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Assessment of the Health Effects of Atmospheric Sulfur Oxides and Particulate Matter: Evidence from Observational Studies

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Steadily rising energy costs have increased the need for reliable information on the health effects of atmospheric sulfur oxides and particulate matter. Because ethical and practical considerations limit studies of this question under controlled conditions, observational studies provide an important part of the relevant information. This paper examines the currently available epidemiologic evidence from population studies of the health effects of these pollutants.

Nonexperimental studies also have important limitations, including the inability to measure accurately the exposure burden of free living individuals, and the potential for serious confounding by other factors affecting health. We begin with a discussion of some of these methodologic issues. The evidence is then reviewed, first in association with fluctuations in 24 hr mean concentration of sulfur oxides and particulate matter, and then in association with differences in mean annual concentration. In the last section, this evidence is summarized and used to approximate the exposure-response relationship linking pollutant concentrations with mortality and morbidity levels.

Introduction

In view of the potential for adverse health effects of air pollution, and the expense of control measures, reliable assessment of the health effects of different air pollutants is an important public health problem. Lowrance (*1*) has defined four tasks in this assessment: identifying the health effects; quantifying these effects at various ambient concentrations; estimating how many people are exposed at these levels; and calculating the overall health risk associated with a given degree of air quality. This paper addresses the quantification of the health effects of sulfur oxides and particulate matter, especially at ambient concentrations near the present air quality standards.

The health effects of these air pollutants can be studied to some extent in controlled conditions. Laboratory studies of animals allow careful control of the concentration of individual pollutants and conditions of exposure, as well as detailed study of the effects on study animals. These studies have been useful for identifying possible mechanisms of action and potential health effects. However, it is

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difficult to use animal studies to quantify these effects in human populations, primarily because the basis for extrapolating from animal to man is uncertain. The uncertainty of such extrapolation is increased by significant interspecies variability in the response to pollutants.

Laboratory studies with human subjects avoid extrapolation from animal to man but raise other concerns, such as ethical considerations and practical difficulties in studying long-term exposures. In addition, laboratory studies cannot duplicate the activity patterns and pollutant mixture experienced by free living populations. Within these constraints, studies involving human subjects can be used to establish the response to short-term exposure.

Studies of occupational groups have been suggested as another source of information. Although these studies may provide good estimates of exposure, the mix of pollutants and concentrations is usually different from ambient air. Exposures are for 8 hr or less rather than on a more continuous basis. Temperature and humidity conditions are also likely to differ from those experienced by the general population. Furthermore, the working population differs from the general population in important ways. The very young, elderly and ill persons are not included. There is considerable selection by the employer and self-selection by the worker, so that those with current disease or who are more sensitive or susceptible are not as well represented as in the general population. As a result, one cannot conclude from a negative study in an occupational group that the same exposure is safe for the general population. If an association between an air pollutant and a health effect is found in an occupational setting, there may be a greater association in general populations.

Because of the limitations of each of these types of investigation, epidemiologic studies in general population groups provide much of the relevant information about the health effects of sulfur oxides and particulate matter at levels of exposure near present ambient standards. Here, too, there are limitations with respect to estimating exposure and measuring effects. Other risk factors, such as cigarette smoking and occupational exposures, must be considered, and confounding factors, such as socioeconomic status, race and weather must also be evaluated. In these studies, exposures are not subject to manipulation, though ambient levels can change during the course of a study. This makes it difficult to determine whether mean concentration, peak concentration, variability, or some other aspect of air pollution concentration is the most important determinant of health effects. Observational studies cannot demonstrate cause and effect, rather we infer causality based on the precepts proposed by the Surgeon General's Advisory Committee on Smoking and Health (*2*) and by Hill (*3*): the strength of the association, the consistency of the data, the specificity of the results, the temporality of the observations, the demonstration of a biological gradient and the plausibility and coherence of the results. Ideally, findings will be replicable by specific experimentation, and conclusions will be further strengthened when different approaches or methods yield similar results.

The next section of this paper briefly summarizes the methodological issues which should be considered in evaluating nonexperimental studies of the effects on health of exposure to atmospheric sulfur oxides and particulate matter. We then review the evidence from selected studies of the association between mortality and morbidity levels and 24-hr mean concentration of sulfur oxides and particulate matter the evidence linking mortality and morbidity levels to annual mean concentrations. The evidence is summarized in the final section.

Methodological Issues in Observational Studies

Observational (nonexperimental) studies of the association between health and air pollution are sometimes viewed as natural experiments in which the exposure to pollutants varies over groups or time. However, this view ignores several special characteristics of observational studies of air pollution. One of the most important is inaccurate measurement of the exposure burden of individuals. Pollution data are usually obtained from one or several outdoor monitoring stations, but the exposure burden can vary greatly between individuals living in the same neighborhood because of special features of the outdoor micrometeorology and the indoor environment (*4-6*). The effects of errors in the independent variable on the estimated associations between air pollution and health effects depends on both the size and expectation of the errors. Many health endpoints, including lung function, hospital admission and frequency of symptoms, also are measured with substantial variability. When an association between air pollution and health is found, collinearity (high correlation) of sulfur oxide and particulate concentrations (*7*) and the possibility of complex chemical interactions reported from laboratory studies (*8, 9*) frequently make it difficult to associate the effect with either pollutant alone (*10*).

Observational studies of respiratory disease or

lung function must consider a host of confounding variables (*11*), many of which have greater health effects than air pollution. When these variables are ignored or inadequately measured, resulting bias can easily be greater than the association of interest. In addition, many observational studies use linear or other simple models to summarize complex data sets without assessing the adequacy of the model. Unless data displays, simple groupings or other analyses are used to show that these models are properly summarizing the data, one can only have limited confidence in the results.

These factors, taken together, create additional uncertainty in interpreting observational studies in comparison with laboratory experiments. The most difficult problem in interpreting the evidence from a group of observational studies is determining how effectively these potential problems have been addressed in each study.

There is an unavoidable element of subjectivity in the assessment of evidence. In an effort to reduce that subjectivity we have included in the assessment those studies which satisfy five criteria.

(1) They have been reported in the open literature.

(2) Concentrations of both sulfur dioxide and particulate matter were reported.

(3) Major confounding factors were controlled, particularly temperature in studies of acute exposure, and smoking, race and socioeconomic status in studies of chronic exposure.

(4) The findings pertain to concentrations less than 1000 $\mu m/m^3$ for both sulfur dioxide and particulate matter.

(5) The data collection, analysis and interpretation were free of error or potential bias which could be reasonably expected to substantially affect the results.

Studies failing to meet one or more of these criteria were also included when discussion of their validity and significance was seen as an important part of assessing the evidence from observational studies.

Health Effects of Acute Exposure to Sulfur Oxides and Particulates

The earliest studies of the acute health effects of air pollution focused on dramatic episodes of severe air pollution (*12-18*). The sudden increases in mortality and morbidity that accompanied these episodes and the frequency and severity of respiratory complaints left little doubt that air pollution was, at least in part, the cause of the adverse health effects. Investigators also recognized that weather, particularly extreme temperatures, could influence mortality and morbidity rates.

A substantial reduction in ambient sulfur oxide and particulate concentrations, achieved in most English and American cities by the 1970's, produced a gradual decline in severity and eventual disappearance of episodes in which either sulfur dioxide or particulate matter exceeded 1000 $\mu g/m^3$ (measuring particulate matter either by the British Black Smoke method or as Total Suspended Particulates). Episode studies were gradually supplanted by studies of fluctuations in daily mortality over extended periods, and investigations of potentially more sensitive indices of health effects, including lung function and respiratory disorders. Sensitive population subgroups, such as asthmatics and children, have also been studied. The pollution concentrations in studies of acute exposure have typically been measured by 24-hr mean concentrations, though high level exposures for shorter periods might be important.

Counts of total daily mortality show a seasonal pattern with a peak in winter, and rates on successive days are interdependent. Early studies used the deviation of daily mortality from the 15-day moving average to eliminate seasonal effects. More recently, investigators have used sophisticated time-series-analysis techniques in an effort to eliminate seasonal effects and other long-term trends affecting daily mortality. Elimination of seasonal effects by these methods may be incomplete, and this becomes especially important when investigators attempt to identify pollution effects that are small relative to effects of temperature, season and even day of the week. We will return to this issue in the discussion of individual studies.

Morbidity data are more difficult to gather than daily mortality figures. For that reason, investigations of morbidity effects of acute exposure to sulfur oxides and particulate matter have usually been small, permitting relatively simple analysis. These studies would be unlikely to detect small increases in morbidity at relatively low air pollution concentrations.

Studies reported in this section used three separate measures of particulate pollution. The British studies used the British Black Smoke method and reported particulate levels in $\mu g/m^3$ (BS). Some American studies used the filter soiling method and reported particulate concentrations in units of Coefficient of Haze (CoHs). Other American studies measured Total Suspended Particulates (TSP) by the high-volume sampler method. Results are reported for each study in the original units, and the relationship between the different measures is considered when summarizing the evidence.

Mortality Effects of Acute Exposure to Sulfur Oxides and Particulate Matter

In this section, we examine studies of the association between daily mortality rate, as measured by the recorded number of deaths, and 24-hr average concentration of sulfur dioxide and particulate matter. The clearest evidence comes from studies of relatively high pollution concentrations, while studies of lower concentrations have been equivocal, primarily because collinearity of temperature and other weather variables with pollution concentrations have made it difficult to interpret associations between daily mortality and air pollutant concentrations.

Studies of Daily Mortality in London. Two important British studies bearing on mortality effects of acute exposure to SO_2 and particulate matter at concentrations near present 24-hr air quality standards were reported by Martin and Bradley (*19*) and Martin (*20*). Martin and Bradley related daily mortality from all causes (and from bronchitis and pneumonia) to the concentrations of SO_2 and black smoke (BS) in London during the winter of 1958-59. The authors found a considerable number of coincident peaks in pollution concentration and daily mortality. The correlation of mortality from all causes with air pollutant concentration, measured on the log scale, was 0.61 for BS and 0.52 for SO_2. The correlation between mortality and mean daily temperature was –0.03 (not significant), while the correlation of mortality with humidity was 0.19 (significant at the 0.05 level). The authors noted that about two-thirds of the air pollution episodes were accompanied by thick fog, and the correlation between mortality and visibility was found to be –0.55. Visibility is influenced both by fog and particulate pollution.

Although the authors emphasized the relationship between differences in pollution concentration and differences in death rate on successive days, their paper provided total deaths, smoke concentration and SO_2 concentration from November 1, 1958 to February 28, 1959. We have re-examined their data after excluding the month of February, as an epidemic of Type A influenza had a significant influence on daily mortality in that month.

For the remaining 92 days, the deviation of each day's total mortality from the 15-day moving average (truncated at each end of the series) was computed. The average deviation is given for intervals of BS concentration in Table 1 and SO_2 concentration in Table 2.

Although Lawther (*21*) has suggested that the number of deaths increased significantly when BS rose above 750 $\mu g/m^3$ and SO_2 concentrations exceeded 710 $\mu g/m^3$, these tables do not suggest those values. If one begins with a threshold hypothesis, that mortality is not affected until air pollution concentrations exceed threshold levels, one might choose threshold values of 500 $\mu g/m^3$ of BS and 300 $\mu g/m^3$ of SO_2 from these data. However, the data are also consistent with a monotonic exposure-response hypothesis, that mortality level increases with air pollution concentration over a broad range of values, including those just cited.

A similar analysis was carried out by Martin for the winter of 1959-60 (*20*). That winter had fewer incidents of high pollution. The significant positive correlation between mortality and pollution was still present, although the author reported that the correlation coefficients were somewhat lower than in the previous year. Tables 3 and 4 show Martin's results combining high pollution days from 1958-59 and 1959-60, excluding days with pollution concentrations lower than the previous day. The mean deviation is positive in every group reported. Bronchitis mortality was also found to be significantly, though less strongly, correlated with pollution level. Pneumonia mortality was not found to be correlated with pollution.

Table 1. Average deviation of daily mortality from 15-day moving average, by concentration of smoke (London, Nov. 1, 1958, to Jan. 31, 1959).[a]

Smoke concentration, $\mu g/m^3$ (BS)	Number of days	Mean deviation
100–199	6	–20.82
200–299	12	–13.65
300–399	18	–10.80
400–499	19	–7.15
500–599	9	10.89
600–699	6	19.72
700–799	7	4.17
800–1199	10	21.49
1200+	5	38.36

[a]Data of Martin and Bradley (*19*).

Table 2. Average deviation of daily mortality from 15-day moving average, by concentration of SO_2 (London, Nov. 1, 1958, to Jan. 31, 1959).[a]

Smoke concentration, $\mu g/m^3$	Number of days	Mean deviation
100–199	17	–13.01
200–299	29	–12.16
300–399	22	6.87
400–499	11	9.32
500+	13	27.21

[a]Data of Martin and Bradley (*19*).

Table 3. Average deviation of daily mortality from 15-day moving average, by concentration of smoke (BS) (London, 1958-60).[a]

Smoke concentration, $\mu g/m^3$ (BS)	Number of days	Mean deviation
500–599	9	5.2
600–699	6	13.0
700–799	9	9.2
800–1099	8	15.6
1100+	7	40.0

[a]Data of Martin (*20*).

Table 4. Average deviation of daily mortality from 15-day moving average, by concentration of SO_2 (London, 1958-60).[a]

SO_2 concentration, $\mu g/m^3$	Number of days	Mean deviation
400–499	9	9.0
500–599	6	11.6
600–799	9	16.0
800–899	6	19.2
900+	5	39.6

[a]Data of Martin (*20*).

These two studies represent an important part of the evidence for mortality effects of short-term elevations in SO_2 and particulate pollution. Although temperature was not an important confounding factor in the two winters studied, fog was an important factor in many air pollution episodes, especially in the winter of 1958-59. Reported analyses have not adequately controlled for the effects of fog on mortality. During this period, daily mean concentrations of SO_2 and BS were highly correlated ($r = 0.89$ for the winter of 1958-59). Consequently, these associations cannot be attributed to either pollutant individually.

Additional evidence for acute effects of short-term elevations in sulfur dioxide and particulate matter concentrations was provided by the analysis of a pollution episode in London in December, 1975 (*22, 23*). Maximum 24-hr concentrations of 994 $\mu g/m^3$ (SO_2) and 546 $\mu g/m^3$ (BS) were reported, and an increase of 100 to 200 deaths above expected totals was observed during the week in which the episode occurred. A doctors' strike in the period immediately prior to this episode had an unknown impact on the mortality data.

Studies of Daily Mortality in New York City. The other principal source of information on variation in daily mortality comes from a series of studies in New York City. This information includes reports (*24-26*) of several air pollution episodes not discussed here, since pollutant concentrations were too high to contribute significantly to our assessment. However, Glasser and Greenburg (*27*) carried out an analysis of daily mortality in New York City during the five-year period 1960-64, using only data from the months October through March. The 24-hr average pollution concentrations were based on hourly SO_2 and bihourly smoke shade (CoHs) readings from a single monitoring station. Death rates were analyzed both as deviations from a 15-day moving average and as deviations from the five-year average for that day. The two analyses were said to have qualitatively similar results. In cross-tabulation of daily mortality by SO_2 and smoke shade level, SO_2 appeared to be more strongly related to mortality and was used as an index of pollution in some analyses. Multiple regression analysis showed a stronger association of mortality with SO_2 than with either temperature or rainfall.

