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Adverse health impacts of air pollution – continuing problems

by David V Bates, MD

Evidence has been published that current levels of fine particulate pollution are associated with a wide range of adverse health outcomes, including accelerated mortality. Tropospheric ozone, often in association with aerosol sulfates, is similarly and independently associated with increased emergency visits and hospital admissions for acute respiratory disease, and there are sound reasons for suspecting that asthma may be worsened by exposure to it. Whether nitrogen dioxide is important at current levels in inducing adverse health effects is unclear. Although the combination of sulfur dioxide and particulate pollution that results from uncontrolled coal burning has been known for 30 years to be harmful, the independent role of sulfur dioxide cannot yet be precisely defined. A first report has appeared that ambient levels of volatile organic compounds may be associated with symptoms. Current efforts to assess the costs, in economic terms, of the adverse health effects attributable to air pollution are likely to be intensified.

I have called this review “Continuing Problems” because, after the industrialized nations had controlled the emissions from coal burning (and black smoke was no longer to be seen), there was a tendency to assume that the control of air pollution was a matter of little moment. Respected authorities indicated that there would be little benefit in further attempts to reduce air pollution, or that global carbon dioxide accumulation represented a far greater threat than anything in the troposphere.

Contemporary air pollution is complex; and the evidence of adverse health impacts is diverse and difficult to grasp. Nevertheless it is important that it be understood and that anyone responsible for urban planning should be aware of the limitations that air pollution may impose.

Diversity of health impacts

The demonstrated impacts of air pollution on health are diverse. They include (i) effects on daily mortality (excluding accidents and suicides), (ii) hospital admissions on a daily basis, (iii) hospital emergency visits on a daily basis, (iv) changes in lung function on a daily basis, (v) increased medication use for asthmatics, (vi) respiratory symptoms in children (daily diary entries), (vii) school and kindergarten absences, (viii) longitudinal survival data, (ix) development of asthma in longitudinal popula-

tion studies, and (x) cross-sectional comparisons of symptoms and lung function.

The interrelationships between these indices are seldom clear; but some aggregation is possible. Thus respiratory symptoms in children are likely to be related to school and kindergarten absences. Changes in lung function on a daily basis might be associated with both of these, as well as with hospital emergency visits. But it is less clear whether the pollutants that might be responsible for all of these should be expected to increase hospital admissions among the elderly. As I have pointed out elsewhere (1), it is to be expected that an impact of a pollutant on daily mortality would also produce an increase in hospital admissions, and it might also be associated with an increase in hospital emergency visits. In the sections that follow, an attempt is made to relate these different outcomes to specific air pollutants.

New methods of study

In the last few years, the study of air pollution and its effects has been transformed by the development of new methods of study. These have included (i) multiple logistic regression, (ii) automated questionnaire analysis, (iii) use of large data banks (outcome and exposure), (iv) time-series analyses (modeling), (v) refinement of exposure analysis, and (vi) neural network analysis. The first

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of these has permitted corrections to be applied for domes-
tic factors or for smoking; the second has permitted
extremely fast analysis of large numbers of question-
aire respondents on respiratory symptoms or personal factors; the
third has permitted analyses of very large data banks on
hospital admissions or emergency visits; the fourth,
which has been recently applied very successfully in
relation to daily mortality data, requires familiarity with
sophisticated computer applications; the fifth can involve
personal exposure measurements, or measurements in
the home in that it has come to be realized that improve-
ment in exposure data may greatly increase the power of
epidemiologic studies, and the sixth has, for the first
time, been applied to the analysis of data from a panel
study of asthmatics (2). Even this list is not exhaustive,
as data have recently been accumulated from autopsy
studies of lungs from a sample of young subjects who
died violently in Los Angeles (3).

Dimensions of the continuing problem

Particulates
The recent demonstration by time-series analyses that
particles less than 10 μm in size (PM<sub>10</sub>) are consistently
associated with daily mortality (excluding accidents and
suicides) has placed a severe strain on regulatory author-
ities. The phenomenon has been shown to apply to many
different locations in the United States, from Philadel-
phia in Pennsylvania to San Jose in California, but also
in Amsterdam and in Santiago, Chile, and in at least 16
other locations. Conferences have been held to discuss
the evolving data (4).

