably close to traffic, continuous monitoring of particle numbers as well as mass concentrations should be undertaken.

A1.3 To assist in characterising the type of particles, Black Smoke samplers should be retained, ensuring that some are co-located with PM_{10} samplers and with those for gaseous pollutants.

A1.4 Studies should be undertaken of the physical and chemical characteristics of suspended particulate matter in a number of different locations, including busy streets, urban background and rural areas. Particle size distributions by mass and number, particle morphology, surface properties and the adsorption of gases and acidic components should be included in such studies, with particular attention to ultrafine particles.

A1.5 Investigations are required on the assessment of personal exposures to SPM in selected circumstances, as in streets, for comparison with nearby fixed samplers. Studies of personal exposure to particles indoors and out should also be studied. The points made above regarding mass and number distributions apply here also.

A1.6 Atmospheric particles are highly variable in physical and chemical composition and size. Furthermore, the environment in which they are formed is also highly variable in composition and time. Studies of the loading of other substances upon such particles will necessitate stringent definition and control of these variables to be of value in the assessment of their toxicological effects in humans.

A1.7 The role of metals in surface layers of ultrafine particles should be defined. There is a need to know whether they catalyse chemical reactions, interact with tissues or induce toxicological sequelae.

A1.8 The toxicological properties of ultrafine particles should be studied. The possible toxicological interactions between such particles and gaseous pollutants are especially worthy of study.

A1.9 The practicability of carrying out controlled human exposures to a broader range of suspended particulate matter components, observing short-term effects on lung function or symptoms, should be considered. Examination of the effects of exposure upon more sensitive indicators of small airway function is stressed.

A1.10 The effects of co-exposure to allergens and ambient particles should be studied.

A1.11 Epidemiological studies should be developed to investigate further the association between exposure to particles and acute effects on health using routinely collected daily data on mortality, hospital admissions and general practitioner consultations.

A1.12 Epidemiological studies designed to address the following important questions are urgently needed:

a. Which component of the air pollution mixture has the greatest effect on health?

b. Is there evidence for a threshold of effect with regard to effects of particles?

c. Is the rate of change of particle concentrations an important factor in controlling the response?

d. Which individuals are most affected by raised levels of particles?

A1.13 Studies on effects of day-to-day changes in PM_{10}, $PM_{2.5}$ and allergen exposure concentrations should also be undertaken among panels of asthmatic or other sensitive subjects. It is important to examine the possibility that within asthmatic subjects there is a range of sensitivity to particles.

A1.14 Studies of the effects upon health of episodes of air pollution characterised by raised levels of particles should be undertaken.

A1.15 Opportunities for exploring chronic effects of long-term exposure to suspended particulate matter, through the use of routinely available mortality or morbidity statistics or follow-up of special surveys should be considered.

Appendix 2

Glossary of Terms and Abbreviations

AAS	Atomic Absorption Spectroscopy
Aerodynamic diameter	The aerodynamic diameter of a given particle is the diameter of a spherical particle of unit density which sediments at the same rate as the given particle
Aerosol	An atmosphere containing particles which remain airborne for a reasonable length of time
AI	Alveolar-interstitial: term used in deposition models to describe peripheral site of deposition of inhaled particles
Aldehydes	A group of chemical compounds, several of which are irritants, eg, formaldehyde
Alkanes	Saturated hydrocarbons of the methane series. All their carbon atoms are joined by single bonds. Also called paraffins
Alkenes	Unsaturated aliphatic hydrocarbons containing one double bond. Also known as olefins
Alveolar macrophages	Phagocytic scavenger cells of the alveoli as opposed to those of the blood, secrete cytokines and proteases
Aromatic	Denoting a compound characterised by the benzene ring
AUN	Automatic Urban Network
BAL	Bronchoalveolar lavage
bb	Bronchiolar } used in the same way as AI(qv)
BB	Bronchial }
BHR	Bronchial hyperreactivity
Black Smoke (BS)	Non-reflective (dark) particulate matter, measured by the smoke stain method
Bronchodilators	Agents that increase the diameter of the air passages (bronchi) of the lungs
CHESS	Community Health and Environmental Surveillance System (US)
Cg	Gas concentration
CMD	Count Median Diameter. Term used to describe the size distribution of particles in an aerosol. 50% of particles, by numbers, are of diameter less than the count median diameter
COMEAP	Committee on the Medical Effects of Air Pollutants
COPD	Chronic obstructive pulmonary disease (often taken to mean chronic bronchitis and emphysema)
Cp	Particle concentration
C5a	The biologically active fragment of the discrete protein C5 which is a component of the complex series of plasma enzymes known as the Complement System
Da	A unit of mass, the Dalton, one-twelfth the mass of the nuclide of carbon-12, equivalent to 1.657×10^{-24} gm
Dibenzofuran	Organic compound containing a furan and two benzene rings
Dioxins	Highly toxic compounds found as trace contaminants in some herbicides and emitted from combustion processes