Tables 5 and 6 summarize the analysis by Glasser and Greenburg. These results have been interpreted as showing a mortality effect for smoke shade above 5 CoHs and SO_2 above 786 $\mu g/m^3$, though they are again supportive of a monotonic exposure response relationship. Although the observations of daily mortality are correlated, Glasser and Greenburg computed standard errors for the mean deviations by assuming independence. Most

Table 5. Average deviation of daily mortality from normal, by level of smoke shade (CoHs) (New York, 1960-64, October through March).[a]

Smoke shade level (CoH)	Number of days	Mean deviation (SE)
<1.0	26	-2.8 (3.5)
1.0–1.9	160	-1.6 (1.4)
2.0–2.9	318	-2.4 (1.0)
3.0–3.9	239	1.5 (1.2)
4.0–4.9	83	2.5 (2.3)
5.0–5.9	19	18.8 (4.3)
6.0+	9	17.2 (7.8)

[a]Data of Glasser and Greenberg (*27*).

Table 6. Average deviation of daily mortality from normal, by level of SO_2 (New York, 1960-64, October through March).[a]

SO_2 concentration, $\mu g/m^3$	Number of days	Mean deviation (SE)
<262	112	-3.5 (1.6)
262–524	311	-3.1 (1.0)
525–786	172	1.8 (1.4)
787–1048	66	9.4 (2.0)
>1048	80	11.9 (2.5)

[a]Data of Glasser and Greenberg (*27*).

of these standard errors were near 2.0, though the entry 18.8 in Table 5 had a quoted standard error of 4.3. The authors also stratified days by temperature into three groups: those more than five degrees below normal, within five degrees of normal, and more than five degrees above normal. The result of the stratified analysis differed little from the unadjusted analysis. However, this simplified approach to covariance adjustment may not eliminate the confounding effects due to temperature. Multivariate analyses of the New York data described below suggest that more careful control for temperature and other meteorologic factors has a substantial effect on the results.

To analyze possible mortality effects of even lower levels of pollution, the 15-day moving average method is not sufficiently sensitive. Furthermore, some authors have argued that more sophisticated adjustment techniques are necessary to ensure that seasonal and temperature effects are eliminated in the adjusted analysis. To achieve that objective, Schimmel and coworkers (*28-30*) have reported three analyses of mortality data from New York City in which the adjustment methodology was refined over time. Buechley et al. (*31*) and Buechley (*32*) have also analyzed some of the same data.

Schimmel and Murawski (*29*) emphasized the common seasonal trends in mortality, pollution and temperature in New York City, and the possibility that nonlinear relationships would make linear regression unsatisfactory as an adjustment technique. They eliminated periods associated with heat waves and analyzed the remaining data in three time periods, 1963-66, 1967-69 and 1970-72. While smoke shade level varied little over the three periods, the average SO_2 level declined dramatically, as shown in Table 7.

Schimmel and Murawski estimated the percentage of premature deaths due to air pollution to be 2.78, 2.48 and 3.20, based on regression analysis of the three periods using a model with no lag effects. The percentage attributed to SO_2 was 0.58, 1.22 and 0.62, values not significantly different from zero. Since the percentage of excess deaths attributed to air pollution differed little in periods with three-fold differences in SO_2 concentration, they concluded that SO_2 concentration is merely an index variable for other unmeasured extraneous variables and not a cause of adverse health effects at these levels.

Schimmel (*30*) continued his analysis of these data by utilizing time series techniques to eliminate any seasonal or other cyclical effects contributing to associations between pollution and mortality. In this analysis, the regression of mortality on SO_2 was not significant and negative coefficients were obtained in some regressions.

Buechley (*31*, *32*) also sought to identify major nonpollutant variables influencing daily mortality and found that mortality was affected by the annual cycle, summer heat waves, influenza epidemics and a temperature variable. These four variables explained 78% of the variation in daily mortality during the 11-year period 1962-72 in New York City. Although SO_2 concentration and particulate level also entered significantly into the regression equation, Buechley found that the coefficient for SO_2 concentration in regression analysis of daily mortality during the winter of 1971-72 was slightly higher than the corresponding coefficient for the winter of 1967-68, even though the mean SO_2 concentration in the second winter was only 10% of that in the earlier period.

Both Schimmel (*30*) and Buechley (*32*) concluded that the associations they found between mortality and air pollution could be explained by joint association with temperature and other weather variables. Their work highlights the limitations of observational studies when the study objective is accurate estimation of small primary relationships when other independent variables are more strongly associated with mortality. These other variables influence the estimate of the primary relationship, and the proper method of adjustment is unknown. Thus, it will be difficult to reliably quantify small mortality effects of fluctuations in ambient pollution concentrations by analyzing observational data.

Table 7. Average pollution levels during three time periods analyzed by Schimmel and Murawski.[a]

Time period	SO_2 level, $\mu g/m^3$	CoHs level
1963–66	112	2.07
1967–69	359	2.27
1970–72	155	2.13

[a]Data of Schimmel and Murawski (*29*).

Morbidity Effects of Acute Exposure to Sulfur Oxides and Particulate Matter

Levels of air pollution which acutely affect mortality rates should affect other health indices, including incidence and prevalence of respiratory disease as measured by emergency room visits or hospital admissions, prevalence and severity of respiratory symptoms as measured by question-

naire during regular contact with a panel of participants, or changes in various aspects of lung function. Unlike mortality rates, these health data must often be specially obtained by the investigator. This has limited the size of morbidity studies. Many studies have used the diary or panel method, in which a group of participants regularly record or report symptoms. Substantial nonparticipation rates have been a problem in many of these studies, and make it difficult to interpret the symptom reports by those from whom observations are obtained.

Illness data were obtained in many of the early severe pollution episodes (*13*, *15*, *33*). This information did little more than confirm the mortality results, though there was some evidence that the increase in illness was not as large in percentage terms as the increase in deaths, and the effects were not so sudden. Martin (*20*) examined hospital admissions for the winters of 1958-59 and 1959-60 and found, after adjustment for day of the week and correction for 15-day moving average, significant correlations for both cardiovascular and respiratory conditions with BS and sulfur dioxide. The average deviations by pollution concentration, given in Tables 8 and 9, show more irregularity than the mortality data.

Table 8. Average deviation of respiratory and cardiac morbidity from 15-day moving average, by smoke concentration (BS) (London, 1958-60).[a]

Smoke concentration, $\mu g/m^3$ (BS)	Number of days	Mean deviation
500–599	9	3.2
600–699	6	–0.7
700–799	9	2.4
800–1099	8	4.9
1100+	7	12.9

[a]Data of Martin (*20*).

Table 9. Average deviation of respiratory and cardiac morbidity from 15-day moving average, by SO_2 concentration (London, 1958-60).[a]

SO_2 concentration, $\mu g/m^3$	Number of days	Mean deviation
400–499	9	2.2
500–599	6	5.1
600–799	9	6.9
800–899	6	12.8
900+	5	12.8

[a]Data of Martin (*20*).

In a second important British study, Lawther et al. (*34*, *35*) collected daily self-reported health status from 194 persons with chronic respiratory disease during the winters of 1959-60 and 1964-65. Health status was reported relative to the previous day, and worsening of health status by self-evaluation was clearly associated with increases in air pollution. The authors reported that this effect could be seen on days when the 24-hr average level of SO_2 exceeded 500 $\mu g/m^3$ and smoke exceeded 250 $\mu g/m^3$ (BS). The strength of this response declined as the winter progressed and there was some evidence for an adaptation or desensitization effect or even loss of interest by participants. Lawther et al. commented that these responses could have resulted from brief exposure to maximum concentrations several times the 24-hr average.

Studies of Bronchial Asthma. Some studies of pollution and asthma have reported negative or equivocal results (*36*, *37*). However, Cohen et al. (*38*) found a weak association between air pollution and the frequency of asthma attacks in a study of patients living near a coal-fueled power plant in West Virginia. Temperature was most strongly correlated with frequency of attacks among 20 patients having at least one attack during the study. In a multiple regression analysis, either SO_2 or TSP concentration was significantly correlated with attack rate after adjustment for temperature ($p < 0.01$). When days were classified as high and low particulate concentration (above or below 150 $\mu g/m^3$ TSP), or as high and low SO_2 concentration (above or below 200 $\mu g/m^3$), symptom prevalence was significantly higher on the high pollution days.

These values should not be interpreted as threshold values, since the dividing line seems arbitrary and the table comparing the two groups of days does not seem to be temperature adjusted. The authors provide little information about changes in panel membership over time, and also give insufficient information about their data analysis methods. In particular, they combined data from children and adults participating in the study. The sensitivity of asthmatics to exogenous allergens, respiratory infections, dust, animals, smoking, cold weather and psychological factors also suggests caution in attributing changes in symptom prevalence to changes in air pollution concentration.

Studies of Acute Respiratory Disease. Few studies relating acute exposure to moderate levels of air pollution to increased incidence of acute respiratory disease have been published. Although early studies by Dohan and Taylor (*39*) and Dohan (*40*) found an association between the level of suspended sulfates and work absences for respiratory disease among outdoor telephone workers, Ipsen et

al. (41) conducted a near replication of their study and found that apparent associations between absenteeism and air pollution were eliminated by adjustment for temperature, humidity and wind velocity.

Studies of Pulmonary Function. Van der Lende et al. (43) obtained results in a study of respiratory symptoms and lung function in the Netherlands which could represent an acute effect of air pollution. Examination of a large general population group in 1969 and again in 1972 failed to show the expected small decrease in levels of Forced Vital Capacity (FVC) and Forced Expiratory Volume in one second (FEV_1), but rather small significant increases. The authors suggested that this could be attributed to improvement in air quality, from reported maximum 24-hr smoke level of 160 $\mu g/m^3$ (BS) and SO_2 concentration of 300 $\mu g/m^3$ in 1969 to 40 $\mu g/m^3$ (BS) and 100 $\mu g/m^3$ (SO_2) in 1972. [This and some other continental European studies used OECD calibration curves to express Black Smoke in $\mu g/m^3$. Some reviewers have suggested that the reported values should be increased, perhaps by a factor of 2, to be comparable with the British Black Smoke method (42).]

Expected decreases in pulmonary function were seen in a rural area measured at the same times. The authors explored possible sources of bias in the study but were unable to explain their results on that basis. If real, these changes are most reasonably interpreted as an acute, reversible response to elevated concentrations of air pollution.

Stebbings et al. (44) studied pulmonary function in 272 children during and after an air pollution alert in Pittsburgh in 1975. The 24-hr average SO_2 concentration reached 350 $\mu g/m^3$ and the 24-hr TSP level reached 770 $\mu g/m^3$. The mean $FEV_{0.75}$ and FVC values, instead of increasing as hypothesized, declined throughout the six-day period. Because the investigators did not have a pre-alert lung function measurement, the values obtained during the alert days could not be compared to "normal" lung function values. Since the children were followed for only the week, the possibility of a later increase in lung function values could not be excluded.

In a later report, Stebbings et al. (45) identified a group of children whose lung functions showed large increases after the alert. Since the proportion of such children was significantly greater in the alert than in a control area, they concluded that the alert had been associated with reduced lung function. Since the analysis was selected in response to the data, was based on unvalidated methodology, and failed to explain the anomalous finding of an excess of children in the alert area whose lung function declined during the study, these results do not provide sound evidence for health effects of air pollution at the levels reported.

Health Effects of Chronic Exposure to Sulfur Oxides and Particulate Matter

Studies of health effects of chronic exposure to air pollutants are typically cross-sectional, comparing mortality or morbidity rates within or among a number of communities. The possibility that the estimates of air pollution effects will be biased by other community differences related to health is particularly great in these studies. Concentrations of air pollutants are usually higher in urban than in rural areas, and many authors have noted that smoking patterns, family size, age distribution, occupation, domestic crowding, nutrition, physical activity and other characteristics of the population can differ between rural and urban areas. Although some studies have sought to match communities on important characteristics or use multivariate adjustment techniques to control for the effects of these factors, their effectiveness is typically unknown. This is especially true when complex regression models are used for adjustment, for the adjustment is limited by the degree to which the model correctly specifies the relation between these factors and the outcome under study.

Mortality Effects of Chronic Exposure to Sulfur Oxides and Particulate Matter

The study of Buck and Brown (46) was one of the first to show an association between annual average concentration of SO_2 and Black Smoke and mortality rate across communities in Great Britain. However, mortality data were obtained in 1955-59 and pollution was measured in 1962. Pollution levels were falling during this period. Although it has been argued that mortality effects were seen in boroughs where Black Smoke and SO_2 levels exceeded 200 $\mu g/m^3$, it is likely that exposures prior to and during 1955-59 were somewhat higher than in 1962. Wicken and Buck (47) also found differences in lung cancer and bronchitis mortality rates between areas of high and low pollution after adjusting for age, smoking habits and social class. However, this study was also limited by unavailability of concurrent air pollution measurements in most of the communities studied.

More recently, several investigators have used multivariate regression techniques to analyze mortality data obtained from vital statistics sources. The following sections discuss these investigations.

Analyses of Total Mortality Rates

As noted above, there are many reasons why mortality rates vary among communities. Therefore, study units should be selected to minimize variation due to factors other than air pollution. On the other hand, study units must be selected to conform with the available data. For mortality studies, Standard Metropolitan Statistical Areas (SMSA's) and cities meet this condition but present several difficulties. Investigators, recognizing that the study units differ with respect to factors other than air pollution, attempt to adjust for these differences by including socioeconomic and demographic variables in their analysis. Nevertheless, it is likely that the effects of variables such as personal habits, occupational exposure, and medical care cannot be fully quantified and eliminated in this way. If any of these factors covaries with air pollution levels, a spuriously large effect will be attributed to air pollution.

The evidence in a multiple regression analysis relating mortality to pollution can be expressed through the coefficients of the pollutants and their standard errors. Comparison of the results of regression analyses from major studies relating mortality rates to pollution levels across communities illustrates the problems that arise in interpreting these studies.

The four regression equations summarized in Table 10 are taken from the work of Lave and Seskin (*48*). TSP represents the average of 26 biweekly measurements of 24-hr TSP in each SMSA, while SO_4 is the lowest sulfate determination from these 26 observations. Regressions LS1 and LS2 were both obtained from the analysis of 1960 mortality data for 117 SMSA's. The two regression equations differ only in that the second contains one additional adjustment variable, home heating fuel. Adding this variable reduces the coefficients of the air pollutants by a factor of three and they are not significant in LS2. Lave and Seskin argue that this occurs because home heating fuels are a major pollution source, home heating fuels and pollutants are highly correlated. This contrast illustrates one effect of collinearity on the regression coefficients. Regression LS3 results from fitting the model from regression LS1 to 1961 data. Mortality and pollution values were about the same in the two years, and the coefficients are quite similar also. When the same model is fitted to the 1969 data (regression LS4), the estimated effects are larger even though mean TSP level declined from 118 $\mu g/m^3$ to 96 $\mu g/m^3$ and the average SO_4 level declined from 4.72 $\mu g/m^3$ to 3.46 $\mu g/m^3$. These comparisons show how sensitive these multiple regression analyses are to variable selection, and also raise questions of consistency.

Table 10. Coefficients of TSP and SO_4 in four regressions reported by Lave and Seskin.[a]

Regression	Source	Coefficient (SE)		Other variables[b]
		TSP	SO_4	
LS1	Data from 117 U.S. SMSA's in 1960	0.452 (0.169)	6.31 (2.33)	D, A, R, I, P
LS2	Data from 117 U.S. SMSA's in 1960	0.171 (0.158)	1.84 (2.16)	D, A, R, I, P, HHF
LS3	Data from 117 U.S. SMSA's in 1961	0.516 (0.178)	4.56 (2.49)	D, A, R, I, P
LS4	Data from 117 U.S. SMSA's in 1969	0.818 (0.241)	7.74 (3.67)	D, A, R, I, P

[a]Data of Lave and Seskin (*48*).
[b]Symbols used in this column are defined in Table 12.

