Altounyan address

Air pollution: brown skies research

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It is an honour and a pleasure to give the Altounyan lecture in memory of Roger Altounyan, a pioneer of clinical studies of airway pharmacology. My topic may seem some way from clinical pharmacology, but I think not. The principles behind studying the effects of a pollutant on lung function, in the laboratory at least, are very comparable to those involved in studying the effects of a drug, although somewhat more difficult in practice.

I had other reasons for choosing to talk about air pollution. It seemed appropriate as Roger Altounyan lived in Manchester which is where I spent my childhood and experienced first hand the famous smogs of the 1950s. Also, as a member of a Department of Health advisory group on medical aspects of air pollution episodes (MAAPE) for the last four years it seemed a suitable time to try to pull some of my thoughts together, and many of the data in this article are taken from the four MAAPE reports.[1-4] I have plagiarised freely from the contributions from my colleagues to these reports and gratefully acknowledge this. Finally, there is considerable public interest in the effects of air pollution at the moment and it is important that these are placed in proportion. We have an obligation to the public and to patients neither to overstate nor understate the magnitude of the health effects from air pollution as far as we are in a position to do so. It is also important that money for research should be directed to where it is most likely to be used effectively and successfully.

My aims are to try to give a broad overview of what is happening to ambient pollution levels in the UK and what is known about their health effects, concentrating on the acute effects of air pollution episodes. I shall also discuss the factors that help to determine the advice we should give to patients with chest disease during episodes of air pollution. I shall not discuss to any extent many aspects of air pollution including indoor air pollution, possible carcinogenic effects of air pollutants, animal studies, or mechanisms.
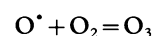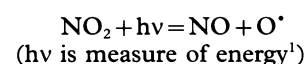
Background

What is air pollution? The common usage of pollutant as shorthand for anything other than oxygen and nitrogen in air somewhat prejudges the issue, since it is not axiomatic that everything we breathe other than oxygen and nitrogen is harmful. One sensible though rather wordy definition is "the contamination of outdoor or indoor air by one or more natural or man made substances in such a way that the air becomes less acceptable for its intended use to maintain health". The "potential" pollutant gases for which there is most information are ozone (O_3), sulphur dioxide (SO_2), and oxides of nitrogen (NO_x), with some data now on acid aerosols and particles, the small particles that can get into the lung and which are usually characterised by their size (for example, PM_{10}, $PM_{2.5}$, etc indicating particles with an aerodynamic diameter of less than 10 and 2·5 μm, respectively).

The effects of polluted air clearly depend on the pollutants it contains and there is no reason to think that the effects of polluted air in mid summer in Los Angeles would be the same as those of polluted air in Sheffield in winter. Different gases such as ozone and SO_2 are likely to have different effects, and the same may be true of particles. The extent to which the effects of particles depend on the nature of the substance forming the particles (which may be organic, inorganic, metal, etc) or generic factors such as particle size and inhaled burden is uncertain at present. It seems likely that their effect will be affected by their chemical composition, to some extent at least, but more data are needed.

The main sources of ambient pollutants are from vehicle exhausts, domestic heating, industrial sources, and background contamination – for example, SO_2 from volcanoes, ozone from the stratosphere. The relative contribution of pollutants from these different sources has changed over the last 20–30 years with an increased contribution from car exhausts and a reduced contribution from industrial sources and domestic heating. For example, emission of oxides of nitrogen from power stations fell by 14% between 1981 and 1991 whilst those from motor vehicles increased by 73%.

Car exhausts release oxides of nitrogen which largely remain as oxides of nitrogen in the winter. In the presence of sunlight in summer, however, they are converted to ozone[13]:

$$NO_2 + h\nu = NO + O^{\bullet}$$
(hν is measure of energy[1])

$$O^{\bullet} + O_2 = O_3$$

The situation in summer is further complicated

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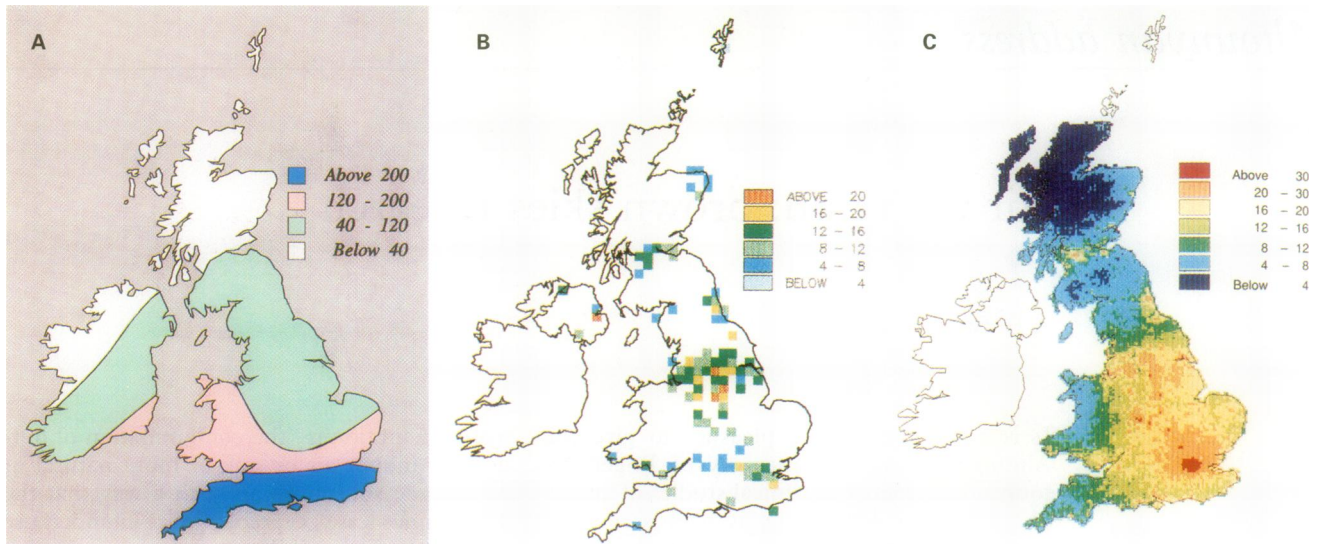NG5 1PB, UK
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Figure 1   Geographical distribution of (A) ozone, (B) SO$_2$, and (C) NO$_2$ in the United Kingdom. Map A shows the number of hours that ozone levels exceeded 80 ppb; maps B and C show annual mean urban/suburban SO$_2$ concentrations and mean NO$_2$ concentrations (from diffusion tubes), both in ppb. The pollutants related to vehicle exhausts (ozone and NO$_2$) are higher in the south of England. Reproduced from MAAPE[1-3] with permission.