Dockery & Pope (5) in a useful summary of current
data, showed that PM<sub>10</sub> was associated with a wide range
of effects in addition to mortality, including hospital
admissions of children with respiratory disease, respira-
itory symptoms, school absences, changes in lung func-
tion, and increased medication use and hospital emerg-
cy visits among asthmatics. Schwartz, who originated
much of this work, has more recently shown that pneu-
monia admissions to hospitals in Detroit (6) cycle with
PM<sub>10</sub> levels. Burnett and his colleagues in Ontario (7)
have shown that aerosol sulfates are not only associated
with respiratory admissions [which had been found pre-
viously (8)], but that cardiovascular hospital admissions
are also affected. This is important additional informa-
tion as it underpins mortality studies, in which cardio-
vascular mortality is always elevated (9). Cardiovascular
deaths outnumber respiratory deaths by a factor of 20 or
so; hence although the effect of PM<sub>10</sub> on cardiovascular
mortality is less marked than on respiratory deaths, the
contribution of cardiovascular mortality to the statistical
power is considerable.

This avalanche of recent work has raised important
and currently unanswerable questions (4) about the
mechanism of action. Animal studies indicate that fine
particles are more toxic to animals than larger ones;
analyses of actual PM<sub>10</sub> particles indicate that the parti-
cles are associated with a wide variety of organic species
and that in some locations aerosol nitrates and sulfates
constitute a considerable fraction of the PM<sub>10</sub>; and the
smaller the particles, the closer the approximation of
indoor and outdoor concentrations of them (an observa-
tion that may be important in relation to a possible im-
 pact of outdoor particles on incapacitated people living
mostly or entirely indoors).

In all the locations that have been studied, automo-
 bile and combustion-generated particles dominate the air
pollution composition. In some locations, there is very
little industry; but in others (as in Provo, Utah, and
Steubenville, Ohio) a local industry such as a steel works
may be an important contributor to PM<sub>10</sub> values.

The consistency and coherence of the current data on
PM<sub>10</sub> leave little room for doubt that the association is
robust, independent of meteorological factors, and not
confounded by the presence of other species, such as
sulfur dioxide or ozone. All of these factors might have
influenced the results in one or another of the studies, but
it seems unlikely that all the reported studies could have
been influenced by them.

The problems of reducing or controlling PM<sub>10</sub> in a
modern city are formidable and have not yet been ad-
dressed in detail.

Photochemical smog: acid aerosols
The understanding of the chemistry of photochemical air
pollution has advanced considerably since its first de-
scription 40 years ago. Careful ozone monitoring in more
locations has revealed the extent of “ozone” episodes.
An ongoing research program on oxidants in the south-
ern part of the United States showed that in June 1990 in
one such episode, in which the highest ozone concen-
tration was centered on Atlanta, ozone at a concentration
greater than 80 ppb (160 μg · m<sup>-3</sup>) extended eastwards
and westwards for a total of a thousand miles.

As a result of two decades of controlled exposure
experimentation, a great deal is known about the acute
effects of ozone on normal subjects. A brief summary of
the knowledge would include the following observations:
(i) at concentrations of 80 ppb (160 μg · m<sup>-3</sup>) with heavy
exercise, ozone lowers the forced expiratory volume in
1 s (FEV<sub>1</sub>) after an hour or so, (ii) the first effect is on
forced vital capacity (FVC) caused by an inhibition of
maximal inspiration and probably instigated by the stim-
ulation of irritant receptors, (iii) the response falls with
consecutive daily exposures, (iv) among normal non-
smoking subjects, there is a wide range of response, but
the results are reproducible in the same individual, (v) ozone induces airway inflammation at low concentrations and the abnormal constituents of bronchial lavage fluid are still present 18 h after the exposure, (vi) there is no close relationship between the decrement in FEV$_{1.0}$ and the severity of the inflammatory response, (vii) prior ozone exposure increases the subsequent response to sulfur dioxide, (viii) ozone exposure increases airway responsiveness to histamine or methacholine in normal subjects, (ix) although the quantitative response (percentage decline) of asthmatics' FEV$_{1.0}$ after ozone exposure is not much different from that in nonasthmatics, it is often imposed on an already lowered value and the preexisting increased airway responsiveness is heightened still further, and (x) there is currently conflicting evidence as to whether acute ozone exposure increases the effect of a subsequent dose of allergen in asthmatics.