DL_{CO}	Diffusing capacity of the lung for carbon monoxide
DoE	Department of the Environment
^{99m}Tc-dTPA	^{99m}Tc-diethylene triaminopentaacetate
Dyspnoea	Difficult or laboured breathing
EPA	Environmental Protection Agency (US)
ERVs	Emergency room visits
ESCA	Electron Spectroscopy for Chemical Analysis
Esters	Compounds formed from an alcohol and an acid by the removal of water
ET	Extrathoracic: parts of the air passages (nose and mouth, pharynx, larynx) outside the thorax
EUN	Enhanced Urban Network
FEV_1	The volume of air expired during the first second of a maximal or "forced" expiration
Fly ash	A fine ash produced, eg, when pulverised fuel is burned in power stations. Particle diameter 1-20 μm
FP	Fine particulate. See $PM_{2.5}$
FVC	Forced vital capacity. The volume of air expired in a forced expiration following maximum inspiration
Gaussian error	The representation of the random or unexplained part of a regression model as following the Gaussian (Normal) distribution
GEE	Generalised estimating equations
Geometric standard deviation (σg)	A measure of dispersion (variability) usually used for deviation data that are approximately symmetric on the log scale, as in the log-normal distribution
G10	10th Generation of branches in the airways
H^+	Hydrogen ion
Henry's Law	A law which states that the solubility of a gas in a liquid solution is proportional to the partial pressure of the gas
HIS	US Health Interview Survey
Hygroscopic growth	Growth of particles due to uptake of water from the atmosphere
ICD	International Classification of Diseases
ICRP	International Commission for Radiological Protection
Inhalable particles	Particles which may be breathed in. "Inhalability" is the orientation-averaged aspiration efficiency for the human head
KM	A measure of particulate loading based on optical reflectance and similar to Black Smoke
kPa	KiloPascal: a unit of pressure. A Pascal = 1 Newton per square metre (100KPa = 1 atmosphere = 760 mm.Hg)
LDH	Lactate dehydrogenase
Longitudinal studies	Studies where a defined group (cohort, panel) is followed up continuously or repeatedly
LRT	Lower respiratory tract
LUDEP	Computer model predicting regional deposition of aerosols across populations
MAAPE	Advisory Group on the Medical Aspects of Air Pollution Episodes

Mass concentration	The concentration of particles in air expressed as mass per unit volume
Mast cells	Cells which when cross-linked by antigen to IgE mediate an immune response. These cells produce histamine and cytokines
Methacholine	A cholinergic agent with actions similar to those of acetylcholine
Micrometre (μm)	A thousandth of a millimetre, also known as a micron
MMAD	Mass Median Aerodynamic Diameter. Term used to characterise the distribution of sizes of particles in an aerosol. MMAD is the size where half the mass of the cloud is contained in particles smaller than the stated aerodynamic diameter and half in larger particles
MMD	Mass Median Diameter. As for MMAD except that the diameter considered is the actual diameter rather than the aerodynamic diameter
MMEF	Maximal mid-expiratory flow
MMMFs	Man-made mineral fibres
MRAD	Minor restricted activity day
Multiple logistic methods	Regression modelling expressing, as a linear function of several explanatory variables, the log of the odds of occurrence of a binary outcome (eg, presence/absence of symptoms)
NEP	Neutral endopeptidase. An enzyme that modulates neuropeptidase activity by proteolytic activation
Neutrophils	Granular white blood cells with the properties of chemotaxis, adherence to immune complexes and phagocytosis: also produce antimicrobial substances including oxidants and proteases
NHANES	National Health and Nutrition Examination Survey (US)
nm (Nanometre)	A unit of linear measure equal to one-billionth of a metre, 10^{-9} metre
nmol	Nanomole, 10^{-9} mole. [A mole is the relative molecular mass in grams]
NO	Nitric oxide, properly called nitrogen monoxide
NO_2	Nitrogen dioxide
NO_3	Nitrate
Non-parametric methods	Statistical methods not involving assumptions regarding the distribution of the data
NO_x	Total oxides of nitrogen. Conventionally the mixture of NO and NO_2 in the atmosphere
Number concentration	The concentration of particles in air expressed as number of particles per unit volume
Number median diameter (NMD)	Term used to characterise the distribution of sizes of particles in an aerosol: that size where half the total number of particles are of diameter greater and half of diameter less than NMD. Count Medium Diameter (CMD) has the same meaning as NMD
O_3	Ozone
PAHs	Polycyclic aromatic hydrocarbons
Phenols	A generic term for any organic compound containing one or more hydroxyl (OH) groups attached to an aromatic ring
PMNs	Polymorphonuclear neutrophil leukocytes (see neutrophils)
PM_{10}	Particulate matter less than 10 μm aerodynamic diameter (or, more strictly, particles which pass through a size selective inlet with a 50% efficiency cut-off at 10 μm aerodynamic diameter).
$PM_{2.5}$	As with PM_{10} but with 2.5 μm as the cut-off point