by the fact that, close to busy traffic, ozone is also removed by nitric oxide (NO) from car exhausts with the production of NO$_2$:

$$NO + O_3 = NO_2 + O_2$$
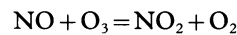
NO$_2$ is also formed from the interaction of NO with peroxy radicals (RO$_2$) which form in the presence of hydrocarbons:

$$NO + RO_2 \rightarrow NO_2 + RO$$
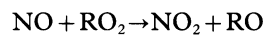
Thus, NO$_2$ produced in urban areas drifts away to rural areas with ozone forming in the air masses en route; as a consequence ozone concentrations in the UK are usually higher in rural areas.[1]

Air pollution episodes in the UK can be broadly divided into three types[4]:

1. Summer smogs characterised by high levels of ozone and sometimes NO$_2$. Ozone accumulates in hot anticyclonic weather and concentrations are usually higher in the afternoon and early evening.
2. Vehicle smog episodes characterised by high levels of NO$_2$ and often with an increase in carbon monoxide and particles. Such episodes usually occur when the weather is stable and still, as in the 1991 December episode in London.
3. Winter smog episodes characterised by high levels of SO$_2$ and often associated with vehicle pollutants (PM$_{10}$, CO, and NO$_2$). They occur in urban areas under stable weather conditions, particularly where coal is still used for domestic heating.

Information on the composition of polluted air in the UK has been very limited until recently and, indeed, is still fairly sparse for anything other than ozone, oxides of nitrogen, and SO$_2$. Measurements of ozone in the past were very largely confined to rural areas since they were the responsibility of the Department of the Environment who were concerned with the effects of pollutants on vegetation. Smoke

and SO$_2$ have been measured in urban areas for more than 40 years. Since both ozone and NO$_2$ relate to traffic, ambient concentrations tend to be higher in the south of England (fig 1). In addition, precursors of ozone drift from Europe to southern England under certain weather conditions, also contributing to ozone levels. The Midlands has high SO$_2$ production from power stations but, since ambient concentrations close to the ground are influenced more strongly by domestic heating, the highest concentrations of SO$_2$ in the UK are seen in Belfast where there is no natural gas, and coal and smokeless fuel are still used for domestic heating.

The changes in ambient concentrations of ozone, SO$_2$, and NO$_2$ in London over the last 20 years are shown in fig 2 and expressed as the number of occasions that levels exceeded 50 ppb for eight hours and 125 and 100 ppb for one hour[4] (measures of pollution can be expressed in various ways but the message is roughly the same). Ozone exceedences vary enormously from year to year but, if anything, are falling in urban areas and increasing slightly in rural areas. SO$_2$ levels have fallen dramatically since the 1970s, as has black smoke. There may have been a small rise in ambient levels of oxides of nitrogen though data are limited. NO$_2$ levels may be higher indoors if there is a gas or paraffin cooker or room heaters using bottled gas, whereas SO$_2$ and ozone concentrations are lower indoors.

Assessing the health effects of air pollution

Several approaches are used to determine the health effects of air pollution and air pollutants including animal studies and studies in vitro which I will not discuss further (but are well covered in the MAAPE reports). The main methods available to study human exposure include chamber studies and epidemiological studies.
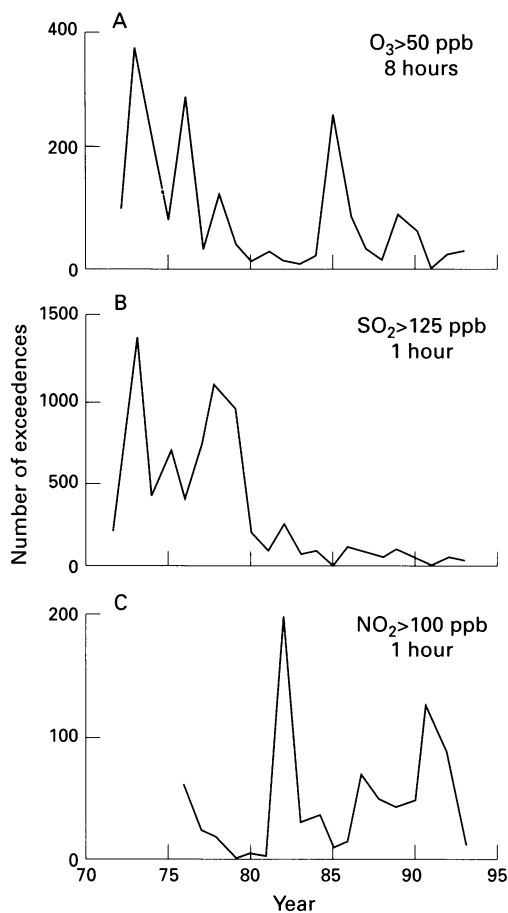
Figure 2 Data from Central London showing the number of occasions in which concentrations of (A) ozone, (B) SO₂, and (C) NO₂ have exceeded 50, 125, and 100 ppb for eight, one, and one hours, respectively. These figures represent the air quality standard for ozone and the levels for SO₂ and NO₂ when air quality moves from the good to the poor band. Since pollution episodes often last several days, one episode may account for a large number of exceedances. Reproduced from MAAPE⁴ with permission.