Epidemiologic studies have slowly yielded data that have elucidated the acute consequences of exposing the population to levels of ozone up to 120 ppb (240 μg · m$^{-3}$). Hospital emergency visits (in a medically unprotected population) for asthma are increased (10, 11), and hospital admissions for acute respiratory disease increase monotonically as the ozone level rises (12, 13), as illustrated in figure 1. Ozone and PM$_{10}$ are independently associated with increased admissions for pneumonia among the elderly (6); the same two pollutants are independently associated with lower respiratory symptoms in children (14); and medication use by asthmatic children in a summer camp was monotonically related to ozone levels (15). These results are hardly surprising in light of the ability of ozone to cause inflammation in the lung, and the modern understanding of asthma as essentially an inflammatory process (16).

The principal uncertainty in relation to photochemical air pollution is the consequence (or lack of it) of living in a high oxidant region. Long-term animal studies, particularly with primates (17), are not reassuring. One autopsy study has suggested that a respiratory bronchiolitis similar to that seen in ozone-exposed primates and in young cigarette smokers may be occurring in young adult humans (3). In one epidemiologic study, evidence was found that, for nonsmoking adults, living in higher oxidant regions was associated with an increased occurrence of newly acquired asthma (18). But in my opinion, at this time, all of this evidence was considered suggestive rather than definitive. No one can pretend it is reassuring.

A reduction in ozone levels is going to be difficult to achieve (19). Eliminating photochemical pollution with a large population that demands mobility will require a revolution in transportation. With so great an investment by powerful industries in the current infrastructure, one can predict that such a reduction will be a long time coming.

When ozone coexists with sulfur dioxide, its presence drives the reaction to sulfuric acid (20), and acid aerosols can be measured in the summer whenever the phenomenon occurs (21). A recent study concluded that these aerosols, unlike ozone and PM$_{10}$, were not related to acute respiratory symptoms in children (14). However, there is evidence that they may be influencing hospital admissions for acute respiratory disease (13).

**Oxides of nitrogen**

In some ways, nitrogen dioxide is the most difficult pollutant to assess because actual exposures may be more influenced by sources within the home than by outside levels, because the results of acute exposure studies have been conflicting (something that has not occurred in the case of ozone), and perhaps because it is uncertain what acute outcome should be measured since the gas is relatively insoluble and would probably impact distal rather than proximal airways. These are not reasons to ignore the pollutant, however, since dense traffic can produce transient high concentrations and evidence of acute health effects does exist. In one study (22), in which average weekly nitrogen dioxide exposures were monitored by Palms' tube detectors being pinned to clothing, an association was found between such exposures and the occurrence of respiratory symptoms in children. Samet (23) has shown convincingly that low levels of nitrogen dioxide in the home do not influence respiratory events in the first two years of life, but Neas' study (24), which also involved careful nitrogen dioxide measurements in the home, found an association with lower respiratory infections in the highest exposed group of schoolchildren. In this study, outdoor nitrogen dioxide levels were shown to be an important component of indoor exposure. It has recently been shown that prior exposure to nitro-
Sulfur dioxide

The levels of sulfur dioxide have been greatly reduced in the industrialized west, but they are still elevated in Eastern Europe and China, and transient high concentrations can be encountered in downdraft conditions close to any major emission source.

It is remarkable that it should still be difficult to decide exactly how important this pollutant is. When associated with severe particulate pollution due to open coal burning, it can be shown to be associated with adverse health effects. Holland & Reid’s 1965 data from Britain (30), which showed a reduced FEV$_{1,0}$ in more polluted regions, has an exact counterpart in modern Beijing, where the FEV$_{1,0}$ of nonsmoking women was predictable on the basis of the regional sulfur dioxide concentration (31). The Groupe Coopératif PAARC study in France showed the same result 20 years ago (32). Another study from Wuhan in contemporary China (33) found convincing evidence of FVC and FEV$_{1,2}$ decrements in children when those living in more-polluted areas were compared with children in cleaner regions. Yet the role of sulfur dioxide (except as a possible surrogate for sulfuric acid aerosol) in relation to mortality in acute episodes seems to be essentially subservient (or even irrelevant) when compared with that of particulates. And although there is no doubt that asthmatics are more sensitive to sulfur dioxide than nonasthmatics, comparisons between East and West Germany did not indicate higher prevalences of asthma in the Eastern regions where coal-burning pollution was much greater. In northern Bohemia, it has been shown that neonatal mortality is greater in the most polluted region (34).