Table 11. Coefficients of TSP and SO_4 in regressions analysis by Lipfert and Crocker et al.

Regression	Source	Coefficient		Other variables[a]
		TSP	SO_4	
L1	Data from 60 U.S. SMSA's in 1969[b]	0.73	5.4	D, A, R, I
L2	Data from 60 U.S. cities in 1969[b]	0.78	8.2	D, A, R, I
L3	Data from 136 U.S. cities in 1969[b]	1.00	-2.0	A, R, I, H, B
L4	Data from 181 U.S. cities in 1969[b]	0.72	-4.3	A, R, I, H, B, C, log D
C1	Data from 60 U.S. cities in 1960[c]	0.11	-0.31[d]	MD, MI, E, CH, C, CT, R, MA, DF

[a]Symbols used in this column are defined in Table 12.
[b]Data of Lipfert (*49*, *50*).
[c]Data of Crocker et al. (*51*).
[d]Coefficient of SO_2.

Results of four regression analyses reported by Lipfert (*49*, *50*) are shown in Table 11. The first (L1) is based on analysis of 1969 mortality data from 60 U.S. SMSA's, using a model much like regression LS4 in Table 10. Very similar coefficients are obtained. The first two models in Table 11 differ only in that the first uses mortality data from 60 SMSA's while the second uses mortality data from 60 U.S. cities. The coefficient of SO_4 is larger in the second regression using smaller geographic areas. Model L3 differs from L2 in that more cities are included and age of housing and birth rate are added as independent variables, while cigarette consumption is added in L4. Though the coefficient of TSP changes very little, the coefficient of SO_4 is negative in these regressions.

The final regression in Table 11 is taken from an analysis of 60 U.S. cities in 1970 by Crocker et al. (*51*). In addition to variables used by other investigators, this model includes variables for climate, education, availability of medical care and nutritional habits. Although Crocker uses SO_2 and not SO_4 as a pollution variable, neither pollutant contributes significantly to the regression. Crocker et al. report a correlation between SO_2 and SO_4 of 0.74.

The association between air pollutant concentration and mortality rates in different analyses can be summarized by the elasticity. An elasticity is a dimensionless number that represents the expected percent change in the dependent variable, mortality, associated with a 100% increase from the mean value in each of the pollutant variables in the regression. Elasticity is computed by multiplying each air pollutant regression coefficient by the average value of that pollutant in the data set, adding these quantities for all pollutants, and dividing by the average mortality over study units. So long as the set of pollution variables chosen contains variables capturing the total association between all air pollutants and mortality, the elasticity will be relatively insensitive to the choice of a subset of these highly collinear pollutant variables. Thus, the elasticities can be viewed, at least approximately, as measuring the total mortality effect of all pollutants included.

Table 13 gives elasticities for the nine regression analyses summarized in Tables 10 and 11. Regressions LS1, LS3, and LS4 were the simplest models used by Lave and Seskin and had the largest elasticity. In regressions using more variables, such as home heating fuel in regression LS2, smaller elasticities were obtained. (When occupation was added to the model for regression LS1, elasticity declined to 0.05). Regressions L1 and L2 included population density, percentage above 65, percentage nonwhite and percentage with income below $3,000 as independent variables. When birth rate and age of homes were added (L3) or cigarette smoking (L4), elasticity declined to 0.06 and 0.04, respectively. The effect of cigarette smoking should especially be noted. Finally, in the analysis by Crocker et al. (*51*) using several other added independent variables (C1), the elasticity was nearly zero. These variables included measures of medical care, diet, climate and cigarette consumption and could easily be defended as critically important in any analysis controlling for other factors expected to influence mortality.

Though it has sometimes been argued that smoking is not associated with air pollution concentration, Crocker et al. report a correlation of 0.23 between cigarette consumption and sulfur dioxide in the 60 cities in their study. Certainly the two variables are not causally related, but both may reflect other characteristics of the population.

Schwing and McDonald (*52*) report on a study of

Table 12. Definitions of other independent variables used in multiple regressions in Tables 10 and 11.

Variable	Definition
D	Population density in person/mile^2
A	Percentage of population 65 or older
R	Percentage of population nonwhite
I	Percentage of population with income below $3000/year
P	Log arithm of SMSA population
HHF	Percentage of homes using each of several home heating fuels
H	Percentages of housing units built before 1960
B	Births/1000 population/year
MD	No. of physicians per capita
MI	Median income
E	Percentage of persons 25 or older with high school diploma
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C	No. of cigarette packs purchased per capita
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MA	Median age

Table 13. Elasticities for air pollutants in nine regression analyses of mortality.

Regression	Elasticity
LS1	0.09
LS2	0.03
LS3	0.09
LS4	0.12
L1	0.10
L2	0.09
L3	0.06
L4	0.04
C1	0.004

46 SMSA's (1959-61) in which 23 explanatory variables are used, including climate, socioeconomic, occupational and smoking variables and eight air pollutants. This study differs from those summarized in Tables 10 and 11 in that the investigators included all 23 variables in their models. To counter severe collinearity, the authors used two methods of analysis, ridge regression and constrained least squares, rather than ordinary least squares. (The previously reported studies all used ordinary least squares.)

Ridge regression is a numerical method for stabilizing estimates of regression coefficients from a data set that has collinear explanatory variables. While the method does achieve stability, it does so by selecting an arbitrary constant that has the effect of shrinking each estimated coefficient toward zero. Though ridge regression leads to smaller standard errors for the estimated coefficients, these coefficients are no longer interpretable as partial regression coefficients, that is, measures of the effects of changes in a single variable while the other variables are held fixed. As emphasized throughout this presentation, collinear data sets are fundamentally insufficient to allow assignment of mortality effects to individual members of a group of collinear explanatory variables.

Schwing and McDonald also use constrained least squares, constraining the air pollution coefficients to positive values. This may be unreasonable when eight air pollutants are studied simultaneously. Thurston et al. (*53*) report that respirable sulfate as a fraction of total sulfate is not constant over different levels of air quality. They note that in "dirty" cities the fraction is 0.6 to 0.7 while in "clean" cities the fraction is 0.8 to 0.9. Thus, if the respirable sulfate affects mortality, an indicator of overall air quality such as TSP could take a negative sign, when both TSP and respirable sulfates are included in the model, to account for the difference in the respirable sulfate fraction between cities.

Schwing and McDonald report an elasticity of 0.22 from ridge regression and an elasticity of 0.045 from constrained least squares. These values are still an order of magnitude larger than that reported by Crocker et al. (0.004).

This discussion has been provided to illustrate the limitations of multiple regression analyses of vital statistics data, using explanatory variables defined by data availability rather than intrinsic interest, and complicated by severe collinearity of pollutant and other explanatory variables. The model can only be approximately correct, the surrogate explanatory variables can never lead to an adequate adjusted analysis, and it is impossible to separate associations of mortality rate with pollutant and confounding variables. This group of studies, in our opinion, provides no reliable evidence for assessing the health effects of sulfur dioxide and particulate matter.

Morbidity Effects of Chronic Exposure to Sulfur Oxides and Particulate Matter

This section focuses on those studies that provide the air pollution and health-status data necessary to assess the morbidity effects of chronic exposure to sulfur oxides or particulates. These studies most commonly represent the cumulative exposure to air pollutants as an arithmetic average concentration of sulfur compounds and particulates during an interval including the study period. Since chronic exposure may refer to the lifetime of an individual, this measure of exposure may be misleading when pollution concentrations have changed substantially during the years preceding the study. Morbidity outcomes are generally limited to respiratory symptoms and measured lung function. Respiratory symptoms are most commonly assessed with self- or interviewer-administered questionnaires. The standard questionnaire developed by the British Medical Research Council (*54*) has been used typically, with modifications or additions. [A standard questionnaire has recently been developed under the joint sponsorship of the American Thoracic Society and the Division of Lung Diseases, National Heart, Lung and Blood Institute, and is recommended for all U.S. population studies (*55*).] Lung function is generally measured by spirometry from which both forced expiratory volume and flow rates can be determined. Relationships between air pollution and nonrespiratory or systemic morbidity are usually not explored.

Most of the studies reviewed are cross-sectional investigations of morbidity prevalence. Many of the difficulties of inferring a cause-effect relationship between air pollution and health outcome in such studies have been discussed above. Typically, a few cities or areas with different air pollution concentrations are compared. The study populations are either matched on, or analyses standardized for, differences in variables such as age distribution, race, socioeconomic characteristics, occupational categories, and smoking habits. Often only two cities or areas with contrasting air quality are compared. Rarely are more than half a dozen areas compared. The effect of limited observations at differing air pollution levels is partially mitigated by the ability to gather extensive information on outcome variables such as ventilatory function and symptom

prevalence and on potentially confounding factors such as cigarette smoking and occupation. Nevertheless, when only a few observations have been made at different air pollution levels, it is difficult to construct generalizable quantitative dose-response relationships.

The major studies suggesting morbidity effects of exposure to elevated concentrations of particulate matter and/or sulfur oxides have been reported from three countries; Great Britain, Poland and the Unites States.

British Studies. Lunn et al. (*56*, *57*) studied schoolchildren living in four areas of Sheffield, England with different air pollution concentrations. These concentrations are shown in Table 14 for the two winters studied. Questionnaires were answered by parents and the investigators found substantially higher prevalence of symptoms of respiratory disease in the three more polluted areas than in the less polluted area (Table 15). These children were followed up in 1967-69 when they were nine years old (*57*). As a result of the institution of smoke control, smoke levels were reduced to about half their former levels. When children from the three dirtier areas were pooled and compared to children from the clean area in the second study, there were no differences in symptom prevalence rates. Pollution concentrations in the later period were 48 $\mu g/m^3$ (BS) and 123 $\mu g/m^3$ (SO_2) in the clean area and averaged about 140 $\mu g/m^3$ (BS) and 200 $\mu g/m^3$ (SO_2) in the dirty areas.

Douglas and Waller (*58*) reported on a study of a sample of children born during one week in March 1946. Air pollution was assessed by creating an index based on coal consumption. The authors created four pollution categories, and found that the prevalence of lower respiratory disease, but not upper respiratory disease increased with increasing pollution when the children were studied at ages 6, 7, 11 and 15.

Comparison of the index to measured BS and SO_2 concentrations in 1962 established a gradient of mean annual pollutant concentrations across the four pollution categories. The lowest pollutant concentrations in 1962 among the categories with increased morbidity were 130 $\mu g/m^3$ (BS) and 130 $\mu g/m^3$ (SO_2). Colley et al. (*59*) followed this cohort at age 20, and Kiernan et al. (*60*) followed it again at age 25. Neither investigation found an association of respiratory disease symptom with previous air pollution exposure, although at age 20 the prevalence of respiratory symptoms was slightly higher among those who had lived in high pollution areas (11.5%) than among those from low pollution areas (10.2%), and a similar relationship was found at age 25. Respiratory symptom prevalence was associ-

Table 14. Air pollution concentrations in communities studied by Lunn et al.[a]

	Concentration (24-hr average), $\mu g/m^3$							
	Greenhill		Longley		Park		Attercliffe	
	1964	Winter 1965-66	1964	Winter 1965-66	1964	Winter 1965-66	1964	Winter 1965-66
BS	97	(70–78)	230	177	262	220	301	249
SO_2	123	(109–134)	181	194	219	241	275	301

[a]Data of Lunn et al. (*56*).

Table 15. Symptoms by area in the study of Lunn et al.[a]

	Greenhill			Longley			Park			Attercliffe		
Symptom	N[b]	P[c]	SE[d]	N	P	SE	N	P	SE	N	P	SE
Nasal discharge	408	6.4	1.2	192	5.2	1.6	130	15.4	3.2	82	14.6	3.9
≥ 3 colds	413	34.4	2.3	194	43.8	3.4	130	48.5	4.4	82	46.3	5.5
Eardrum finding	381	9.4	1.5	178	10.7	2.3	125	14.4	3.1	75	17.2	4.4
Frequent cough	411	22.9	2.1	194	36.1	3.4	130	34.6	4.2	82	50.0	5.5
Cold going to chest	412	34.7	2.4	194	42.8	3.6	130	40.0	4.3	82	53.7	5.5
Lower respiratory infection	413	23.0	4.3	192	36.0	5.8	127	35.0	7.1	82	30.0	9.2

[a]Data of Lunn et al. (*56*).
[b]The number of responses obtained.
[c]The percentage of positive responses.
[d]The estimated standard error of the observed percentage.

ated with cigarette smoking at these ages. Because pollution concentrations in 1962 were presumably much lower than those in earlier years, the concentrations cited probably understate the exposure of study participants. We note that exposure during childhood to air pollution concentrations in excess of 130 $\mu g/m^3$ (BS) and 130 $\mu g/m^3$ (SO_2) resulted in no significant increase in respiratory illness by adulthood compared to those exposed to lower air pollution concentrations.

Lambert and Reid (*61*) mailed self-administered questionnaires to 18,379 men and women in Britain to assess the relationship of smoking and air pollution to bronchitis symptoms. The reply rate was 74% from the 35-69 year-old age group studied. From the 9,975 replies analyzed, the authors conclude that the prevalence of respiratory symptoms increased with pollution levels independently of cigarette smoking. Air pollution was found to have a greater effect on the symptoms of smokers than nonsmokers, in terms of the absolute difference in symptom prevalence rates.

The exposure levels in this study are approximate, since only 30% of the population surveyed was covered by actual air pollution measurements. The pollutants measured, BS and SO_2, were taken from 1965 data of the British National Air Pollution Survey. The balance of the population was assigned to exposure categories based on the Douglas-Waller (*58*) index which was developed from 1952 domestic coal consumption. A comparison of symptom-prevalence ratios from measurements of BS, SO_2, and index values shows similar ratios and similar gradients for symptoms with increasing pollution. The lack of complete air pollution data adds uncertainty to the exposure estimates, but in those areas where BS and SO_2 measurements were available, increased prevalence of symptoms was found in association with BS and SO_2 levels between 100 and 150 $\mu g/m^3$, as an annual average.

Polish Studies. A study of two areas of contrasting air quality in Cracow, Poland, was conducted by Sawicki. The study began with a cross sectional survey in 1968 and continued with a prospective study until 1973 (*62*). Annual average particulate values in 1968 were 90 and 170 $\mu g/m^3$. In 1968, chronic bronchitis prevalence was greater in the more polluted area for men, but not for women. The difference was statistically significant for men who were nonsmokers or present smokers. These data are given in Table 16. Asthmatic disease prevalence was also greater among smokers living in the more polluted area and FEV_1 as a percentage of FVC was lower for most age-sex-smoking-history groups.

Between 1968 and 1973, the annual mean concentration of SO_2 and BS declined slightly for Cracow as a whole but increased slightly at the sites close to the homes of most study participants. In 1973, respiratory disease was again more prevalent among those living in the areas of high pollution for many, but not all of the age, race, and sex groups studied. Mean FEV_1 level was not significantly different in the two areas. The prevalence of obstructive disease was higher in the more polluted area only for present smokers. The authors concluded that smoking and, to a lesser extent, occupational exposure and age had the greatest effect on respiratory illness prevalence, while air pollution at the place of residence was listed as one of several factors having a smaller effect on respiratory illness.