Figure 3 Percentage change from baseline in (A) forced vital capacity (FVC) and (B) forced expiratory volume in one second (FEV₁) in 64 healthy men exposed to ozone 350 ppb for 2·25 hours. The histogram shows the wide range of response between healthy subjects. Reproduced from Weinmann et al⁵ with permission.

CHAMBER STUDIES

In chamber studies subjects are exposed to a known concentration of pollutant(s) such as ozone, SO_2, and NO_2 for a given period of time; they are the main method by which the acute effect of a single pollutant can be studied in isolation.

Ozone

Subjects have inhaled different concentrations of ozone for up to six hours, usually with intermittent exercise. The main findings are:

1. Ozone causes cough, breathlessness, and pain on inspiration and a restrictive ventilatory defect rather than bronchoconstriction – that is, an inability to inhale fully to total lung capacity (fig 3).⁵ (This is in keeping with the fact that the main pathological changes appear to occur at bronchiolar level in animal studies.) Athletic performance is reduced with high concentrations of ozone.

2. The effects of ozone are strongly related to the concentration of ozone inhaled, the duration of exposure, and minute ventilation during exposure; the response is therefore markedly increased by exercise.
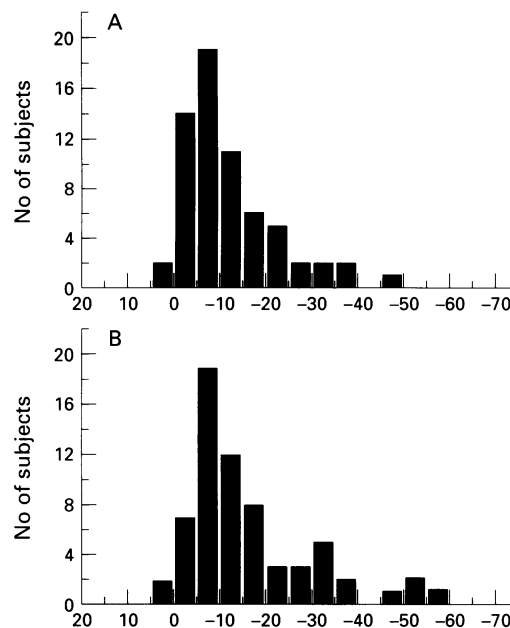
The effect on lung function wears off over 12–24 hours.

3. The response to ozone shows large inter-subject variability, the basis of which is not understood. In most studies asthmatic subjects have not been more sensitive to ozone than non-asthmatic subjects. Exposure has usually been associated with a small increase in bronchial responsiveness (on average around one doubling dose of histamine or methacholine), but this again has been broadly similar in asthmatic and non-asthmatic subjects.

4. The response to ozone shows tolerance in that exposure to the same concentration of ozone on five successive days causes a maximum effect on the first or second day with the effect becoming negligible by day 5.⁶

