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Adverse health impacts of air pollution – continuing problems

by David V Bates, MD¹

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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 by 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 domestic factors or for smoking; the second has permitted extremely fast analysis of large numbers of questionnaires 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 improvement 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_{10}) are consistently associated with daily mortality (excluding accidents and suicides) has placed a severe strain on regulatory authorities. The phenomenon has been shown to apply to many different locations in the United States, from Philadelphia 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_{10} was associated with a wide range of effects in addition to mortality, including hospital admissions of children with respiratory disease, respiratory symptoms, school absences, changes in lung function, and increased medication use and hospital emergency visits among asthmatics. Schwartz, who originated much of this work, has more recently shown that pneumonia admissions to hospitals in Detroit (6) cycle with PM_{10} levels. Burnett and his colleagues in Ontario (7) have shown that aerosol sulfates are not only associated with respiratory admissions [which had been found previously (8)], but that cardiovascular hospital admissions are also affected. This is important additional information as it underpins mortality studies, in which cardiovascular mortality is always elevated (9). Cardiovascular deaths outnumber respiratory deaths by a factor of 20 or so; hence although the effect of PM_{10} 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_{10} particles indicate that the particles 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_{10} ; and the smaller the particles, the closer the approximation of indoor and outdoor concentrations of them (an observation that may be important in relation to a possible impact of outdoor particles on incapacitated people living mostly or entirely indoors).

In all the locations that have been studied, automobile 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_{10} values.

The consistency and coherence of the current data on PM_{10} 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_{10} in a modern city are formidable and have not yet been addressed in detail.

Photochemical smog: acid aerosols

The understanding of the chemistry of photochemical air pollution has advanced considerably since its first description 40 years ago. Careful ozone monitoring in more locations has revealed the extent of "ozone" episodes. An ongoing research program on oxidants in the southern part of the United States showed that in June 1990 in one such episode, in which the highest ozone concentration was centered on Atlanta, ozone at a concentration greater than 80 ppb ($160 \mu\text{g} \cdot \text{m}^{-3}$) 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 ($160 \mu\text{g} \cdot \text{m}^{-3}$) with heavy exercise, ozone lowers the forced expiratory volume in 1 s ($\text{FEV}_{1.0}$) 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 stimulation 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 PM₁₀ 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 must be 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.

ONTARIO HOSPITAL ADMISSIONS AND AIR POLLUTION

Figure 1. Daily respiratory admissions to 168 Ontario hospitals over a period of six years in relation to the daily maximum 1-h ozone level. The respiratory admissions apply to all acute respiratory conditions, but there was also a significant association with admissions for asthma when considered separately. [Reprinted from reference 12 with the permission of *Environmental Research*]

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 PM₁₀, 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 Palmes' 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-

gen dioxide at concentrations that produce no acute effect increases the subsequent response to ozone 2 h later in normal subjects (25). This is an interesting observation, since sequential nitrogen dioxide and ozone exposures are probably a frequent event in the population. Moseholm et al (2), using neural network analysis, found evidence of an influence of nitrogen dioxide levels (together with sulfur dioxide) in an eight-month panel study of 27 nonatopic adult asthmatics in Denmark. In addition it has recently been found that nitrogen dioxide exposure increases the severity of the late asthmatic reaction when an allergen is administered (26). A recent study in Birmingham in England (27) found that residence close to a major traffic artery was a risk factor in the emergency visits of asthmatics to hospitals. This finding might have been due either to a higher PM_{10} or higher nitrogen dioxide exposure. In a study of five German cities, Schwartz and his colleagues (28) concluded that both particulates and nitrogen dioxide were associated with increased respiratory symptoms among children.

A severe inversion episode in London in December 1991 (29) led to nitrogen dioxide levels of 400 ppb ($750 \mu\text{g} \cdot \text{m}^{-3}$) for eight consecutive hours on two consecutive days. It is not known whether this episode was associated with any measurable adverse health effects.

I conclude that it would be premature to rule out the occurrence of any adverse health effects from nitrogen dioxide in the general population, even though such effects cannot, at this time, be precisely delineated. The analysis of the London episode may throw some additional light on this question.

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 Cooperatif 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 $FEV_{1.0}$ 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 sur-

rogate 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 $12.7 \mu\text{g} \cdot \text{m}^{-3}$ and the corresponding sulfur dioxide concentration was $39.1 \mu\text{g} \cdot \text{m}^{-3}$ (13.65 ppb), the highest values being $188.3 \mu\text{g} \cdot \text{m}^{-3}$ for smoke and $126.3 \mu\text{g} \cdot \text{m}^{-3}$ 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_4 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 cur-

rent 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 (51). 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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References