Rudnik et al. (*63*) reported extensively on the early phase (1970-1976) of a long-term study of the factors which influence development of childhood

Table 16. Prevalence of chronic bronchitis by sex and smoking status in 1968.[a]

	Low pollution area						High pollution area					
	Men			Women			Men			Women		
Smoking status	N[b]	P[c]	SE[d]	N	P	SE	N	P	SE	N	P	SE
Total	323	11[e]	1.7	362	4	1.0	262	19[e]	2.4	396	5	1.1
Nonsmokers	56	4	2.6	266	2	0.9	58	7	3.4	264	3	1.0
Ex-smokers	46	4	2.9	18	11	7.4	40	5	3.4	34	6	4.1
Present smokers	221	14[e]	2.3	78	10	3.4	164	27[e]	3.5	98	10	3.0
Period of smoking												
1-10 years	56	5	2.9	41	7	4.0	42	7	3.9	42	5	3.4
11-20 years	89	9[e]	3.0	21	14	7.6	38	29[e]	7.4	18	6	5.6
> 21 years	76	28	5.2	16	13	8.4	84	36	5.2	38	18	6.2

[a] Data of Sawicki (*62*).
[b] Number of persons studied.
[c] Prevalence of chronic bronchitis.
[d] Standard error of the observed rate.
[e] Rates which are significantly different at the 0.05 level.

Analyses of Total Mortality Rates

As noted above, there are many reasons why mortality rates vary among communities. Therefore, study units should be selected to minimize variation due to factors other than air pollution. On the other hand, study units must be selected to conform with the available data. For mortality studies, Standard Metropolitan Statistical Areas (SMSA's) and cities meet this condition but present several difficulties. Investigators, recognizing that the study units differ with respect to factors other than air pollution, attempt to adjust for these differences by including socioeconomic and demographic variables in their analysis. Nevertheless, it is likely that the effects of variables such as personal habits, occupational exposure, and medical care cannot be fully quantified and eliminated in this way. If any of these factors covaries with air pollution levels, a spuriously large effect will be attributed to air pollution.

The evidence in a multiple regression analysis relating mortality to pollution can be expressed through the coefficients of the pollutants and their standard errors. Comparison of the results of regression analyses from major studies relating mortality rates to pollution levels across communities illustrates the problems that arise in interpreting these studies.

The four regression equations summarized in Table 10 are taken from the work of Lave and Seskin (*48*). TSP represents the average of 26 biweekly measurements of 24-hr TSP in each SMSA, while SO_4 is the lowest sulfate determination from these 26 observations. Regressions LS1 and LS2 were both obtained from the analysis of 1960 mortality data for 117 SMSA's. The two regression equations differ only in that the second contains one additional adjustment variable, home heating fuel. Adding this variable reduces the coefficients of the air pollutants by a factor of three and they are not significant in LS2. Lave and Seskin argue that this occurs because home heating fuels are a major pollution source, home heating fuels and pollutants are highly correlated. This contrast illustrates one effect of collinearity on the regression coefficients. Regression LS3 results from fitting the model from regression LS1 to 1961 data. Mortality and pollution values were about the same in the two years, and the coefficients are quite similar also. When the same model is fitted to the 1969 data (regression LS4), the estimated effects are larger even though mean TSP level declined from 118 $\mu g/m^3$ to 96 $\mu g/m^3$ and the average SO_4 level declined from 4.72 $\mu g/m^3$ to 3.46 $\mu g/m^3$. These comparisons show how sensitive these multiple regression analyses are to variable selection, and also raise questions of consistency.

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This discussion has been provided to illustrate the limitations of multiple regression analyses of vital statistics data, using explanatory variables defined by data availability rather than intrinsic interest, and complicated by severe collinearity of pollutant and other explanatory variables. The model can only be approximately correct, the surrogate explanatory variables can never lead to an adequate adjusted analysis, and it is impossible to separate associations of mortality rate with pollutant and confounding variables. This group of studies, in our opinion, provides no reliable evidence for assessing the health effects of sulfur dioxide and particulate matter.

Morbidity Effects of Chronic Exposure to Sulfur Oxides and Particulate Matter

This section focuses on those studies that provide the air pollution and health-status data necessary to assess the morbidity effects of chronic exposure to sulfur oxides or particulates. These studies most commonly represent the cumulative exposure to air pollutants as an arithmetic average concentration of sulfur compounds and particulates during an interval including the study period. Since chronic exposure may refer to the lifetime of an individual, this measure of exposure may be misleading when pollution concentrations have changed substantially during the years preceding the study. Morbidity outcomes are generally limited to respiratory symptoms and measured lung function. Respiratory symptoms are most commonly assessed with self- or interviewer-administered questionnaires. The standard questionnaire developed by the British Medical Research Council (*54*) has been used typically, with modifications or additions. [A standard questionnaire has recently been developed under the joint sponsorship of the American Thoracic Society and the Division of Lung Diseases, National Heart, Lung and Blood Institute, and is recommended for all U.S. population studies (*55*).] Lung function is generally measured by spirometry from which both forced expiratory volume and flow rates can be determined. Relationships between air pollution and nonrespiratory or systemic morbidity are usually not explored.

Most of the studies reviewed are cross-sectional investigations of morbidity prevalence. Many of the difficulties of inferring a cause-effect relationship between air pollution and health outcome in such studies have been discussed above. Typically, a few cities or areas with different air pollution concentrations are compared. The study populations are either matched on, or analyses standardized for, differences in variables such as age distribution, race, socioeconomic characteristics, occupational categories, and smoking habits. Often only two cities or areas with contrasting air quality are compared. Rarely are more than half a dozen areas compared. The effect of limited observations at differing air pollution levels is partially mitigated by the ability to gather extensive information on outcome variables such as ventilatory function and symptom

prevalence and on potentially confounding factors such as cigarette smoking and occupation. Nevertheless, when only a few observations have been made at different air pollution levels, it is difficult to construct generalizable quantitative dose-response relationships.

The major studies suggesting morbidity effects of exposure to elevated concentrations of particulate matter and/or sulfur oxides have been reported from three countries; Great Britain, Poland and the Unites States.

British Studies. Lunn et al. (*56*, *57*) studied schoolchildren living in four areas of Sheffield, England with different air pollution concentrations. These concentrations are shown in Table 14 for the two winters studied. Questionnaires were answered by parents and the investigators found substantially higher prevalence of symptoms of respiratory disease in the three more polluted areas than in the less polluted area (Table 15). These children were followed up in 1967-69 when they were nine years old (*57*). As a result of the institution of smoke control, smoke levels were reduced to about half their former levels. When children from the three dirtier areas were pooled and compared to children from the clean area in the second study, there were no differences in symptom prevalence rates. Pollution concentrations in the later period were 48 $\mu g/m^3$ (BS) and 123 $\mu g/m^3$ (SO_2) in the clean area and averaged about 140 $\mu g/m^3$ (BS) and 200 $\mu g/m^3$ (SO_2) in the dirty areas.

Douglas and Waller (*58*) reported on a study of a sample of children born during one week in March 1946. Air pollution was assessed by creating an index based on coal consumption. The authors created four pollution categories, and found that the prevalence of lower respiratory disease, but not upper respiratory disease increased with increasing pollution when the children were studied at ages 6, 7, 11 and 15.

Comparison of the index to measured BS and SO_2 concentrations in 1962 established a gradient of mean annual pollutant concentrations across the four pollution categories. The lowest pollutant concentrations in 1962 among the categories with increased morbidity were 130 $\mu g/m^3$ (BS) and 130 $\mu g/m^3$ (SO_2). Colley et al. (*59*) followed this cohort at age 20, and Kiernan et al. (*60*) followed it again at age 25. Neither investigation found an association of respiratory disease symptom with previous air pollution exposure, although at age 20 the prevalence of respiratory symptoms was slightly higher among those who had lived in high pollution areas (11.5%) than among those from low pollution areas (10.2%), and a similar relationship was found at age 25. Respiratory symptom prevalence was associ-

Table 14. Air pollution concentrations in communities studied by Lunn et al.[a]

	Concentration (24-hr average), $\mu g/m^3$							
	Greenhill		Longley		Park		Attercliffe	
	1964	Winter 1965-66	1964	Winter 1965-66	1964	Winter 1965-66	1964	Winter 1965-66
BS	97	(70–78)	230	177	262	220	301	249
SO_2	123	(109–134)	181	194	219	241	275	301

[a]Data of Lunn et al. (*56*).

Table 15. Symptoms by area in the study of Lunn et al.[a]

Symptom	Greenhill			Longley			Park			Attercliffe		
	N[b]	P[c]	SE[d]	N	P	SE	N	P	SE	N	P	SE
Nasal discharge	408	6.4	1.2	192	5.2	1.6	130	15.4	3.2	82	14.6	3.9
≥ 3 colds	413	34.4	2.3	194	43.8	3.4	130	48.5	4.4	82	46.3	5.5
Eardrum finding	381	9.4	1.5	178	10.7	2.3	125	14.4	3.1	75	17.2	4.4
Frequent cough	411	22.9	2.1	194	36.1	3.4	130	34.6	4.2	82	50.0	5.5
Cold going to chest	412	34.7	2.4	194	42.8	3.6	130	40.0	4.3	82	53.7	5.5
Lower respiratory infection	413	23.0	4.3	192	36.0	5.8	127	35.0	7.1	82	30.0	9.2

[a]Data of Lunn et al. (*56*).
[b]The number of responses obtained.
[c]The percentage of positive responses.
[d]The estimated standard error of the observed percentage.

ated with cigarette smoking at these ages. Because pollution concentrations in 1962 were presumably much lower than those in earlier years, the concentrations cited probably understate the exposure of study participants. We note that exposure during childhood to air pollution concentrations in excess of 130 $\mu g/m^3$ (BS) and 130 $\mu g/m^3$ (SO_2) resulted in no significant increase in respiratory illness by adulthood compared to those exposed to lower air pollution concentrations.

Lambert and Reid (*61*) mailed self-administered questionnaires to 18,379 men and women in Britain to assess the relationship of smoking and air pollution to bronchitis symptoms. The reply rate was 74% from the 35-69 year-old age group studied. From the 9,975 replies analyzed, the authors conclude that the prevalence of respiratory symptoms increased with pollution levels independently of cigarette smoking. Air pollution was found to have a greater effect on the symptoms of smokers than nonsmokers, in terms of the absolute difference in symptom prevalence rates.

The exposure levels in this study are approximate, since only 30% of the population surveyed was covered by actual air pollution measurements. The pollutants measured, BS and SO_2, were taken from 1965 data of the British National Air Pollution Survey. The balance of the population was assigned to exposure categories based on the Douglas-Waller (*58*) index which was developed from 1952 domestic coal consumption. A comparison of symptom-prevalence ratios from measurements of BS, SO_2, and index values shows similar ratios and similar gradients for symptoms with increasing pollution. The lack of complete air pollution data adds uncertainty to the exposure estimates, but in those areas where BS and SO_2 measurements were available, increased prevalence of symptoms was found in association with BS and SO_2 levels between 100 and 150 $\mu g/m^3$, as an annual average.

Polish Studies. A study of two areas of contrasting air quality in Cracow, Poland, was conducted by Sawicki. The study began with a cross sectional survey in 1968 and continued with a prospective study until 1973 (*62*). Annual average particulate values in 1968 were 90 and 170 $\mu g/m^3$. In 1968, chronic bronchitis prevalence was greater in the more polluted area for men, but not for women. The difference was statistically significant for men who were nonsmokers or present smokers. These data are given in Table 16. Asthmatic disease prevalence was also greater among smokers living in the more polluted area and FEV_1 as a percentage of FVC was lower for most age-sex-smoking-history groups.

Between 1968 and 1973, the annual mean concentration of SO_2 and BS declined slightly for Cracow as a whole but increased slightly at the sites close to the homes of most study participants. In 1973, respiratory disease was again more prevalent among those living in the areas of high pollution for many, but not all of the age, race, and sex groups studied. Mean FEV_1 level was not significantly different in the two areas. The prevalence of obstructive disease was higher in the more polluted area only for present smokers. The authors concluded that smoking and, to a lesser extent, occupational exposure and age had the greatest effect on respiratory illness prevalence, while air pollution at the place of residence was listed as one of several factors having a smaller effect on respiratory illness.

Rudnik et al. (*63*) reported extensively on the early phase (1970-1976) of a long-term study of the factors which influence development of childhood

Table 16. Prevalence of chronic bronchitis by sex and smoking status in 1968.[a]

	Low pollution area						High pollution area					
	Men			Women			Men			Women		
Smoking status	N[b]	P[c]	SE[d]	N	P	SE	N	P	SE	N	P	SE
Total	323	11[e]	1.7	362	4	1.0	262	19[e]	2.4	396	5	1.1
Nonsmokers	56	4	2.6	266	2	0.9	58	7	3.4	264	3	1.0
Ex-smokers	46	4	2.9	18	11	7.4	40	5	3.4	34	6	4.1
Present smokers	221	14[e]	2.3	78	10	3.4	164	27[e]	3.5	98	10	3.0
Period of smoking												
1-10 years	56	5	2.9	41	7	4.0	42	7	3.9	42	5	3.4
11-20 years	89	9[e]	3.0	21	14	7.6	38	29[e]	7.4	18	6	5.6
> 21 years	76	28	5.2	16	13	8.4	84	36	5.2	38	18	6.2

[a]Data of Sawicki (*62*).
[b]Number of persons studied.
[c]Prevalence of chronic bronchitis.
[d]Standard error of the observed rate.
[e]Rates which are significantly different at the 0.05 level.

chronic nonspecific respiratory disease (CNSRD). The authors discussed an early pilot study that was used to test and develop the design and instruments for the main study. The main study, scheduled for completion in 1982, compares 3805 eight to ten year olds, on respiratory symptoms, illness, and lung function (PEFR), in the Polish communities of Cracow (two areas), Nowy Targ, and Limanowa. The arithmetic mean air pollution values for each of two years in these communities are shown in Table 17. The authors provide detailed information on the distribution and seasonal pattern of the air pollution observations.

Most of the symptoms analyzed and past respiratory illness were less prevalent in the cleaner communities of Nowy Targ and Limanowa than in the two areas in Cracow. There was some indication that symptom rates were lower in the cleanest city of Limanowa than in Nowy Targ. Peak expiratory flow rate (PEFR) was lower in Cracow. In fact, PEFR of children without symptoms in Cracow was lower than in symptom-positive children in the cleaner areas. The authors concluded that living in the more polluted community had a deleterious effect on respiratory symptoms, illness, and lung function. The effect of living in Cracow was greater than the other social, economic and environmental factors investigated by the authors. Unfortunately, PEFR as measured with Wright peak flow meters is subject to considerable variation due to variability between machines. It is not clear from these reports how this phenomenon was controlled.

U.S. Studies. A series of studies conducted in a New Hampshire pulp mill town, beginning in 1961, represent some of the earliest work on the health effects of chronic exposure to sulfur oxides and particulates in this country. In the initial study, Ferris and his colleagues (*64*, *65*) compared symptom prevalence and lung function in three areas with different pollution levels within Berlin, New Hampshire and found no associations after control for cigarette smoking. In a subsequent study (*66*), a random survey was carried out in the relatively clean city of Chilliwack, British Columbia. Though the pollution levels were considerably lower than those in Berlin, the prevalence of chronic respiratory disease was not significantly different in the two towns after adjustment for age and smoking habits.