A retrospective analysis by Hazucha⁷ of data from 24 studies covering 200 subjects who had exercised for two hours whilst inhaling ozone shows very clearly the extent to which exercise affects the response to ozone (fig 4). When healthy subjects exercised for six hours the airway response was even greater – a mean fall in forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) of 10% after breathing 70 ppb ozone for six hours with heavy exercise.⁸ To put these findings in perspective, ozone levels in the UK are usually below 60 ppb but exceed 100 ppb during some photochemical pollution episodes (the highest hourly average since the National Ozone Network was established is 160 ppb at Lullington Heath although 258 ppb was recorded at Harwell in 1976). The highest level in 1995 was 128 ppb on the south coast.
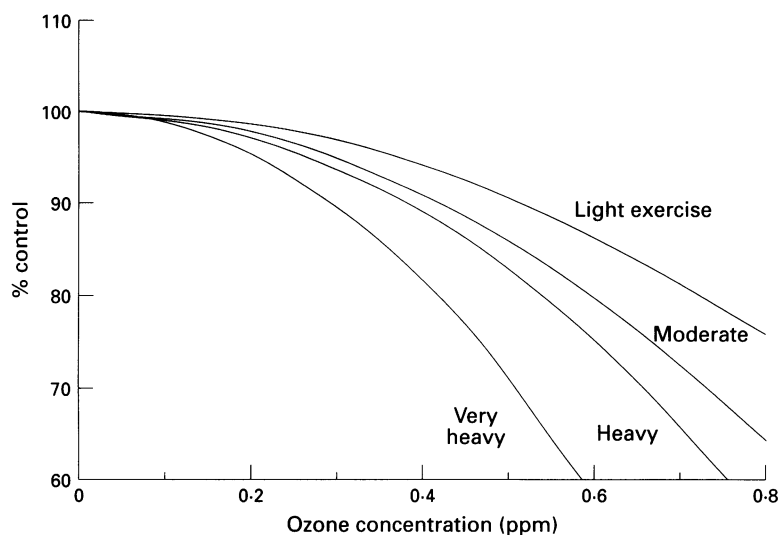
Figure 4 Analysis of change in forced expiratory volume in one second (FEV₁) in relation to ozone concentration and exercise intensity. The regression curves were obtained from a retrospective analysis of published data from 24 studies covering 200 subjects who had inhaled ozone for two hours. Reproduced from Hazucha with permission.[7]
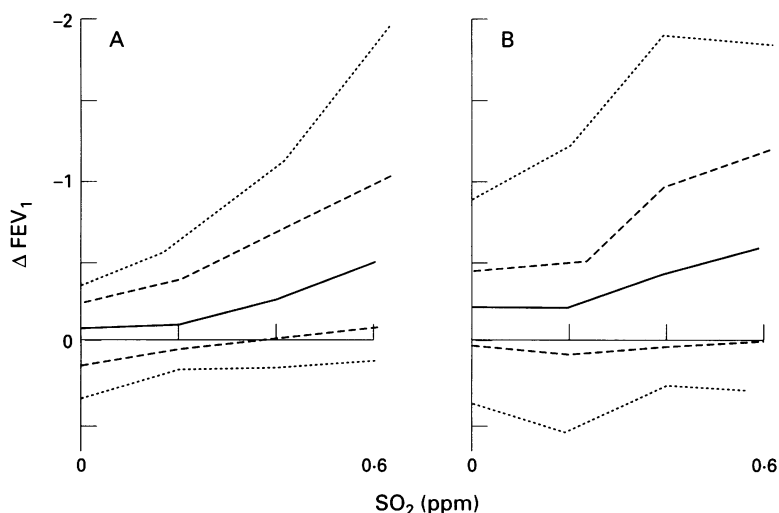

Figure 5 Mean (———) ± 1 SD (- - - -) change in forced expiratory volume in one second (FEV₁) in patients with (A) moderate and (B) severe asthma following inhalation of increasing concentrations of SO₂ up to 0·6 ppm. Data for the most sensitive patient are also given (····). Modified from Linn et al[10] with permission.

SO₂ and sulphuric acid

In contrast to ozone, patients with asthma are considerably more sensitive to SO_2 than healthy subjects who show little response to SO_2 concentrations below 1000 ppb.[2] In one study half the asthmatic patients showed a doubling in specific airway resistance in response to 750 ppb SO_2 or less,[9] and some asthmatic patients bronchoconstrict to concentrations around 200 ppb or possibly less.[2] The response to SO_2 occurs rapidly, seems not to increase with increased duration of exposure and, indeed, may show tolerance with prolonged exposure.[2] It is inhibited by β agonists.

There is considerable variation in SO_2 responsiveness between asthmatic subjects with some showing a fall in FEV_1 of about one litre with the levels of SO_2 that are seen from time to time in Belfast (500–600 ppb). The range of change in FEV_1 with increasing doses of SO_2

in asthmatic subjects studied by Linn et al[10] is shown in fig 5.

A few chamber studies have looked at the response to sulphuric acid.[2] Most recent studies have shown no change in lung function in normal subjects following inhalation of sulphuric acid at concentrations up to 1500 µg/m³ and in asthmatic patients up to 3000 µg/m³, but there are considerable differences between studies and some have shown changes at much lower concentrations, as low as 100 µg/m³ in one study. Some studies have also shown a small increase in bronchial responsiveness.[2] The variable response to sulphuric acid may be due to methodological factors including differences in osmolarity of the aerosol and wide intersubject variation in oral ammonia which neutralises acid. Data on ambient concentrations of sulphuric acid in the UK are sparse but maximum levels are thought to be below 30 µg/m³.

Oxides of nitrogen

There has been particular interest in the effect of oxides of nitrogen since this is most closely related to vehicle exhausts. Chamber studies have been carried out at concentrations of NO_2 ranging from 100 to 7000 ppb.[3] In healthy subjects there is no convincing evidence of a change in lung function at concentrations below 2500 ppb, although concentrations above 1000 ppb have usually caused a small increase in bronchial reactivity. Patients with asthma have rarely shown any change in lung function at concentrations below 4000 ppb, although more studies have shown an increase in bronchial reactivity (roughly a third of all studies) and in one study this occurred at a concentration of only 100 ppb.[11] The analysis of this study has been criticised and several groups have failed to reproduce the findings. Indeed, more recent studies have shown no increase in bronchial reactivity at concentrations up to 3000 ppb.[12] This large variation and lack of a dose response relation is curious and suggests that difference in methodology combined with a relatively small number of subjects in many studies may be responsible. It is interesting that the studies that showed an increase in bronchial responsiveness were, in general, those that did not involve exercise and used histamine or methacholine to assess bronchial reactivity rather than an indirect challenge such as exercise or distilled water. Exercise therefore appears to attenuate rather than enhance the effect of NO_2, in contrast to its effect on ozone and SO_2. Overall, these data suggest that, for short term exposure at least, concentrations of NO_2 below 4000 ppb are unlikely to be associated with anything other than a small change in bronchial responsiveness. During the 1991 pollution episode in London the maximum hourly NO_2 concentrations reached 423 ppb.[4]

Despite the great interest in endogenous NO, formal studies looking at the effect of inhaling NO are limited and the findings are conflicting.[3] High concentrations have been associated with a small fall in oxygen saturation.