The aforementioned Danish panel study found evidence of an influence of sulfur dioxide (together with nitrogen dioxide) on decrements of evening peak flow rates (2). In many other studies (35, 36), including my own in Vancouver (37), associations between adverse health outcomes and sulfur dioxide have been difficult to interpret, as the PM$_{10}$ cannot be excluded as a confounder. In Birmingham in England, Walters and his colleagues (38) showed that, in winter, sulfur dioxide and smoke were independently related to asthma admissions to hospitals, and smoke levels were also associated with all acute respiratory admissions. In this study, the daily mean smoke level was 12.7 µg · m$^{-3}$ and the corresponding sulfur dioxide concentration was 39.1 µg · m$^{-3}$ (13.65 ppb), the highest values being 188.3 µg · m$^{-3}$ for smoke and 126.3 µg · m$^{-3}$ for sulfur dioxide (44.2 ppb). These levels were within guidelines of the European Commission except for one day. Stepwise multiple regression models were used.

The SO$_2$ molecule (a constituent of PM$_{10}$) has been noted to be associated with increased hospital admissions in the summer in several studies (8, 12, 13). In the case of sulfur dioxide, animal studies are generally unhelpful — except perhaps for the indication that chronic mucus hypersecretion might be a consequence of exposure to high concentrations.

It seems that it is premature to conclude that sulfur dioxide emissions can be disregarded, and efforts must continuously be made to reduce the emissions of this pollutant.

Volatile organic compounds

Judging from the hearings before United States senate committees when the Clean Air Act amendments of 1990 were being discussed, public anxiety about exposure to these compounds runs far ahead of any definite evidence of ill effects. However, a recent study in the Kanawha Valley of West Virginia (39), where there is a high aggregation of chemical manufacturing plants, produced the first evidence from daily diary data showing that ambient exposures to volatile organic compounds were associated with increased upper and lower airway symptoms and headache, sensory irritation, and skin rashes. Petroleum-related volatile organic compounds (toluene,
xylene, benzene, $n$-pentanal) were associated with respiratory symptoms, and industry-related volatile organic compounds (chloroform, methylchloride, methylene chloride) were associated with eye and nose irritation. There was no indication of any long-term effects, but they have not yet been looked for.

**Lead**

Although the removal of lead from gasoline represents a major step forward in limiting the damage of air pollution from this element, it is unclear to what extent the initial United States decision to reduce the lead content of gasoline was based on health concerns (40). There is overwhelming evidence of the general dissemination of airborne lead (even as far as Greenland) as a consequence of its use in gasoline and near unanimity in epidemiologic studies that the lead level of children (even from very low levels) is related to behavioral difficulties and also some decrement in intelligence (41). The reduction and elimination of lead dissemination from gasoline in third world cities should be regarded as commanding the highest priority.

**Carbon monoxide**

The redesign of automobile fuel delivery systems has resulted in a considerable lowering of ambient carbon monoxide levels in modern cities. At present, elevations of carboxyhemoglobin sufficient to worsen myocardial ischemia (about 3%) can occur under specific situations, particularly the use of a car heater in stationary traffic. Elevations of carboxyhemoglobin of about 2% were observed in Germany among nonsmokers during an air pollution episode (42); the first time this had been documented. And there is recent evidence that daily hospital admissions in major cities may be associated with elevated carbon monoxide levels (43); but in this instance it is possible that the carbon monoxide level, as an indicator of inversion conditions, was a surrogate for fine particulate levels. Fortunately, carbon monoxide does not accumulate in the global atmosphere.

**Universal difficulties**

**Assessing the economic disbenefits of air pollution**

It has become apparent that once the simpler measures have been taken to limit the emissions of pollutants from single sources, further control measures are more costly and much more difficult to implement. Specifically, reducing nitrogen dioxide emissions from cars and trucks is not simple, and reducing PM$_{10}$ may prove to be even more difficult.