The average values of FEV_1 and peak expiratory flow rate (PEFR) were higher in Chilliwack than in Berlin for 30 of 32 subgroups defined by sex and smoking history after controlling for age and height. The authors suggested that differences in ethnicity, weather, medical facilities and other factors may have confounded the examination of the effect of air pollution.

The Berlin, New Hampshire population was followed up in 1967 and again in 1973 (*67-69*). During the period between 1961 and 1967, all measured indicators of air pollution fell. In the 1973 follow-up, sulfation rates nearly doubled from the 1967 level (0.469 to 0.901 mg SO_3/100 cm^2/day) while TSP values fell from 131 to 80 $\mu g/m^3$ (Table 18). Concentrations of SO_2 were estimated by assuming that all atmospheric sulfur was in the form of SO_2. For all three periods, concentrations of SO_2 at these sites were below the present annual ambient air standard.

During the 1961 to 1967 period, standardized respiratory symptom rates decreased and there was an indication that lung function also improved. Thus, the higher pollution concentrations seen in 1961 were judged to be associated with increased incidence of respiratory symptoms and impairment of lung function. Between 1967 and 1973, age-sex standardized respiratory symptom rates and age-sex-height standardized pulmonary function levels were unchanged. The authors concluded that either

Table 17. Two-year mean air pollution values.[a]

	SO_2 $\mu g/m^3$		BS, $\mu g/m^3$	
	1974	1975	1974	1975
Cracow-1	111.4	108.1	169.7	150.9
Cracow-2	138.2	148.5	204.9	227.4
Nowy Targ	57.1	66.8	82.0	79.8
Limanowa	41.5	64.3	53.4	49.2

[a]Data of Rudnick et al. (*65*).

Table 18. Pollution levels, Berlin, New Hampshire, during three study periods.

Year (s)	Total dustfall, g/m^2/30 days	TSP, $\mu g/m^3$	Sulfation (lead peroxide), mg SO_3/100 cm^2/day	Sulfation converted to SO_2, $\mu g/m^3$[a]
1961	18.4	180	0.731	55
1966–67	14.3	~131	0.469	37
1973	—	80	0.901	66

[a]Assuming all sulfur in the form of SO_2.

the change in air pollution concentration during the latter period was not associated with a change in respiratory health or that the study was too small to detect an effect. The comparison of health status between 1961 and 1967 suggests morbidity effects at 180 $\mu g/m^3$ (TSP) and 55 $\mu g/m^3$ (SO_2). These effects could represent a combination of transient (acute) and irreversible (chronic) effects of air pollution exposure. The TSP value of 180 $\mu g/m^3$ was based on sampling during the summer months and probably underestimated the annual average concentration. The comparison of 1967 to 1973 is uninformative because of offsetting changes in pollution concentrations, although SO_2 concentrations were below present ambient standards in both periods.

Mostardi and Leonard (*70*) compared the results of pulmonary function testing in 42 high school students from an urban area with pollution concentrations of 100 $\mu g/m^3$ (SO_2) and 109 $\mu g/m^3$ (TSP) and 50 students from a rural area with pollution concentrations of 72 $\mu g/m^3$ (SO_2) and 83 $\mu g/m^3$ (TSP) (maximum annual average over five years). This study was flawed by failure to consider smoking effects.

Subsequently, Mostardi and Martell (*71*) reported on 173 and 161 students respectively from the same urban and rural areas. They tested FVC and $FEV_{0.75}$ on subjects residing for 4 years or more in the areas. The groups were analyzed separately by sex and nonsmoking males were separately considered. The two groups had similar anthropometric characteristics. Approximately 20% lower values of $FEV_{0.75}$ and 10% lower values of FVC were reported in the more polluted area for the total group, for males, females, and for non-smoking males. While a higher proportion of smokers was found in the urban area (12% vs. 6% in the rural area) the authors claim this did not influence their results. They did not mention race in this study. In the first report (*70*) the authors found that the lung function differences persisted after exclusion of the three black students in the urban area.

The observed differences of 20% for $FEV_{0.75}$ and 10% for FVC in two communities with relatively small differences in ambient concentrations of SO_2 and TSP are striking. Other studies discussed here suggest that air pollution at these levels would not have this large an impact on lung function. This implies that other community differences such as racial composition or socioeconomic status may have contributed to the intercommunity differences. The observed differences cannot be reliably attributed to differences in air pollution concentrations.

The remainder of the evidence for health effects of sulfur oxides and particulate matter comes from the Community Health and Environment Surveillance System (CHESS) program, sponsored by the Environmental Protection Agency during the late 1960's and early 1970's. Much of this work was published in a monograph (*72*) and subsequently summarized in three brief papers (*73-75*). These studies have been severely criticized. The most important criticism is that methodology and quality control for aerometric measurements was seriously flawed. In particular, spills of reagent and other errors in handling measuring equipment led to underreporting of SO_2 values by 50 to 100%, while smaller biases were identified in the procedures for particulate measurement, resulting in underreporting by an estimated 10 to 30%. A number of other problems of study design, participant follow-up and data quality control were detected, raising doubts about the accuracy and proper interpretation of reported results. Ultimately, the CHESS studies were the subject of a special Congressional hearing (*76*) and an investigation by an expert panel convened by a Committee of the U.S. House of Representatives (*77*). The principal criticism of the CHESS report arising from this review was that the data had been overinterpreted in the CHESS monograph.

As we have indicated, observational studies of the health effects of air pollution are particularly difficult to conduct because individual exposure is poorly measured and populations may not be comparable in ways related to respiratory health. In view of the special problems occurring in the studies published in the CHESS monograph and the failure of subsequent publications to meet these criticisms, we believe that these studies cannot be used to assess the exposure response relationship between sulfur oxide and particulate concentrations and morbidity. This decision substantially reduces the evidence for morbidity effects of chronic exposure to particulates and SO_2 at levels near present air quality standards, in that most of these studies reported health effects in association with pollutant concentrations near these standards. A more extensive discussion of this controversy can be found in the above cited congressional reports and a recent review article (*78*).

Two studies which were part of the CHESS program were published separately (*79*, *80*). Information in these articles addresses some of the criticisms of the CHESS program. Hammer et al. (*79*) surveyed children in four metropolitan New York communities chosen for socioeconomic similarity.

Some of the aerometric data used in Hammer's analysis are shown in Table 19. The TSP values for 1968-70 were obtained by extrapolating from the TSP values at the Manhattan station using dustfall values in each borough and the ratio of dustfall to TSP at the Manhattan station. Values of SO_2 in

Table 19. Approximate air pollution concentrations.[a]

Pollutant		Air pollution concentration, μg/m³ 1968-1970	1971	1972
SO_2	Riverhead	N/A[b]	23	22
	Queens	175	51	50
	Bronx	250	51	38
TSP	Riverhead	N/A[b]	34	36
	Queens	85	63	89
	Bronx	110	86	60

[a]Data of Hammer et al. (79).
[b]Not available.

Queens and Bronx were obtained from stations in the boroughs. Data for Riverhead were provided by Suffolk County (New York). The fourth community, Sheepshead, was geographically contiguous to the area studied in Queens, and was assumed to have similar pollution values. All data for 1971 and 1972 were obtained from the CHESS monitoring network. Although Riverhead unquestionably had substantially less air pollution than the other three communities, both historically and during the study, the values cited can be regarded only as approximations to the ambient concentrations in the study communities. Questions on respiratory disease were answered retrospectively by parents. Significant differences were found in rates of lower respiratory disease in the low pollution community compared to the three high pollution communities for all ages from 1 to 12. Sex and education of head of household were considered in the analysis. Although smoking may have been a factor in older children, this study suggests morbidity effects at pollution concentrations of about 175 μg/m³ (SO_2) and 85 μg/m³ (TSP), using the average of the annual exposures over the years 1968 to 1970.

Interpretation of this study is complicated by a 10-fold decline in SO_2 and 3-fold decline in TSP over the 12 year period and by the lack of direct local measurement of air pollution concentration. More detailed information might improve exposure estimation for each child by age and period of exposure.

Hammer (80) also conducted a retrospective study, using parent-answered questionnaires covering four years recall of acute lower respiratory disease in 10,000 children aged 1 to 12 years. The two communities chosen for comparison differed in particulate air pollution concentration but had low SO_2 concentrations (Table 20).

The values for 1968-1970 cited in Table 20 were obtained by fitting trend lines to a few data points. As with the New York study, we can be confident that the cleaner community (Charlotte) had lower TSP concentrations, while in this study both communities had very low SO_2 concentrations. However, the TSP concentrations cited are approximate.

Hammer found that lower respiratory disease morbidity was less prevalent for children in the cleaner community (Table 21). A separate analysis of children with bronchial asthma produced more equivocal findings.

Among asthmatics, morbidity rates in the more polluted community were greater for only about half of the comparisons made. In the case of asthmatic blacks, bronchitis rates were greater in the cleaner community. On the whole, this study showed an association between TSP concentration and morbidity level.

Among the remaining studies in the CHESS program, the study of chronic respiratory disease prevalence in the Salt Lake Basin (81) is deserving of further attention. Although large and statistically significant differences were found in disease prevalence between communities with high and low levels of SO_2 and sulfates, these pollutants were among those found to be especially inaccurately measured by the CHESS aerometric network, and Utah State Aerometric was incomplete for the relevant years. Nevertheless, the health data have not been convincingly criticized, and an air pollution gradient was recognized to exist across the study communities, despite problems of precise measurement. Further work with these data may increase the acceptance of this study.

At the August 1980 meeting of the Clean Air Scientific Advisory Committee, EPA officials reported that unacceptably high data entry error rates had been detected in some CHESS data sets, and that data sets for the major CHESS studies would be reentered and reanalyzed to establish the validity of earlier results reported from the CHESS program. Unfortunately, this report further weakens the credibility of CHESS results. Although we cite results from two CHESS studies, continued use of these findings is contingent upon successful validation of the data sets by the staff of the EPA.

The studies that have been reviewed in this section provide the observational evidence for mor-

Table 20. Approximate air pollution values for Birmingham and Charlotte, 1968-71 average.[a]

Pollutant	City	Air pollution values, μg/m³ 1968-70	1971
TSP	Charlotte	<25	<25
	Birmingham	<25	<25
SO_2	Charlotte	81	74
	Birmingham	141	133

[a]Data of Hammer (80).

Table 21. Age-adjusted rates (%) of one or more episodes of lower respiratory disease, by race and age interval.[a]

Race	Age, yr	Any lower respiratory Disease, %		Bronchitis, %	
		Charlotte	Birmingham	Charlotte	Birmingham
White	1–4	35.0	38.9	23.1	27.7
	5–8	29.9	36.3	20.4	26.2
	9–12	22.0	26.4	14.9	18.6
Black	1–4	27.8	24.0	13.7	10.6
	5–8	16.4	20.6	7.8	7.9
	9–12	12.7	15.9	6.3	6.9

[a]Data of Hammer (*80*).

bidity effects of chronic exposure to SO_2 and particulate matter. In the next section, we summarize and interpret all of the evidence for health effects of acute and chronic exposure.

Summary and Conclusions

Individual studies providing evidence on the association between health effects and the ambient concentration of sulfur oxides and particulate matter have been described in preceding pages. This section is devoted to a summary of that evidence in an effort to present a perspective on using the available data to establish concentrations for both acute and chronic exposure associated with increased morbidity or mortality. The analysis in this section has been influenced by the many thoughtful reviews published in recent years (*78*, *82-89*).

For the purposes of this discussion, acute exposure is measured by the 24-hr average concentration of each pollutant. Current National Ambient Air Quality Standards for maximum 24-hr average concentration are 260 $\mu g/m^3$ for TSP and 365 $\mu g/m^3$ for SO_2. Exposures over shorter periods may be important, perhaps as measured by the peak hourly concentration in each 24-hr period. Exposures calculated from different short term averaging periods are highly correlated in most situations.

The choice of method for measuring chronic exposure is less straightforward, and can have a significant influence on the determination of concentrations associated with health effects. Most studies reported arithmetic average concentrations of each pollutant over some sampling period including the study period. Although the sampling period did not cover an entire year in every instance, we express the values reported in the various studies as an annual mean concentration. Current National Ambient Air Quality Standards for annual mean concentration are 75 $\mu g/m^3$ for TSP (computed as the geometric mean of 24-hr samples) and 80 $\mu g/m^3$ for SO_2 (arithmetic mean). Since arithmetic means were used almost exclusively for reporting particulate and sulfur oxide concentrations in the studies of chronic exposure, these values have been used in summarizing the evidence. Differences between geometric and arithmetic means are usually unimportant compared to other sources of uncertainty in measuring exposure.

Many of the studies cited failed to obtain concurrent aerometric data. When available, those data were collected at one or a few sites distant from the homes of study participants. The air monitoring techniques were often primitive by current standards, with a resulting potential for substantial bias or variability in measuring concentration. Even when ambient concentrations are optimally measured, the implications for individual exposure are uncertain. Consequently, very great uncertainties about the actual air pollution exposures of study participants in most of the studies discussed weaken analyses of the relationship between exposure and health effect response.

For studies using Black Smoke (BS) to measure particulate concentrations, the conversion to TSP values is highly uncertain and depends upon conditions in the study environment. We convert BS to TSP values using the results of Commins and Waller (*89*). Since their study was conducted in London between 1955 and 1963, the applicability to other sites or times is unknown. Although we use their conversion to unify the discussion, this introduces additional uncertainty. For the one New York study using Coefficient of Haze (CoHs), we use the conversion developed in New York by Ingram and Golden (*90*). They equate 5 CoHs to 580 $\mu g/m^3$ (TSP).

Some studies have reported sulfate concentrations, and there has been considerable interest in the fine particulate fraction (*91*). However, the correlation between TSP concentrations and its components has been consistently high in observational studies. Thus, these studies provide no basis for separately assessing the health effects of different fractions by size or chemistry of ambient par-

ticulate matter. Further understanding of the proper measure of particulate concentration in terms of health significance will come from advances in understanding of lung physiology and from exposure studies with animals.

Assessing causal relationships from studies of association is a familiar problem for epidemiologists, and the problem is especially difficult in air pollution research. When exposures are near present air quality standards, the health effects of air pollution exposure are likely to be small. Many other individual characteristics influence lung function and the risk of respiratory disease. Some of these, like smoking, occupational differences, and socioeconomic status, are well known but difficult to measure, others like passive smoking have been recognized only recently. The association of lung function and respiratory disease with these characteristics is often much greater than the likely effects of air pollution. The possibility in any observational study that these factors have been inadequately controlled adds additional uncertainty to the interpretation of the nonexperimental studies. Thus, the determination of concentrations associated with adverse effects is tempered by recognition of these potential nonsampling errors.

For all of these reasons, the epidemiologic data base is extremely weak. In particular, it is insufficient to distinguish between a threshold hypothesis, that health effects are seen only above certain concentrations, and a monotonic exposure-response hypothesis, that health effects increase (perhaps very slightly) with air pollution concentration over a very wide range. Although we favor the latter hypothesis as more physiologically plausible, we have chosen to interpret the evidence in terms of concentrations at which health effects have been detected. These values should not be interpreted as threshold values. Finally, SO_2 and particulate concentrations were highly correlated in many of the studies cited. Thus we cite concentrations jointly of SO_2 and TSP at which health effects have been detected, and then discuss the evidence for health effects of the individual pollutants.