Effect of pollutants on bronchial inflammation

Recent studies have focused on the effects of inhalation of specific pollutants on changes in cell composition or activity and release of inflammatory markers in nasal and broncho-alveolar lavage (BAL) fluid or bronchial biopsy samples and these have been reviewed.[13] A large number of end points have been measured in the different studies and the concentration of pollutants inhaled has often been high. In broad terms, ozone at ambient concentrations has been shown to cause a neutrophilia[14] and an increase in various mediators associated with inflammation, and very high concentrations of SO_2 have also caused an increase in inflammatory cells (lymphocytes, mast cells, and macrophages). Exposure to NO_2 has caused less consistent evidence of inflammation though lipid peroxidation products have been increased, presumably as a result of its oxidant activity; it may modify the immunological response in the lung but the results to date are inconsistent.

Interactions between pollutants and between pollutants and antigen

Since pollutants are rarely breathed in isolation the effect of interactions between pollutants is important though difficult to study because of the large number of possible permutations of pollutants, concentrations, and exposure times, and whether they are inhaled in combination or sequentially. Because of their diverse nature, the possible permutations are considerably greater if particles are considered. By analogy with pharmacological studies, interactions can be described as additive, antagonistic, or synergistic. Several studies have shown an additive effect between two pollutants but none has convincingly shown synergism or potentiation. Nitric acid fog *reduced* the subsequent response to ozone when compared with clean air, an effect which appears to be due to fog, however, rather than the nitric acid.[15]

Some recent studies have looked at the effect of exposure to pollutants on the response to antigen challenge. This is particularly important with respect to ozone since both are increased in summer and will often be increased together. The response to allergen was greater after exposure to ozone 120 ppb for one hour in six of seven asthmatic subjects studied by Molfino *et al* in 1991.[16] This study was small but the findings have been confirmed in a larger study by Jörres *et al*[17] in patients with asthma and rhinitis exposed to 250 ppb ozone for three hours. A recent study in 10 subjects with asthma has shown a small increase of 4% and 5% in the early and late response to antigen following exposure to NO_2 at 400 ppb for one hour,[18] although a further study also in 10 subjects with asthma failed to show any significant change in the early response to antigen after six hours exposure to NO_2 (400 ppb) or SO_2 (200 ppb), though the combination caused a significant increase in the response to antigen.[19] Further studies on larger numbers of subjects are needed to clarify the interaction between pollution exposure and the response to antigen.

Limitations of chamber studies

Although chamber studies have the advantage of being able to study a single pollutant or a combination of pollutants in a standardised way, their limitations need to be recognised.

1. Early studies often contained a small number of subjects with variable control of drug treatment in patients and the analysis (particularly of bronchial reactivity) was not always appropriate. Many recent studies have rectified these problems and have included a large number of subjects and the findings are consequently more convincing.
2. There is clearly a limit to how many hours and how many days subjects are prepared to spend in a chamber, and there may be a reluctance to involve patients with more severe disease or young children in such studies yet these are the groups where information is needed most.
3. The effects of SO_2 and ozone are increased when subjects exercise, but exercise itself causes bronchoconstriction in asthmatic subjects. Although the same amount of exercise is carried out in the control study, it adds another confounding factor when looking for relatively small signals.
4. Perhaps the major problem, however, is that the response in the chamber is likely to be influenced by long and short term variations in ambient exposure to pollutants prior to the study and this is very difficult to standardise. The airway response to breathing clean air in a chamber for two hours will presumably depend on whether the subject was exposed to high or low pollutant levels in the days before the study.
5. Finally, of course, chamber studies only tell us about the pollutants we study in the chamber and not what happens in real life with the mixture of pollutants present in ambient air. Particles have rarely been studied in chamber experiments and they present particular problems methodologically because of the enormous possible permutations of size and content. They may be the most important constituent of polluted air, however, as far as health is concerned.