1. Bates DV. Health indices of the adverse effects of air pollution: the question of coherence. *Environ Res* 1992;59:336–49.
2. Moseholm L, Taudorf E, Frosig A. Pulmonary function changes in asthmatics associated with low-level SO₂ and NO₂ air pollution, weather, and medicine intake: an 8-month prospective study analyzed by neural networks. *Allergy* 1993;48:334–44.
3. Sherwin RP, Richters V. Centriacinar region (CAR) disease in the lungs of young adults: a preliminary report. In: Berglund RL, Lawson DR, McKee DJ, editors. *Tropospheric ozone and the environment*. Pittsburgh (PA): Air & Waste Management Association, 1991:178–96.
4. Bates DV. Commentary: summary of the colloquium on particulate air pollution and human mortality and morbidity, Irvine, California, 24–25 January 1994. *Inhal Toxicol* 1995;7:vii–xi.
5. Dockery DW, Pope CA III. Acute respiratory effects of particulate air pollution. *Annu Rev Public Health* 1994;15:107–32.
6. Schwartz J. Air pollution and hospital admissions for the elderly in Detroit, Michigan. *Am J Respir Crit Care Med* 1994;150:648–55.
7. Burnett RT, Dales RE, Krewski D, Vincent R, Dann T, Brook JR. Associations between ambient particulate sulfate and admissions to Ontario hospitals for cardiac and respiratory diseases. *Am J Epidemiol*. In press.
8. Bates DV, Sizto R. Hospital admissions and air pollutants in southern Ontario: The acid summer haze effect. *Environ Res* 1987;43:317–31.
9. Schwartz J. What are people dying of on high air pollution days? *Environ Res* 1994;64:26–35.
10. White MC, Etzel RA, Wilcox WD, Lloyd C. Exacerbations of childhood asthma and ozone pollution in Atlanta. *Environ Res* 1994;65:56–68.
11. Cody RP, Weisel CP, Birnbaum G, Liroy PJ. The effect of ozone associated with summertime photochemical smog and the frequency of asthma visits to hospital emergency departments. *Environ Res* 1992;58:184–94.
12. Burnett RT, Dales RE, Raizenne ME, Krewski D, Summers PW, Roberts GR, et al. Effects of low ambient levels of ozone and sulphates on the frequency of respiratory admissions to Ontario hospitals. *Environ Res* 1994;65:172–94.
13. Thurston GD, Ito K, Hayes CG, Bates DV, Lippmann M. Respiratory hospital admissions and summertime haze air pollution in Toronto, Ontario: consideration of the role of acid aerosols. *Environ Res* 1994;65:271–90.
14. Schwartz J, Dockery DW, Neas LM, Wypij D, Ware, JH, Spengler JD, et al. Acute effects of summer air pollution on respiratory symptom reporting in children. *Am J Respir Crit Care Med* 1994;150:1234–42.
15. Thurston G, Lippmann M, Bartoszek M, Fine J. Summer haze associations with asthma exacerbations, peak flow changes, and respiratory symptoms in children at a summer asthma camp. In: Program abstracts of the Sixth Conference of the International Society for Environmental Epidemiology: Re-