Health Effects of Acute Exposure to SO_2 and Particulate Matter

The studies providing evidence for health effects resulting from acute exposure to SO_2 and particulate matter are summarized in Table 22. The selection criteria excluded studies of SO_2 or TSP exposures above 1000 $\mu g/m^3$, and the list is strikingly short. The two mortality studies cited (from the same group) found increased mortality associated with TSP concentrations of 500-600 $\mu g\ m^3$ in conjunction with SO_2 concentrations of 300-400 $\mu g/m^3$. These studies summarize a relatively small body of data from two winters in London. The individual studies do not suggest a threshold phenomenon. Although there is some suggestion of an association at lower concentrations, the evidence is very scanty. For all of the reasons discussed above, this interpretation is subject to considerable uncertainty, and this explains in part the divergent views expressed by different reviewers. Time series analyses of daily mortality records over several years have sometimes suggested small mortality effects of air pollution concentrations at much lower concentrations, particularly in association with particulate concentration in the New York studies, but the results have been highly dependent on model selection and are internally inconsistent.

Only two reports of associations between morbidity and 24 hour average pollutant concentrations are cited in Table 22, and one of these is again the study by Martin. Thus, the acceptable epidemiologic evidence for health effects in association with acute elevations of SO_2 or TSP concentrations below 1000 $\mu g/m^3$ consists of only two studies. Other reports, including those of Cohen (*38*), Van der Lende (*43*), and Glasser and Greenberg (*27*) are suggestive but subject to numerous ambiguities related to meth-

Table 22. Summary of evidence for health effects of acute exposure to SO_2 and particulate matter.

Type of study	Reference	Effects observed	24-hr average pollutant levels at which effects were detected, $\mu g/m^3$	
			TSP	SO_2
Mortality	Martin and Bradley (*19*)	Increases in daily total mortality above the 15-day moving average	600	300
	Martin (*20*)	Increases in daily total mortality above the 15-day moving average	600	400
Morbidity	Martin (*20*)	Increases in hospital admissions for cardiac or respiratory illness	600	400
	Lawther et al. (*34*, *35*)	Worsening of health status among 195 bronchitics	350	500

odology and interpretation. Although severe air pollution episodes have frequently been associated with excess mortality and morbidity, there is only a small body of evidence to document such effects at concentrations below 1000 $\mu g/m^3$.

Health Effects Associated with Chronic Exposure to SO_2 and Particulate Matter

As noted above, the evidence for mortality effects of chronic exposure to SO_2 or particulate matter is inconclusive. Though several studies have found associations, the methodological uncertainties are so great as to make these studies essentially valueless for quantifying the exposure-response relationship. The morbidity studies that have found differences in levels of health effects in association with differences in pollutant concentrations are summarized in Table 23, and displayed in Figure 1. In these studies, upper and lower respiratory symptoms, chronic bronchitis and reduced pulmonary function were observed in association with TSP concentrations in excess of about 180 $\mu g/m^3$. In one study, acute respiratory disease was increased in association with reported TSP concentration of 135 $\mu g\ m^3$ though these values were estimated from relatively weak aerometric data. As with the studies of acute effects, most of these studies could be interpreted as demonstrating that the prevalence of adverse health effects increases monotonically with exposure over the entire range of exposure studied. These studies provide little evidence to assess the health effects associated with elevated SO_2 concentrations along with moderate particulate concentrations. Although Hammer (*79*) and the Salt Lake Studies (*72*) did report such associations, the problems with methodology and aerometric measurement in those studies limit their value in this assessment. Though exposure to these pollutants at concentrations below those cited may imply some increase in risks, it will be difficult to resolve this question in an observational setting, because health effects of pollutants at these concentrations are likely to be small relative to effects of other factors which vary over communities.

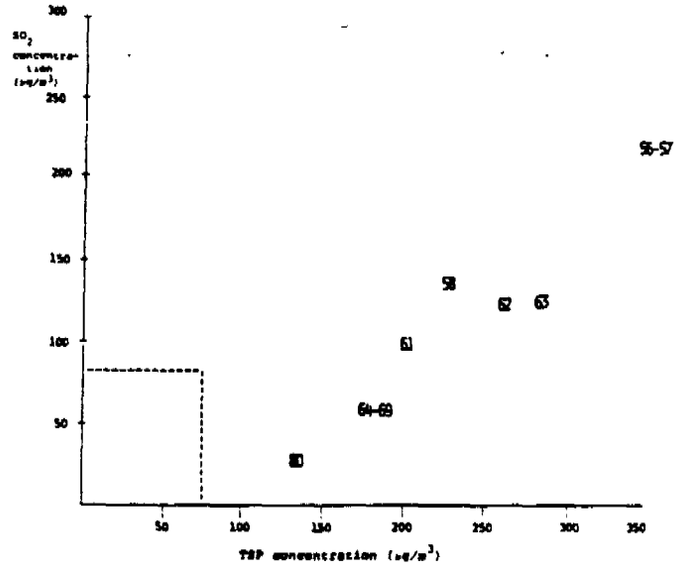

FIGURE 1. Plot of studies in which increased levels of adverse health effects were associated with chronic exposure to higher concentrations of TSP and SO_2. Studies are plotted at the lowest concentrations at which increases were seen and by the reference numbers in the bibliography. The dashed lines correspond to the current National Ambient Air Quality Standards for annual mean concentration.

Table 23. Summary of evidence for health effects of chronic exposure to SO_2 and particulate matter.

Type of study	Reference	Effects observed	Annual average pollutant levels at which effects noted, $\mu g/m^3$	
			TSP	SO_2
Cross-sectional (four areas)	Lunn et al. (*56, 57*)	Increased frequency of respiratory symptoms; decreased lung function in five-year-olds	360	225
Cross-sectional study across Britain	Lambert and Reid (*61*)	Increased prevalence of respiratory symptoms	200	100
Cross-sectional (two areas)	Sawicki (*62*)	More chronic bronchitis, asthmatic disease in smokers; reduced FEV%	270	125
Cross-sectional (four areas)	Rudnik et al. (*63*)	Increased history and symptoms of respiratory illness	285	125
Longitudinal and cross-sectional	Ferris et al.	Higher rate of respiratory symptoms; and decreased lung function	180	55
Cross-sectional (two areas)	Hammer (*60*)	Increased frequency of acute lower respiratory disease	135	<25

Summary

The studies summarized in Table 22 indicate that increased mortality and morbidity are associated with exposure to 24-hr average TSP concentrations of 500-600 $\mu g/m^3$ and SO_2 concentrations of 300-400 $\mu g/m^3$ and a temporary decrease in lung function has been associated with a TSP concentration of 250 $\mu g/m^3$ and a SO_2 concentration of 300 $\mu g/m^3$. This conclusion is based on only two independent studies. There is little evidence concerning health effects of short term exposure to only one of these pollutants. Various studies not accepted in this assessment have reported health effects at lower pollutant concentrations, but we believe that the evidence from these studies is inconclusive.

The studies summarized in Table 23 indicate that increased morbidity is associated with chronic exposure to TSP concentrations exceeding 180 $\mu g/m^3$ (annual average). Though effects were found both with and without parallel increases in SO_2 concentration, there is no basis in these studies for evaluating the effects of elevated SO_2 concentrations without increased particulate pollution. Once again, one cited study (*80*) and several studies not accepted for this assessment have reported health effects at lower concentrations and with elevated SO_2 concentrations, particularly the studies in the CHESS program. In our opinion, the evidence for health effects at these lower concentrations is inconclusive, but should be the subject of continuing investigation. Though we have focused on the evidence from observational studies, the evidence from animal studies and controlled studies of human exposure must also be considered, particularly in relation to the less severe effects of short-term high exposures. These studies will also play an important role in future efforts to link health effects with chemical or size fractions of the SO_2-TSP pollution complex. Nonexperimental studies provide little information on this issue because of the collinearity of the components of interest. This will be especially important in studying fine particulates.

Although we have given single numbers as concentrations above which various health effects occur, these numbers are based on very sparse data from studies not designed to establish such values. Thus, the numbers are subject to uncertainty which is difficult to quantify.

In view of the limitations of studies based on multivariate analysis of data obtained from sources not oriented to air pollution research, future studies will be most informative if they involve thorough and detailed investigation of well defined populations.

Direct measurement and careful control of potential confounding factors will be especially important, as will improved measurement of the air pollution exposure of individuals. The need for such research may grow as energy usage patterns shift in response to limited availability of oil and natural gas.

The public health significance of this question is sufficient to justify the commitment of additional resources to improving the data base on health effects of sulfur oxides and particulate matter.

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Mathematical Models of the Uptake of Carbon Monoxide on Hemoglobin at Low Carbon Monoxide Levels

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Coburn's differential equation for the uptake of carbon monoxide by hemoglobin and two particular types of solution of this equation were considered and the solutions verified for a group of healthy adults consisting of 73 nonsmoking pedestrians or car passengers exposed to low levels of carbon monoxide as experienced in the city of Lyon. The CO levels at the breathing level and the walking speed of the subjects was continually measured, and the carboxyhemoglobin levels determined at the beginning and the end of each test journey. The values of all the other relevant parameters were also determined. The half-life of carboxyhemoglobin was studied as a function of the degree of activity, the age, the sex and the height of the subjects. Finally a mathematical model was set up to represent a periodic uptake of CO which made it possible to estimate the variations in the carboxyhemoglobin level for any subject during a period of a day or a week without any need to know the initial level.

There is normally a very small concentration of CO in the air as a result of natural phenomena, its level being between 0.01 and 1 ppm. Measurements carried out on the Isle of Sark (*1*), where motor vehicle traffic is prohibited, confirmed that the CO levels were always less than 1 ppm. Measurements made in urban areas in various places in the world over many years have resulted in a considerable quantity of information on CO levels. The exact location where the measurements are made is important, since the highest concentrations are found in the midst of a stream motor vehicles and also inside such vehicles, as confirmed by this investigation. Pedestrians walking along the sidewalks are exposed to a lesser concentration of CO than are motorists. People who are obliged to remain at certain critical locations such as toll booths, garages or in traffic jam in enclosed and poorly ventilated streets are exposed to high CO levels due to road traffic (*2,3*). In order to obtain some idea of the conditions, a person moving within a city will experience CO levels having an average level for the hour in excess of 30 ppm (*4*). American standards for permissible levels to which the public may be exposed are in fact sometimes exceeded (*5,6*).

Dangerous HbCO Level and Particularly Vulnerable Subjects

The effect of carbon monoxide is to reduce oxygenation of the tissues and this effect may be experienced immediately or after a longer period of time. Any increase above the endogenous level can in theory be harmful for a person having an extreme requirement for oxygen, and who cannot compensate a reduced supply of oxygen by physiological means. Such subjects consist mainly of people suffering from coronary atheromatic ischaemia or from cerebral vascular deficiencies. Also at risk

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here are people suffering from pernicious anaemia or from respiratory deficiencies, patients recovering from major surgery or premature babies. Aronow and Isbell (7) refers to a "critical" carboxyhemoglobin level of between 0.025 and 0.030 for angina pectoris sufferers, such a level giving rise to an appreciable reduction in the time elapsing before the onset of a painful attack following a given physical effort. The World Health Organization (5) estimates that the level for the population exposed to atmospheric pollution should not exceed these limits. In the case of our sample, the 0.025 level was exceeded for 19 out of the 73 subjects (pedestrians or car passengers) as a result of their displacement in the city. However this level can in theory easily be exceeded for subjects remaining in heavily polluted localities. The 0.025 carboxyhemoglobin level would result from an exposure to a 13 ppm CO concentration for more than 24 hr.

Kinetics of the Uptake and Elimination of Carbon Monoxide

Symbols and units used are summarized in Table 1. We used SI units, but for CO concentration used ppm because it is independent of the temperature.

Differential Equation

Coburn et al. (8) have proposed the following differential equation (1) for carboxyhemoglobin level as a function of time:

$$V_b\, M[O_2]/Pc_{O_2}\,(1/D_L + P_B - P_{H_2O}/\dot{V}_A)\, d[CO]/dt + [CO] = Pi_{CO}\, M[O_2]/Pc_{O_2} + \dot{V}_{CO}\, M[O_2]/Pc_{O_2}\,(1/D_L + P_B - P_{H_2O}/\dot{V}_A) \quad (1)$$

Numerical Values of the Different Parameters

The values given below are statistical averages for subjects in good health and very different values can apply in individual cases, particularly in the case of subjects suffering from certain diseases. The value of M can vary from 185 to more than 250, and we assumed a value of $M = 250$. $[O_2]$ was given a value such that: $[O_2] + [CO] + [X] = 8.92$ mmole/liter of blood (200 ml/l.) P_B was assumed to have a value of 99.3 kPa (745 mm Hg) for the town of Lyon, which is at an altitude of 120 m above sea level.

Pc_{O_2} and P_{H_2O} were assumed to have values of 13.3 kPa (100 mm Hg) and 6.3 kPa (47.5 mm Hg), respectively.

The value of P_{iCO} is directly related to that of C by the equation: $P_{iCO} = P_B \times 10^{-6} C$. We also assumed that $y = HbCO = 17\,[CO]/[Hb]$, (or $1000\,[CO]/1.316\,[Hb]$, if [CO] and [Hb] are in ml/100 ml and g/100 ml of blood, respectively), and similarly that $HbX = 17\,[X]/[Hb]$. The value of D_L is related to the height and body surface of the subject and the value decreases with age. A number of relationships have been proposed, and the resulting calculated values may differ 20 to 30% for the same subject. We used the following relationships (9):

For a man aged 18 or more:

$$D_L = 0.329H - 0.000135Y - 0.318$$

For a woman aged 18 or more:

$$D_L = 0.119H - 0.000087Y - 0.015$$

For a child:

$$D_L = 0.117A - 0.022$$

The value of V_b for adults depends on the sex of the subject and we assumed values of $m/13$ and $m/15$ for male and female subjects, respectively. For children we assumed values of $0.071m$, $0.075m$ and $0.080m$ for 15, 10 and 1-6 year old subjects respectively (10).

The value of $\dot{V}_{CO}$ for a standard male subject has been given as 5.2×10^{-6} mmole/sec (0.007 ml/min) (8). We assumed that the value varied with the total hemoglobin level $V_b[Hb]$ (for a standard male subject, $V_b = 5$ liters and [Hb] = 155 g/l. blood), giving:

$$\dot{V}_{CO} = 5.2 \times 10^{-6}\, V_b[Hb]/5(155)$$

The degree of alveolar ventilation is proportional (11) to the oxygen consumption $\dot{V}_A = 19.63\dot{V}_{O2}$, and this consumption depends in turn on the power expended by the subject (12). Thus we have:

$$\dot{V}_A = 4.33 \times 10^{-2}\, P$$

Power Expended

The power expended is the sum of the basal metabolism, the muscular power and the specific dynamic action of the foods: $P = MB + PM + SDA$. The basal metabolism is proportional to the surface area of the body: $MB = Ax$.

Pandolf et al. (13) have established an equation giving the rate of energy expenditure for a subject when standing or when walking at different speeds and when carrying or not carrying a load.

$$\dot{P}\,(SDA = 0) = 1.5m + 2(m + m')\,(m'/m)^2 + e(m + m')\,(1.5V^2 + 0.35\alpha V)$$

Table 1. Symbols and units used.