EPIDEMIOLOGICAL STUDIES

Epidemiological studies take a variety of forms but can broadly be divided into studies of specific air pollution episodes, studies of trends over time (panel studies or time trend series analyses), or comparisons of areas with different pollution profiles (spatial analyses). For some pollutants such as NO_2 there are also some studies of accidental exposure in the workplace or elsewhere. In this review it is only possible to give a flavour of the findings from the large number of studies in this area, including recent studies from the UK, with some broad generalisations.
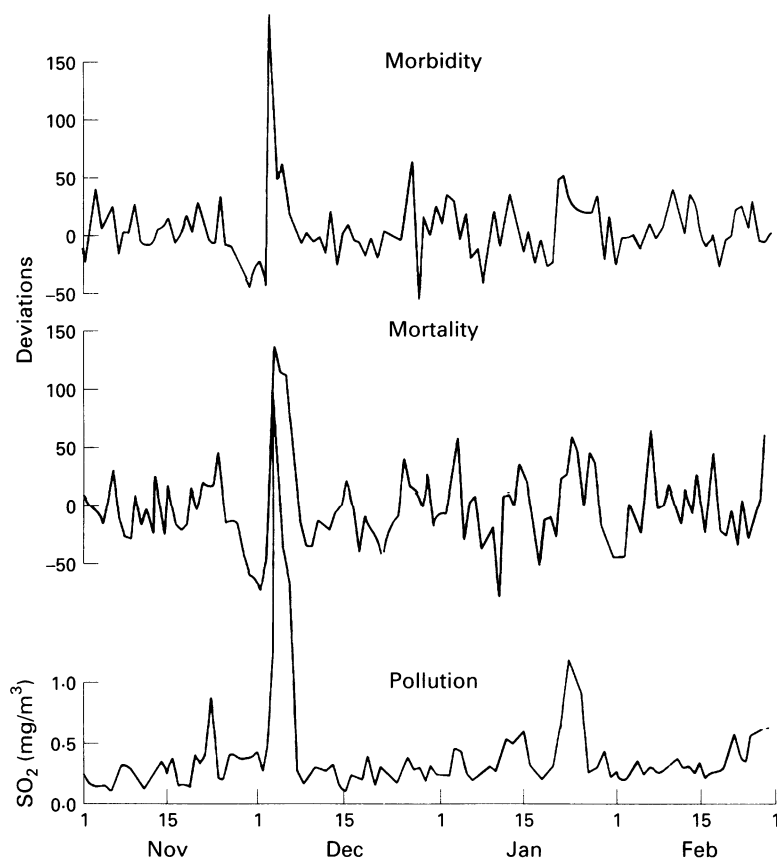
Figure 6   Changes in morbidity (emergency admissions to hospital) and mortality in relation to change in ambient SO_2 in London in the winter of 1962–3. Mortality and morbidity are expressed as percentage deviation from 15 day moving averages. Reproduced from Waller[23] with permission.

The advantage of epidemiological studies is that they are clearly relevant to actual health effects in the area studied. When an adverse effect is seen it may be difficult to determine which pollutant is responsible and hence to know which public health measures should be introduced to reduce the effect. Confounding by other factors such as temperature is also a major potential problem and one that could cause the effects of air pollution or a particular pollutant to be either underestimated or overestimated. Many studies have taken a large number of measurements and carried out a large number of statistical tests to find one or two that are significant. The extent to which this is analogous to data dredging in pharmacological studies is difficult to determine; consistency of findings between studies is necessary for effects to be accepted with confidence.

Accidental exposures

The main source of information on accidental exposure to NO_2 is from accidents involving silage where concentrations can exceed 100 000 ppb.[20] Severe exposure causes acute pulmonary oedema and death, whilst less severe exposure can cause pneumonitis, bronchiolitis obliterans, and delayed death from respiratory failure. The precise concentration at which these effects occur is uncertain because of the nature of the exposure. When Apollo astro-

nauts were accidentally exposed to around 250 000 ppb NO_2 for four minutes they developed some chest symptoms and pneumonitis with evidence of increased collagen breakdown, but made a complete recovery.[21] Ice hockey players and spectators have also been exposed to high concentrations of NO_2 when ice resurfacing machines have been defective; in one study exposure to over 4000 ppb NO_2 caused cough, breathlessness, or chest pain in a third of those exposed.[22]

Air pollution episodes

In the 1950s and 1960s there was a very clear relation between air pollution episodes in the UK and both mortality and morbidity.[2] The 1952 episode, for example, was associated with an excess of some 4000 deaths in greater London alone; most of the deaths occurred in those aged over 65 and the majority were due to cardiorespiratory disease. During that episode mean concentrations of black smoke and SO_2 were 2650 μg/m^3 and 441 ppb, respectively.[4]

Since the introduction of the Clean Air Acts in 1956 and 1968 the number of deaths with each smog episode has declined and 1962 was the last of the old type of smog episodes in which an association with an increase in mortality was reported (fig 6).[23] The health effects of air pollution episodes since then have been very much smaller and separating the signal from the noise in such studies requires considerable epidemiological and statistical expertise. Most of the more recent studies have come from the USA and the rest of Europe. The analysis of the 1991 winter fog episode by Anderson *et al* in a recent issue of *Thorax* is the first recent attempt to look at the health effects of a major pollution episode in the UK.[24] The episode, which was largely confined to London, caused high levels of NO_2 (maximum hourly average 423 ppb) and black smoke (148 μg/m^3) with a smaller increase in SO_2.[24 25] The analysis is complex but suggests that there was an increase in mortality and some measures of morbidity in London during the episode, with the population at risk again appearing to be older subjects and those with chronic cardiorespiratory problems. Confounding by the prevalent cold weather or a coincident cause such as a respiratory virus epidemic can never be excluded entirely when considering increased mortality and morbidity in a single episode. A causal relation to air pollution is plausible, however, with particles being perhaps the most likely culprit since the magnitude of the effect is close to that predicted from studies on particles in the USA.

An opportunistic approach to assessing the effect of an acute pollution episode can sometimes be taken when an episode occurs during the course of a study; when this has occurred it has usually been associated with a small reduction in lung function.[4]

Time trend studies

Time trend studies include panel studies in which individuals – often those considered to be at risk such as patients with asthma – monitor

events such as symptoms or peak flow rate and these are then related to ambient pollutant concentrations. The alternative approach is to study the relation between disease indices such as hospital admissions and ambient pollutant concentrations in a particular area.