Poisson regression analysis	With data expressed as counts, regression modelling where the log of the mean is a linear function of explanatory variables; and the data follow a Poisson distribution
ppb	Parts per billion
ppm	Parts per million
Quinone	Any benzene derivative in which two hydrogen atoms are replaced by two oxygen atoms
RADs	Restricted activity days
Relative humidity (RH)	Actual vapour pressure expressed as a percentage of the saturated vapour pressure. A measure of the degree of saturation of the air with water vapour
Respirable particles	Particles which can penetrate to the deep unciliated regions of the lung
RR	Relative risk: the ratio of the incidence or prevalence in two groups
SE	Standard error
Secondary particle or aerosol	Particles may be formed when two volatile and non-condensible vapour species react to give rise to a product with a very low vapour pressure. Such a product is described as a secondary particle to distinguish it from those arising from the reactions of liquids or solids
Sensitivity analysis	In regression modelling, analysis designed to check how the results may vary with different underlying model assumptions
sGaw	Specific airways conductance. The reciprocal of sRaw [cm. H_2O-1.sec^{-1}]
Smog	A term used to describe a mixture of smoke and fog. Also used to describe photochemical air pollution
SO_2	Sulphur dioxide
SO_4	Sulphate
SO_x	Oxides of sulphur
Spirometry	Measurement of the various subdivisions of lung volume and rates of flow
SPM (Suspended particulate matter)	A general term embracing all airborne particles small enough to remain in suspension for some hours or days
Summertime haze	Atmospheric haze produced during photochemical episodes: comprises secondary aerosols
TEOM	Tapered Element Oscillating Microbalance, an instrument for the continuous measurement of suspended particulate matter in air
Thoracic particle mass	Describes that fraction of the particles which penetrates beyond the nasopharynx and larynx
Time-series studies	Studies of health of defined populations over a specified period of time
TSP (Total Suspended Particulate)	The gravimetrically determined mass loading of airborne particles. Most commonly associated with use of the US high volume air sampler in which particles are collected on a filter for weighing
Ultrafine particles	Particles of less than 50 nm diameter
URT	Upper respiratory tract
$\dot{V}max$	Maximum expiratory flow rate
VOCs	Volatile organic compounds of low molecular weight
WHO	World Health Organization

Concentration Units and Conversion Factors

Concentrations of air pollutants are expressed in two ways, either as the mass of pollutant in a given volume of air (usually expressed as micrograms per cubic metre or $\mu g/m^3$) or as the ratio of the volume of the gaseous pollutant (expressed as if pure) to the volume of air in which the pollutant is contained (usually expressed as a volume mixing ratio or parts per million, ppm, or parts per billion, ppb).

The mass concentration as expressed above will be dependent on the ambient temperature and pressure and ideally these should be specified each time a concentration is measured as a mass/volume. The variation is discussed below and although not large may not be negligible where large variations in temperature and pressure occur.

The volume mixing ratio is independent of temperature and pressure, if ideal gas behaviour is assumed.

The relationship between the two sets of units can be expressed as follows:

$$\mu g/m^3 = ppb \times \frac{molecular\ weight}{molecular\ volume}$$

where:

$$molecular\ volume = 22.41 \times \frac{T}{273} \times \frac{1013}{P}$$

where T is the ambient temperature (°K) and P in the atmospheric pressure (in millibars). Conversion factors for some common gaseous pollutants are given in the Table below for 20°C and 0°C and 1013 mb pressure. Pollutants which are present in particulate form in the atmosphere such as sulphates are normally only expressed in mass/volume units.

Pollutant	Molecular weight	To convert			
		ppb to $\mu g/m^3$		$\mu g/m^3$ to ppb	
		0°C	20°C	0°C	20°C
NO_2	46	2.05	1.91	0.49	0.52
NO	30	1.34	1.25	0.75	0.80
HNO_3	63	2.81	2.62	0.36	0.38
O_3	48	2.14	2.00	0.47	0.50
SO_2	64	2.86	2.66	0.35	0.38
CO†	28	1.25	1.16	0.80	0.86

* ie, to convert ppb of SO_2 at 0°C to $\mu g/m^3$ multiply by 2.86

†for CO the factors apply to the more commonly used conversions of ppm and mg/m^3

Appendix 3

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Appendix 4

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