Symbol	Unit	Definition
A	m^2	Body surface area
$a(t)$		Other form of the coefficient in Coburn's equation
$b(t)$		Other form of the coefficient in Coburn's equation
C	ppm	Carbon monoxide concentration in air
[CO]	mmole/l. of blood	CO level in blood
d		A coefficient depending on the type of meal
D_L	mmole/sec/kPa	Pulmonary CO diffusion capacity
e		A coefficient depending on the condition of ground surface
$f(t)$		Function used for resolving Coburn's equation
$g(t)$		Function used for resolving Coburn's equation
H	m	Height of subject
[Hb]	g/l. of blood	Hemoglobin level
HbCO	fraction	Carboxyhemoglobin level with respect to the total hemoglobin
HbO_2	fraction	Oxyhemoglobin level with respect to the total hemoglobin
HbX	fraction	X hemoglobin level with respect to the total hemoglobin (e.g., nitrosylhemoglobin)
HEL	fraction	Limit endogeneous carboxyhemoglobin level with respect to the total haemoglobin
k	fraction/ppm	A constant for carboxyhemoglobin level
K	fraction/ppm/sec	Rate constant for carboxyhemoglobin formation
K_0	fraction	A coefficient employed in step-by-step calculation: carboxyhemoglobin and oxyhemoglobin levels
K_1	fraction/sec	Coefficient employed in step-by-step calculation: partial rate constant for CO uptake
K_2	fraction^2/sec	Coefficient employed in step-by-step calculation: partial rate constant for CO uptake
m	kg	Weight of subject
m'	kg	Load carried by subject
M		Haldane's constant
MB	W	Basal metabolism
$[O_2]$	mmole/l. of blood	Oxygen level in the pulmonary capillaries
p_d		Fraction of the daily energy allowance for one meal
P	W	Total power expended by the subject
P_B	kPa	Barometric pressure
Pc_{CO}	kPa	Average partial CO pressure in the pulmonary capillaries
Pc_{O_2}	kPa	Average partial oxygen pressure in the pulmonary capillaries
P_{H_2O}	kPa	Vapor pressure of water
Pi_{CO}	kPa	Partial CO pressure in inspired air
PM	W	Muscular power (expended)
sda	W	Instantaneous specific dynamic action per 1 kJ of food ingested at last meal
SDA	W	Specific dynamic action of foods
V	m/s	Walking speed
V_A	mmole/sec	Alveolar ventilation rate
V_b	liters	Blood volume
V_{CO}	mmole/sec	Rate of endogeneous CO production
V_{O_2}	mmole	Volume of oxygen consumed
w_r	kJ/kg	Heat production to food/kg of body weight
x	W/m^2	Basal metabolism per unit body surface area
[X]	mmole/l. of blood	Possible gas level other than O_2 and CO in the pulmonary capillaries (e.g. nitric derivatives)
Y	years	Age of subject
y	fraction	(= HbCO): proportion of carboxyhemoglobin with respect to total hemoglobin
$y(t)$		particular periodic solution of Coburn's equation
y_0	fraction	value of y at time t_0
y_{1m}	fraction	Initial measured value of HbCO
y_{2c}	fraction	Final calculated value of HbCO
y_{2m}	fraction	Final measured value of HbCO
α	per cent	Inclination
δ		Kronecker symbol (1 = standing, 0 = other cases)
τ	sec	Time constant
$\tau_{1/2}$	sec	Half-life

The validity of this equation has been verified for young male subjects of average height and weight (1.75 m, 78.2 kg). The equation gives the value of the total power expended, including the basal metabolism, but for a zero SDA value.

We also considered Scherrer's findings (*12*); he stated that the power expenditure amounts to 1.2 times the basal metabolism for a standing subject and to 1.1 times the same basal metabolism when the subject is sitting and at rest (and 0.9 times when the subject is asleep). We made use of a coefficient d to allow for these factors. Certain authors have shown that a female or an overweight subject expends less energy when at rest as a result of a smaller proportion of muscular tissue which accounts for the difference in metabolism with effort. The additional expenditure of energy as a result of performing work PM is the same (*14*). If we wish to apply the above equation for a subject of either sex then the first term ($1.5m$) in the expression must be a function of the sex. We accordingly replaced the first term by Adx, where x is a function of both age and sex (*15*) and the second term appears only for a stationary, standing subject. We then have:

$$P(\text{SDA} = 0) = Adx + 2\delta(m + m')(m'/m)^2 + e(m + m')(1.5V^2 + 0.35\alpha V) \quad (1)$$

The SDA or additional postprandial heat is defined as the increase in the rate of energy expenditure resulting from the ingestion of a meal, the other conditions being basal. This specific dynamic action varies with time and it rises to a maximum value some 2 hr after the ingestion of a meal (*16*). Furthermore it should be noted that the SDA value depends on the type of food consumed and it can be assumed, as a first approximation, that it is a function of the energy value of the meal, this latter being a function of the age and sex of the subject. It is also proportional to the weight of the individual and we can accordingly refer to w_r, the heat allowance per kilo of weight of the subject. We therefore have:

$$\text{SDA} = mw_r\,(Y, \text{sex})p_r\,\text{sda}$$

where sda is the SDA for 1 kJ of food and p_r is the fraction of the daily energy allowance for each meal.

What is the relative importance of MB, PM and SDA? With our mixed group of subjects made up half of pedestrians and half of car passengers we had values of $\overline{\text{MB}} = 91$, $\overline{\text{PM}} = 80$ and $\overline{\text{SDA}} = 23$. On considering a theoretical subject over a period of one week we obtained average values of MB, PM and SDA of 78, 13 and 17, respectively. Thus the SDA is approximately 20. It represents nearly a quarter of the basal metabolism to which we need to add the muscular work rate which can be greater than the basal metabolism. Thus the SDA is not negligible.

Solving the Differential Equation

Three methods of solving Coburn's equation are considered.

First Method: Step-by-Step Solution. Let y_1 and y_2 be the carboxyhemoglobin levels at times t_1 and t_2, respectively; if C remains unchanged from time t_1 to time t_2 we can write:

$$y_2 = y_1 + (t_2 - t_1)\left\{K_1 - [K_2/(K_0 - y_1)]\right\}$$

where

$$K_0 = \frac{17(8.92 - [\text{X}])}{[\text{Hb}]} \quad (1)$$

$$K_1 = \frac{17}{V_b[\text{Hb}]} \times \left[\frac{Pc_{O_2} + MP_B \times 10^{-6}C}{M\{(1/D_L) + [(P_B - P_{H_2O})/\dot{V}_A]\}} + \dot{V}_{CO}\right] \quad (2)$$

$$K_2 = \left(\frac{17}{[\text{Hb}]}\right)^2 \times \left[\frac{(8.92 - [\text{X}])Pc_{O_2}}{MV_b\{(1/D_L) + [(P_B - P_{H_2O})/\dot{V}_A]\}}\right] \quad (3)$$

The advantage of this method of solving the equation in comparison with the other two methods considered below is that no assumptions need to be made. The disadvantage is that an error is introduced, since no distinction is made between the tangent to the curve and the curve itself at each point.

Second Method: Analytical Solution. If we ignore [CO] (and [X] but it is not strictly necessary) with regard to $[O_2]$, then the basic equation can be put into the form of a linear first order differential equation:

$$(k/K)dy/dt + y = kC + \text{HEL} \quad (4)$$

This is also the form of equation proposed by Chovin and Richalet (*17*) except for the inclusion of

the HEL term, which was based on the results of the experimental investigation by Hanks and Farquhar (*18*). Peterson and Steward (*19*) have verified it for constant concentrations (50 to 200 ppm) in industrial conditions on the whole.

If, in addition, C can be regarded as a linear function of time ($C = at + C_1$) then the analytical solution to the equation becomes:

$$y = \text{HEL} + K\{a[t - (k/K) + C_1\} + \{y_1 - k[a(k/K) - C_1] - \text{HEL}\}\, e^{-Kt/k}$$

where

$$k = \frac{17 \times 8.92 M \dot{P}_B \times 10^{-6}}{Pc_{O_2}[\text{Hb}]}$$

$$K = \frac{17 P_B \times 10^{-6}}{V_b[\text{Hb}]\,[(1/D_L) + [(P_b - P_{H_2O})/\dot{V}_A]}$$

$$\text{HEL} = \frac{17 \times 8.92 M \dot{V}_{CO}}{Pc_{O_2}[\text{Hb}]\,[(1/\dot{D}_L) + [(P_b - P_{H_2O})/\dot{V}_A]}$$

The time constant k/K is then given by:

$$\tau = \frac{8.92M}{Pc_{O_2}} V_b \left(\frac{1}{D_L} + \frac{P_B - P_{H_2O}}{\dot{V}_A}\right)$$

The constant k is such that the HbCO level following an infinite time of exposure to a concentration C will be kC + HEL. In particular, the value of k is a function of the hemoglobin level and is independent of the level of activity. The value of the factor K, which defines the rate of uptake of CO by the hemoglobin, increases with the degree of alveolar ventilation and hence with physical activity. Standard values of k and K are listed in Table 3 below. The limit endogeneous carboxyhemoglobin level HEL also increases with the amount of physical activity, but the level remains very low (≤ 0.002).

This analytical method of solving the equation enables us to determine any HbCO level, if the initial level is known, provided the variation of C is linear and K remains constant during the interval concerned, which are not unreasonable assumptions.

Third Method: Periodic Solution. The two methods of solving the differential equation described above depend on a knowledge of the initial HbCO level. This well-established disadvantage can disappear if we ignore [CO] with regard to $[O_2]$ and if the parameters K, C and HEL are periodic functions of time (k being constant for a given subject). It is possible to find a periodic solution by using some analytical properties. For convenience, we use a more mathematical language in this section. If we rewrite the equation

$$dy/dt + a(t)y = b(t)$$

with

$$a(t) = K(t)/k$$

$$b(t) = K(t)\,C(t) + K(t)\,\text{HEL}(t)/k$$

this is a linear differential equation of the first order, whose general solution is

$$y(t) = y_0 f(t) + g(T)$$

with the new functions (*20*)

$$f(t) = \exp\{-\int_0^t a(u)du \quad f(0) = 1$$

and

$$g(t) = f(t)\int_0^t b(u)/f(u)\,du \quad g(0) = 0$$

If $a(t)$ and $b(t)$ are periodic functions of period T and if $a(t) \geq 0$, it may be easily shown that

$$\hat{y}(t) = g(t)f(t)/[1 - f(t)] + g(t)$$

is a particular solution which is periodic (of period T), and every general solution $y_0 f(t) + g(t)$ converges towards $\hat{y}(t)$ as t is increasing ($t \geq 3$ or $4T$) (*21*). Then the $\hat{y}(t)$ function is a convenient analytical tool to describe the actual variations of the carboxyhemoglobin level $y(t)$ if the data used K,C,HEL are periodic functions of time. So we make the realistic assumption that these data representative of the activity and CO exposure of a person are periodic over a period of 24 hr, or, better, over 7 days; moreover, since these variations are known, it is no longer necessary to measure or to choose arbitrarily the initial HbCO level to describe the variations of the HbCO level in any time interval. In practice, we obtain the values of K, HEL and C every 15 min (during 24 hr or 7 days) and calculate the basal integrals $f(t)$, $g(t)$ at the same moments by numerical methods on a computer.

For the second and third methods, we ignore [CO] with regard to $[O_2]$: the greater the value for HbCO, the more k and HEL are overestimated. We can give $[O_2]$ its initial value $[8.92 - (Hb/17)\ y_1]$ or its mean value. Besides, if we do not ignore [X] when we can estimate it, we must replace 8.92 by 8.92 – [X].

Experimental Verification

In order to validate the theoretical analysis, we carried out tests with a total of 73 subjects whose ages varied from 18 to 60 years and who all stated that they were nonsmokers. This sample was divided into two groups of subjects: one group consisting of car passengers who remained seated in each case for the duration of a test journey within and around the town, and a second group consisting of pedestrians who walked at a nearly constant speed in each case in the actual polluted atmosphere existing in certain streets of the city of Lyon. The pedestrians were accompanied by a technician who ensured that the walking speed was maintained throughout each test journey on making measurements at intervals of 3 to 4 min (the mean speed is 1.09 m/sec).

Samples of blood were taken at the beginning and end of each journey and these samples analyzed in order to obtain values of [Hb]; y_{1m} and y_{2m}. The analysis of the blood samples was based on the method developed by Boudene, Godin and Roussel (*22*), where the proportions of hemoglobin and CO in the blood were determined by means of infrared spectroscopy. The carbon monoxide levels in the atmosphere were measured on a continuous basis by means of a polarography technique by using a portable Ecolyser and a paper recorder.

For each of the subjects we had in addition to our knowledge of the values of [Hb], y_{1m}, y_{2m} and C, information concerning the sex, weight, height and age of the subject, the load carried by the subject, the time of day when the subject undertook the test journey and continuous information on the walking

Table 2. Average values of the different parameters for the sample subjects.

Parameter	Men	Women
n	37	36
Age	32	32
[Hb], g/l	147	133
m, kg	71	57
m', kg	3	3
H, m	1.75	1.62
C, ppm	13.9	13.7
V, m/sec	0.70	0.64
Duration, min	126	123
D_L, mmole/sec/kPa	0.190	0.175
A, m^2	1.85	1.59
V_b, liters	5.46	3.78
$V_{CO} \times 10^{-5}$, mmole/sec	5.55	3.49
y_{1m}	0.019	0.018
$\sigma_{y_{1m}}$	0.007	0.006
y_{2m}	0.023	0.021
$\sigma_{y_{2m}}$	0.008	0.006
$\tau_{1/2}$, min		
Activity A	236	208
Activity B	140	117

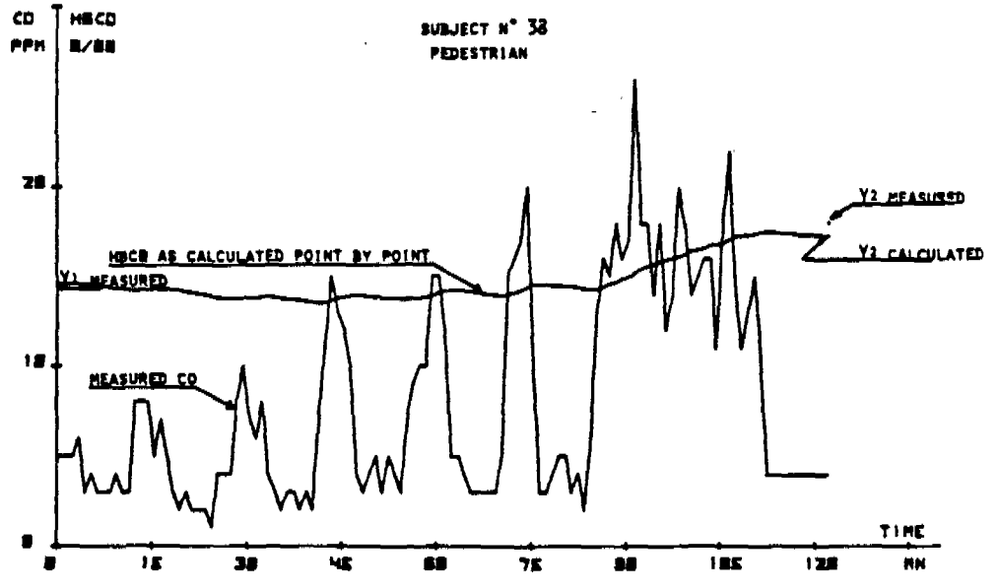

FIGURE 1. Example of an experimental validation of analytical solution.

speed of the pedestrians. Knowing the initial level in each case we calculated the successive carboxyhemoglobin levels throughout the duration of the test and the final level y_{2c} for each subject. An example of the results obtained as a result of making these calculations is given in Figure 1. The calculations were made on using the analytical method without approximate rectification of $[O_2]$ to solve the differential equation and also on using the step by step method on estimating HbX = 0 or HbX = 0.010. In Table 2 we list with respect to the sex of the subjects, average values of the different parameters for the sample subjects: age, [Hb], m, m', H, CO concentration, V, duration of the tests, D_L, A, V_b, $\dot{V}_CO$, y_{1m}, y_{2m} and the half-life $\tau_{1/2}$ for the subjects when at rest (A) and when walking at a speed of 4 km/hr (B).