Summer camp studies in the USA have been used to assess the effect of summer smog and ozone on lung function in children.[1] The camps are often held in areas where ozone levels are high and, as children run around a great deal, their exposure to ozone is high. Studies relating daily peak flow to ozone concentrations have in general shown a fall in peak flow as ozone concentrations increase. The average fall in peak expiratory flow is 77 ml for a 100 ppb increase in ozone concentrations,[1] although there are large intersubject differences. It is not possible from these studies alone to say how much of the effect is due to ozone per se rather than to other pollutants such as NO_2 and acidic aerosols which often track with ozone, and this probably varies with different locations. Chamber studies suggest that ozone has a greater effect than NO_2 or SO_2; however, the magnitude of effect in the summer camp studies has often been greater than that expected from ozone alone on the basis of chamber study data[1] although this was not the case in one study.[26]

Other time series studies have shown an inverse relation between lung function and other pollutants, particularly particles. Pope and Dockery[27] found an increase in cough and a fall in peak expiratory flow in association with an increase in PM_{10} in both symptomatic and, to a lesser extent, asymptomatic school-children, and several studies have shown an increase, albeit small, in hospital admissions in association with PM_{10} and, to a lesser extent, with ozone at concentrations within current guidelines.[28] An increase in particles has been associated with an increase in cardiorespiratory mortality in several studies, and Schwartz[29] found a relative risk of 1·06 for a 100 µg/m³ increase in total suspended particles when the results were subjected to meta analysis.[29] He argued that the effect was due to particles and not to confounding as the risk was consistent between cities with different pollution and weather profiles. The reason for the increase in cardiac deaths in relation to particles is uncertain; Seaton *et al*[30] suggested that ultrafine particles are absorbed into the lung interstitium where they cause inflammation and release of mediators, thereby increasing blood coagulability and predisposing individuals to cardiac events.

Two recent studies have looked at the effect of pollutant levels on health in the UK. A small increase in hospital admissions for respiratory disease in 1988–90 was seen in Birmingham in relation to ambient SO_2 and black smoke levels, although only a small part of the increase was due to asthma.[31] Interpretation is difficult as an influenza epidemic occurred during one of the winters. In a panel study of 75 subjects with asthma living in north west England Higgins *et al*[32] found impaired asthma control in association with increased levels of SO_2 and ozone. Although the findings in both studies were small, the effects were seen at levels of SO_2 and ozone below current guidelines.

Geographical studies
Chronic rather than acute health effects of air pollution can be studied by comparing health indices including mortality between cities or areas with different levels of air pollution as in the six cities study in the USA.[33] The conclusions are critically dependent on adequate allowance for different confounding factors, particularly those related to occupation and social class. Having used complex statistical analyses to correct for confounding, several recent studies conclude that exposure to particles and PM_{10} concentrations are related to mortality and other health indices.[4 33] The effects were best related to small particles ($PM_{2.5}$ and sulphates).

Although there is considerable variation in the findings between studies and, to some extent, between the different epidemiological approaches, there has been reasonable consistency in recent studies in finding a relation between particles and various health indices. The studies have been carefully reviewed in a recent report which concludes that the relation is probably causal and the findings from the USA and elsewhere are probably applicable to the UK.[34]

Air pollution and asthma
There is considerable interest in the relation between air pollution and asthma and a detailed report has just been published.[35] Two questions are important: firstly, whether the recent increase in asthma prevalence is related to atmospheric pollution, and secondly, whether established asthma is made worse by air pollution episodes.

The weight of evidence argues against a causal relationship between air pollution and the initiation of asthma. Asthma prevalence has increased over the last 20 years whilst levels of SO_2 and black smoke have fallen considerably. Recent studies comparing cities in East and West Germany have found that children in East Germany – where levels of SO_2 and black smoke were much higher and still are to some extent – have more bronchitic symptoms and higher total IgE levels but less evidence of atopy; they have fewer positive skin tests and less seasonal rhinitis and apparent asthma, although bronchial responsiveness is similar.[36 37] Comparisons between other cities in Western and Eastern Europe have given broadly similar results.[38] These data do not exclude a role for vehicle exhaust pollutants in increasing the incidence of asthma in Western Europe, and there are some data to suggest that children living near roads are more likely to wheeze.[39] Whether this is due to traffic or confounding factors is difficult to disentangle. The fact that the prevalence of asthma is not higher in urban than in rural areas, or in people occupationally exposed to traffic such as traffic police,[40] suggests that confounding factors may be relevant.

Asthma prevalence is high in New Zealand and Australia[41] where pollution levels are generally low, and the highest reported prevalence of asthma in children in the UK is on the Isle of Skye.[42] Taken together, these data argue against pollution (including vehicle related pollution) being an important initiator of asthma.

As far as the second question is concerned, there are several reasons why air pollution might make asthma worse. An asthmatic patient is likely to be more sensitive to air pollutants such as SO_2 (though not apparently to ozone or NO_2 to any great extent), pollutants may enhance the response to allergen, and the net effect of inhaling a pollutant may be greater because the subject has worse lung function initially. Some studies have shown an increase in morbidity or a fall in peak expiratory flow in asthmatic patients in relation to specific pollutants – for example, SO_2 in Birmingham[43] – whereas other studies are more reassuring. In the 1991 pollution episode in London most of the morbidity appeared to be due to cardio-respiratory disease in older patients rather than asthma in younger people. In general it is likely that some patients with asthma are made worse by certain types of pollution and, although the effect appears to be fairly small for the asthmatic population in general, it may be important for certain individuals.