In this situation, it is natural that there should be an expectation that calculations should be made of the current disbenefits (in economic terms) of air pollution before costly and difficult control measures are instituted. Pioneer efforts to make such calculations 25 years ago (44) were generally disregarded; as recently as 1989, it was a commonly held opinion that such calculations were too unreliable to be used as a guide for policy (45). This situation has been changed by the mandated requirement in the Clean Air Act amendments of 1990 in the United States (see section 812) that the Environmental Protection Agency should provide such estimates. Hall et al (46) published such calculations for Los Angeles; and currently similar estimates are being prepared for San Francisco and New York State. All such calculations will be dominated by how the association between PM$_{10}$ and daily mortality is handled. Should it be assumed that there is no threshold? Is "PM$_{10}$" likely to be the same everywhere? How should the "cost" of a premature death be evaluated in relation to age? Is death accelerated by only a few days in the majority of instances? These and other questions have to be answered before any estimate can be produced. In relation to the last question, a recently published study is of great importance. In a 17-year prospective study of six cities in the United States, in which continuing smoking habits were accurately recorded, Dockery and his colleagues (47) showed that higher PM$_{10}$ levels were associated with reduced survival. Thus the association between PM$_{10}$ and daily mortality in the time-series data did not indicate that death had been brought forward only by a few days (as some had suggested), but was related to long-term survival.

The attempts to estimate the cost of the adverse health effects of air pollutants are likely to be a continuing endeavor. When air pollution is responsible for events other than episodic sudden mortality (as in London in 1952), there is a tendency to ignore the other phenomena with which air pollution is associated. Industrial interests, capable of exerting substantial economic pressure, will attempt to minimize the importance of such effects as the aggravation of asthma or the increased risk of lower respiratory infections among children. For this reason, economic calculations, though inevitably controversial, may prove useful in reminding legislators in all countries that there is further work to be done. A report of the World Bank (48) has commented that the problem of limiting air pollution in Third World countries is that there is a powerful and well-organized lobby with an interest in limiting any proposed regulation and that those concerned with reducing pollution have little understanding of the problem and even less political influence.

**Relationship between asthma and air pollution**

Barnes (49) recently concluded that current levels of air pollution have little to do with asthma. Others who specialize in this complex and multifactorial disease have...
expressed the same view. Yet the prima facie evidence is very strong that asthma is made worse by current levels of oxidant and particulate air pollution, even if prevalence is unaffected. In Great Britain, Anderson concluded that more severe asthma has become more common (50), and in Canada there has been a marked increase in hospital admissions for the condition (31). In view of the fact that asthma is primarily an inflammatory condition, that hospital emergency visits and admissions have been shown to be related to ozone levels (in Ontario, New Jersey, and Atlanta), that particulate pollution (in Seattle and Birmingham, for example) is associated with increased hospital visits and admissions for asthma, and that one prospective study has found that new cases of asthma in a nonsmoking adult population were more common in more polluted regions; it is surprising that these experts have been unwilling to draw the obvious conclusion that asthma is at least aggravated by current levels of air pollution.

Long-term global problems

The scientific community is in agreement that global carbon dioxide levels have risen over the past 50 years and that the impact will have been to cause global warming. But the magnitude of this effect depends on the particular computer model that is chosen, and a long period of observation is needed before one can be sure that global temperature change has occurred. Some experts have urged that this problem over-rides all others and that the effects of current tropospheric pollution are trivial by comparison. Others are more cautious and point out that most computer models fail to take account of concomitant changes that offset the effect on global climate. The ordinary observer is not in a position to be able to decide between these viewpoints; but it would be prudent to insist that atmospheric scientists be given the tools they need to keep the situation under close and continuing surveillance.

Conflict between pollution control and economic development

It was formerly taken for granted that the costs of better air pollution control were a burden on industry and interfered with prosperity and full employment. It is unclear whether this simplistic view of the current world economy is correct, not only because Eastern Europe showed that uncontrolled pollution could occur alongside gross economic inefficiency, but also because, in the industrialized West, there is evidence that more progressive industries are found in countries where the pollution controls are strictest (52).

Few countries take proper account of the long-term costs and inefficiencies that follow human disease, in adults and children, consequent upon air pollution.

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