- search Triangle Park, NC September 18–21, 1994. Abstract 1994:227.
16. Laitinen LA, Laitinen A, Haahtela T. Airway mucosal inflammation even in patients with newly diagnosed asthma. *Am Rev Respir Dis* 1993;147:697–704.
 17. Tyler WS, Julian MD, Hyde DM. Respiratory bronchiolitis following exposures to photochemical air pollutants. *Semin Respir Med* 1992;13:94–113.
 18. Abbey DE, Mills PK, Petersen FF, Beeson WL. Long-term ambient concentrations of total suspended particulates and oxidants as related to incidence of chronic disease in California Seventh-Day Adventists. *Environ Health Perspect* 1991;94:43–50.
 19. National Research Council, USA. Rethinking the ozone problem in urban and regional air pollution. Washington (DC): National Academy Press, 1991; 489 p.
 20. Penkett SA. Atmospheric photochemistry and its role in the generation of acidity in rain. In: Calvert JG, editor. *The chemistry of the atmosphere: its impact on global change*. Oxford: Blackwell Scientific Publications, 1994:327–43.
 21. Keeler GJ, Spengler JD, Koutrakis P, Allen GA, Raizenne M, Stern B. Transported acid aerosols measured in Southern Ontario. *Atmos Environ* 1990;24A:2935–50.
 22. Mukala K, Pekkanen J, Tiittanen P, Alm S, Salonen RO, Husman T, et al. Personal NO₂ exposure and cough in pre-school children. In: Program abstracts of the Sixth Conference of the International Society for Environmental Epidemiology: Research Triangle Park, NC September 18–21, 1994. Abstract 201.
 23. Samet JM, Lambert WE, Skipper BJ, Cushing AH, Hunt WC, Young SA, et al. Nitrogen dioxide and respiratory illness in infants. *Am Rev Respir Dis* 1993;148:1258–65.
 24. Neas LM, Dockery DW, Ware JH, Spengler JD, Speizer FE, Ferris BG, Jr. Association of indoor nitrogen dioxide with respiratory symptoms and pulmonary function in children. *Am J Epidemiol* 1991;134:204–19.
 25. Hazucha MJ, Folinsbee LJ, Seal E, Bromberg PA. Lung function response of healthy women after sequential exposures to NO₂ and O₃. *Am J Respir Crit Care Med* 1994;150:642–7.
 26. Strand V, Svartengren M, Rak S, Bylin G. Effects of NO₂ exposure on immediate and late response to inhaled allergen in subjects with asthma. *Am J Respir Crit Care Med* 1994;149:A154.
 27. Edwards J, Walters S, Griffiths RK. Hospital admissions for asthma in preschool children: relationship to major roads in Birmingham, United Kingdom. *Arch Environ Health* 1994;49:223–7.
 28. Schwartz J, Spix C, Wichmann HE, Malin E. Air pollution and acute respiratory illness in five German communities. *Environ Res* 1991;56:1–14.
 29. Warren Spring Laboratory. Initial analysis of NO₂ pollution episode, December 1991. England: The Environmental Technology Executive Agency of the Department of Trade and Industry, 1992.
 30. Holland WW, Reid DD. The urban factor in chronic bronchitis. *Lancet* 1965;1:445–8.
 31. Xu X, Dockery DW, Wang L. Effects of air pollution on adult pulmonary function. *Arch Environ Health* 1991;46:198–206.
 32. Groupe Cooperatif PAARC. II results and discussion. *Bull Eur Physiopathol Respir* 1982;18:101–16.
 33. He Q-C, Liou PJ, Wilson WE, Chapman RS. Effects of air pollution on children's pulmonary function in urban and sub-urban areas of Wuhan, People's Republic of China. *Arch Environ Health* 1993;48:382–91.
 34. Bobak M, Leon DA. Air pollution and infant mortality in the Czech Republic, 1986–88. *Lancet* 1992;340:1010–4.
 35. Ponka A. Absenteeism and respiratory disease among children and adults in Helsinki in relation to low-level air pollution and temperature. *Environ Res* 1990;52:34–46.
 36. Sunyer J, Anto JM, Murillo C, Saez M. Effects of urban air pollution on emergency room admissions for chronic obstructive pulmonary disease. *Am J Epidemiol* 1991;134:277–86.
 37. Bates DV, Baker-Anderson M, Sizto R. Asthma attack periodicity: a study of hospital emergency visits in Vancouver. *Environ Res* 1990;51:51–70.
 38. Walters S, Griffiths RK, Ayres JG. Temporal association between hospital admissions for asthma in Birmingham and ambient levels of sulphur dioxide and smoke. *Thorax* 1994;49:133–40.
 39. Ozkaynak H, Spengler J, Ware J, Samet J, Wagner G, Schwab M. Associations between children's daily health symptoms and ambient volatile organic compounds: the Kanawha County health study. In: Program abstracts of the Sixth Conference of the International Society for Environmental Epidemiology: Research Triangle Park, NC September 18–21, 1994. Abstract 204.
 40. Bates DV. Environmental health risks and public policy: decision-making in free societies. Seattle (WA): University of Washington Press, 1994: 117 p.
 41. Needleman HL, Gatsonis CA. Low-level lead exposure and the IQ of children: a meta-analysis of modern studies. *JAMA* 1990;263:673–8.
 42. Wichmann H-E, Sugiri D, Islam MS, Haake D, Roscovanu A. Pulmonary function and carboxyhemoglobin during the smog episode in January 1987. *Zbl Bakt Hyg* 1988;B187:31–43.
 43. Morris RD, Naumova EN, Munasinghe RL. Ambient air pollution and hospitalization for congestive heart failure among the elderly in seven large American cities. In: Abstracts of the Sixth Conference of the International Society for Environmental Epidemiology: Research Triangle Park, NC, September 18–21, 1994. Abstract 352.
 44. Lave LB, Seskin EP. Air pollution and human health. *Science* 1970;169:723–33.
 45. Blodgett J. Health benefits of air pollution control: a discussion: congressional research service report for congress, Feb 27th, 1989. Washington (DC): Library of Congress, 1989.
 46. Hall JV, Winer AM, Kleinman MT, Lurmann FW, Brajer V, Colome SD. Valuing the health benefits of clean air. *Science* 1992;255:812–7.
 47. Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, et al. An association between air pollution and mortality in six US cities. *New Engl J Med* 1993;329:1753–9.
 48. Sebastian I. Issues in urban air pollution: Ankara diagnostic report. Washington (DC): World Bank, 1990. Environment working paper, no 38.
 49. Barnes PJ. Air pollution and asthma. *Postgrad Med J* 1994;70:319–25.
 50. Anderson HR. Increase in hospital admissions for childhood asthma: trends in referral, severity, and readmissions from 1970 to 1985 in a health region of the United Kingdom. *Thorax* 1989;44:614–9.
 51. Mao Y, Semenciw R, Morrison H, MacWilliam L, Davies J, Wigle D. Increased rates of illness and death from asthma in Canada. *Can Med Assoc J* 1987;137:620–4.
 52. Porter ME. Essay: America's green strategy. *Sci Am* 1991;264:168.

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