Advice to the public and to patients

I would like finally to discuss the health advice that should be given to patients and the public during air pollution episodes (excluding advice about the production of pollutants which is outside the remit of this article). Information on air quality and the possible health consequences of air pollution episodes should be easily available. Advice has to take account of current uncertainties of the health effects of high pollution episodes as seen in the UK and the fact that, for the great majority of people, observed effects on health have been minimal with current levels of pollutants. If advice is to have health benefits the following criteria should be met:

1. *The pollution episode can be predicted ahead of time*: recent episodes in the UK have lasted a few days so people can be alerted at the start of an episode if not before it.
2. *Advice can be targeted at the groups at risk*: the groups identified as being at risk are patients with asthma and those with severe cardiorespiratory disease where any further decrement in lung or cardiac function could have serious consequences.
3. *Interventions are known to work for an individual*: since it is not usually possible to identify the patient with asthma or other lung diseases who is at particular risk during an air pollution episode, advice has to be tailored to patients with asthma and lung problems in general. The main interventions available are: (1) to advise patients to remain indoors and restrict exercise, or (2) to modify treatment. The effects of ozone and SO_2 on lung function should be less if subjects

rest and remain indoors where levels of ozone and SO_2 are lower, but whether restricting the activity of children or adults during an air pollution episode is feasible or beneficial in practice has not been studied. There is, in some respects, an inbuilt safety factor in that subjects most at risk have more severe lung disease, are less able to exercise, and will spend more time indoors. Unlike ozone and SO_2, the levels of NO_2 may be higher indoors than outside and the effects are not increased by exercise.

Increasing the dose of inhaled steroid and using a β agonist would probably reduce or reverse the adverse effects of pollution in patients with asthma. It has been suggested that all patients with asthma or chronic obstructive pulmonary disease should increase their preventative treatment during an air pollution episode but, since only a small proportion of subjects are affected, many would increase medication unnecessarily. Episodes of pollution are only one of many factors that can cause asthma to deteriorate and they are probably less important than some others such as exposure to allergens, viral infections, or thunderstorms. An alternative and, I believe, better approach is to treat air pollution episodes like any other trigger factor and encourage patients to adjust their inhaled medication according to symptoms and peak expiratory flow.

4. *The advice and/or intervention does not increase anxiety inappropriately or cause adverse effects in some subjects*: asthmatic children are strongly encouraged to participate in sport and normal activities as much as possible for both physical and psychological reasons. Suggesting that asthmatic children should restrict their activities on high pollution days could undermine this message and emphasise their difference from other children. Unless clear benefit is demonstrated with this approach, it seems better not to recommend restrictions unless the child is clearly worse on high pollution days.

So what advice should be given during air pollution episodes? Although lung function may fall in fit people who exercise when ozone levels are high, there is no evidence that healthy people are at risk during air pollution episodes and they can be reassured. Elderly patients with cardiorespiratory disease are probably most at risk, but the difficulty here is to know what intervention would be helpful. Most patients with asthma do not deteriorate during high pollution episodes (or a small effect is masked by increased treatment); some patients may deteriorate, however, whether due directly to pollutants or interactions with pollen or other factors such as temperature. On the present evidence it seems reasonable to say that, unless patients with asthma know they are worse during air pollution episodes, they do not need to alter their lifestyle; they should adjust their treatment according to symptoms and peak expiratory flow. Giving advice for children with brittle asthma who may wish to exercise is more

difficult and the pros and cons of limiting exercise and keeping children indoors need to be discussed with parents.

Conclusions

Direct information on the health effects of air pollution in humans relies mainly on chamber studies and epidemiological studies. Although chamber studies have limitations they allow the acute effects of individual pollutants to be studied in well characterised subjects under controlled conditions. Most chamber studies have shown relatively small falls in lung function and relatively small increases in bronchial reactivity at the concentrations of ozone, SO_2, and NO_2 that occur even during high pollution episodes in the UK. The possible exception is SO_2 where sensitive asthmatic patients may show a greater response at concentrations that are seen from time to time in certain areas and in proximity to power stations. There is no convincing evidence of potentiation between pollutants in chamber studies.

Epidemiological studies are more difficult to carry out and require considerable epidemiological and statistical expertise to deal with the main problem – confounding by other factors. Although the health effects seen with current levels of pollution are small compared with those seen in the 1950s and close to the limits of detection, this should not be interpreted as being unimportant. A small effect may have large consequences when the population exposed is large (the whole population in this case). Recent data suggest that particles have more important health effects than the pollutant gases that have been studied. Much of this information comes from the USA though the findings are probably applicable in the UK.[34] More information is needed on the size of the health effects that occur during the three types of air pollution episodes seen in this country and the relative contributions of particles, pollutant gases, pollen, and other factors such as temperature. Research into air pollution declined in the UK following the introduction of the Clean Air Acts; it is now increasing again following pressure from certain individuals and ginger groups, including the British Lung Foundation, and its potential importance is recognised by the Department of Health.

This article has concentrated on the acute effects of air pollution episodes, though the long term effects of acute episodes of air pollution and chronic high levels of pollutants is equally, if not more, important. Roger Altounyan had severe chest disease attributed to asthma and personal pollution (cigarette smoke). But did the smog episodes in Manchester in the 1950s or subsequent vehicle related pollution play a part and did they interact with the bronchial challenges he underwent over the years (estimated at 3000)?

Air pollution is a product of the way that society chooses to live. Obtaining an accurate picture of the extent to which current levels of air pollution cause acute and chronic effects on health is important if sensible choices are to be made by individuals and society about the processes contributing to air pollution. It is also important for patients with or at risk of developing cardiorespiratory disease.

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