As a verification of the validity of the theoretical calculations we compared the final measured levels with the different calculated values. We applied statistical tests to the pairs of values (y_{1m}, y_{2m}), (y_{2m}, y_{2c}) and (y_{2m}/y_{1m}, y_{2c}/y_{1m}) in order to ascertain if there were any significant differences between them (at 5%) for different subsamples as regards the sex and the type of activity. As a result of this it was found that the initial and final measured levels y_{1m} and y_{2m} were significantly different ($p = 10^{-7}$). The method of calculation employed did not have any effect on the results; the differences in the levels determined by each method were not significantly different from one another. There was no significant difference between the calculated and measured levels either for the whole sample of subjects or, except for the case of male pedestrians, for any subsample. This was found for both the (y_{2m}, y_{2c}) and the (y_{2m}/y_{1m}, y_{2c}/y_{1m}) pairs of values. We calculated also Δ = [sign of $(y_{2m} - y_{1m})$] $(y_{2c} - y_{2m})/y_{1m}$, which is positive when the calculated change is too great. Mean Δ showed that the calculated changes were generally lightly too small and in the case of male pedestrians clearly too small.

The calculated results as a whole were very satisfactory for all subjects and particularly so in the case of female pedestrians. Thus we can conclude that the two method (analytical or step-by-step solutions) were equally valid, at least when the level of HbX + HbCO is low. The analytical solution is therefore to be preferred for environmental pollution since it is easier to use; we can give if necessary to $[O_2]$ its initial or mean value. The differential equation for the uptake-elimination of carbon monoxide by hemoglobin and the use of the selected parameter values to model the phenomena is generally valid, although it would appear that the changes in the HbCO levels are underestimated for male pedestrians (the degree of alveolar ventilation is no doubt insufficient in the model).

Applications

Effects on a Particular Subject

The procedure employed to verify the validity of the theoretical approach can also be applied to real life cases. This requires measuring or estimating the CO concentrations throughout the period of time being considered and assuming an initial HbCO level. We can then determine the effects of the changing environment on a real or imaginary subject.

However, it is often difficult, if not impossible, to obtain information on the CO concentration in the air and on the level of activity of the subject at each instant. We must therefore ask what error would be introduced on using average values of CO concentration and/or of the level of activity of the subject? To answer this question let us consider a female subject exposed to an average CO concentration of 15 ppm and walking along at an average speed of 1 m/sec, with both these values varying from zero to twice the average level. The initial level of HbCO is assumed to amount to either 0.010 or 0.050. When calculating the results for this case it was found that no errors are introduced when assuming these average values despite the random variations in the instantaneous values of CO concentration and the level of the subject's activity. In general it was found that only a small error is introduced by assuming an average value for the level of activity but that a significant error can result when assuming an average value for the CO concentration and the period of integration involved is greater than the half-life (see below). The error, however, becomes negligible for periods of integration which are less than the half-life by an order of magnitude or more.

Graphs for Determining the Uptake and Elimination of CO Under Different Conditions

A desk calculator has to be employed to obtain analytical solutions of the differential equation, and we have therefore produced a series of graphs resulting from theoretical calculations which show the way in which CO is taken up or eliminated from hemoglobin for CO concentrations of 0, 10, 30, 50

and 100 ppm for an average (French) women (1.60 m high, 55 kg in weight):

Level of activity A: Subject seated and at rest. $\dot{V}_A$ = 4.06 mmole/ sec = 5460 ml/min

Level of activity B: Subject walking along at a speed of 4 km/hr. $\dot{V}_A$ = 8.87 mmole/sec = (11930 ml/min)

Level of activity C: Subject involved in some strenuous physical or sporting activity such as cycling (at a speed of 15 to 20 km/hr), football or swimming, resulting in a doubling in the value of $\dot{V}_A$ compared to the value for activity B: $\dot{V}_A$ = 17.74 mmole/sec = 23860 ml/min

Two sets of curves are shown on each of these graphs for the different CO concentrations and levels of activity, one set originating from a zero and the other set from a 0.100 HbCO level.

Reference can be made to this graph in determining the approximate fixation-elimination of CO for a subject for a given initial level of HbCO and for continuously varying concentrations of CO in the atmosphere and of levels of activity of the subject. The graphs include curves for each of the three levels of activity for each of the CO concentrations. As an example of the use of these graphs we can consider (see Fig. 2) the case of an average female subject having an initial HbCO level of 0.020 who is successively exposed to different CO concentrations as follows: 30 ppm for 1 hr while at rest, HbCO = 0.028; 50 ppm for 1 hr while walking along at a speed of 4 km/hr, HbCO = 0.049; 0 ppm for 1.5 hr while at rest, HbCO = 0.037; 100 ppm for 1 hr while at rest. On referring to the appropriate graphs for these exposures it will be found that the final HbCO level for the subject amounts to 0.067.

Model of Periodic Conditions

Ott and Mage (*23*) used a simplified point-by-point determination of the HbCO level, CO concen-

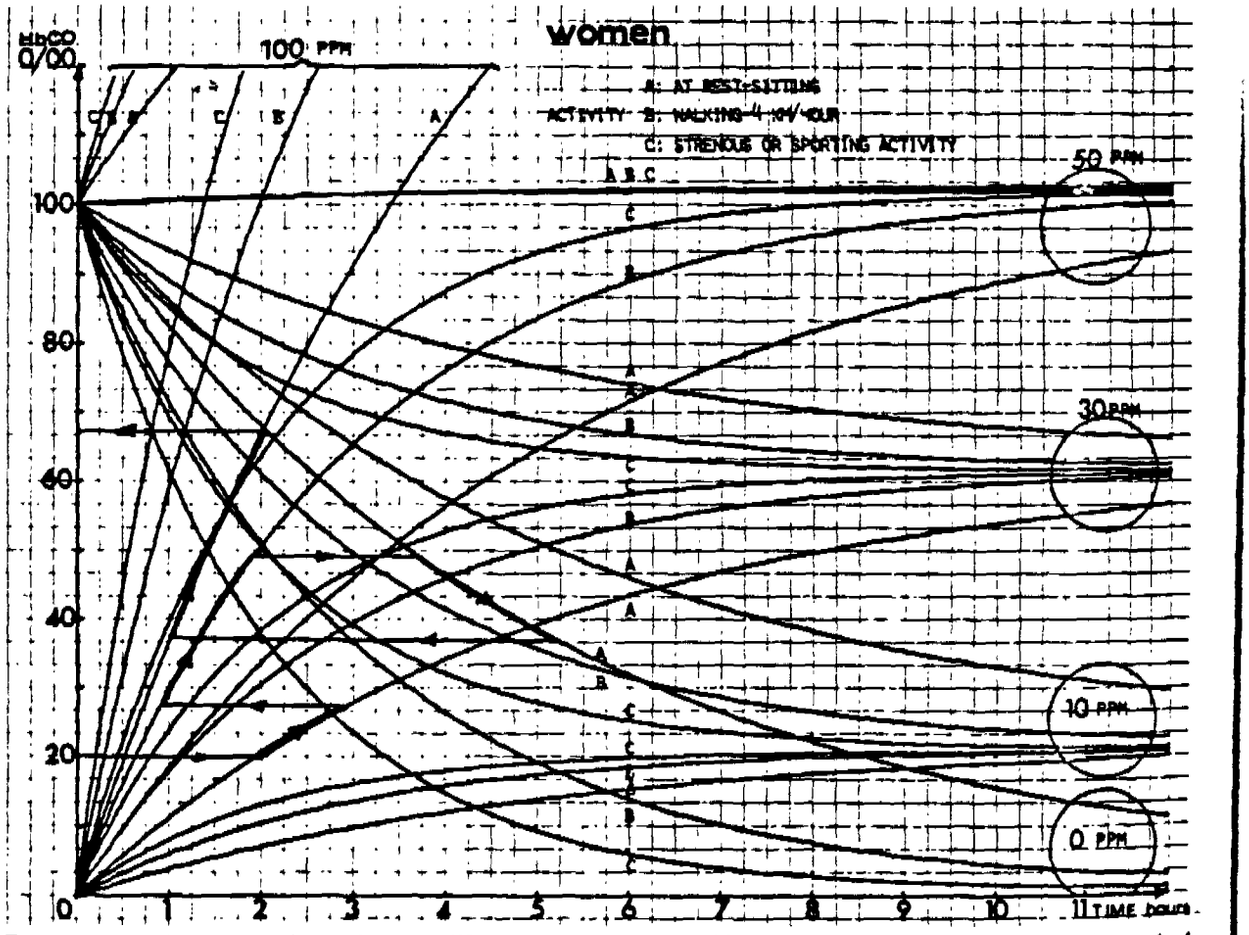

FIGURE 2. Graphs of the uptake-elimination of CO for an average woman, with constant concentration and activity and example of use.

tration being known hour by hour and the physical activity being constant. For a more precise calculation, a point-by-point determination is only possible in the case of relatively short periods of time. For longer periods of time and in cases where the CO concentrations and the levels of activity of the subject vary in a periodic manner it is better if we make use of the periodic method of solving the differential equation. We employed this method for solving the differential equation for two different cases, the time base being a quarter of an hour and the most significant period for the calculations being 1 week. The details of these two cases and the results of the calculations were as follows.

First Case. A customs officer whose place of work was at the side of the road near the French-Swiss frontier lived in the surrounding countryside. The CO concentration at the place of work was measured during the winter of 1978. It was found that the carboxyhemoglobin level varied from 0.002 to 0.033. The level exceeded 0.025 for 3.3% of the total time (corresponding to 14% of the working time) and the average CO concentration (working and rest periods combined) amounted to 3.7 ppm.

Second Case. A saleswoman lived on the outskirts of a large town and worked in a shop located in the main street and in the vicinity of road traffic from Tuesday to Saturday. She travelled to work by bus and spent a part of the weekend in the country. The CO concentrations taken into account were those actually measured at the side-walk of the main street. The CO concentrations in the other locations and the levels of activity taken into account were as estimated. On assuming the subject to be a nonsmoker, it was found that the HbCO level oscillated between values of 0.002 and 0.022. The average CO concentration amounted to 4.7 ppm (Fig. 3).

In order to have some idea of the effects of pollution due to motor vehicle traffic in comparison with the effects of smoking cigarettes (assuming 10 inhalations of 30 ml at 4% CO concentration per

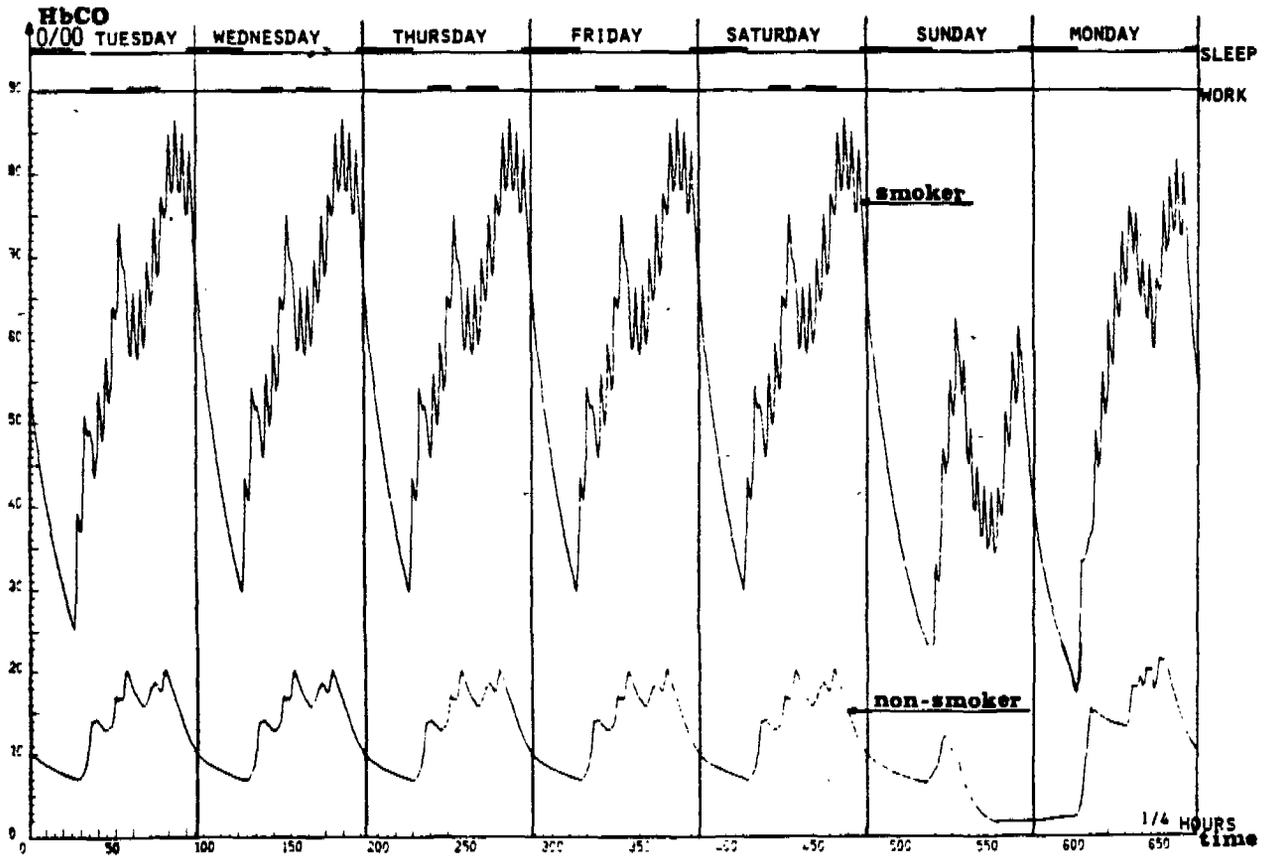

FIGURE 3. Simulation of the periodic variation in HbCO level for a nonsmoking saleswoman and for a subject smoking a total of 103 cigarettes per week.

cigarette) we also considered the case of the same saleswoman smoking at the rate of one cigarette per hour (103 cigarettes per week). The results of the calculations for this case are also shown on Figure 3. The HbCO level oscillated between values of 0.017 and 0.087, while the average CO concentration due to both the motor vehicle traffic and the smoking amounted to 18.3 ppm. The HbCO level exceeded 0.025 for 97% and 0.040 for 79% of the time. The levels were in general some four times greater for the cigarette smoking than for the nonsmoking subject.

The simulation of periodic variations in carboxyhemoglobin levels would appear to be a very useful technique in assessing the effects of carbon monoxide pollution of the atmosphere and of the variations in the actual CO concentration. The calculated HbCO levels given in the examples above are quite consistent with the HbCO levels quoted in the literature (*24-28*). It is necessary, however, to have information on the behavior of the subject on a quarter of an hour to quarter of an hour basis, but there are no problems in making assumptions concerning the behavior of a subject over certain very long periods of time (nighttime and rest periods). It is accordingly possible to determine the effects of any particular variations in CO concentrations during specific periods of time (e.g., during working hours or when travelling). Thus this technique has many potential applications.

Half-life of the Carboxyhemoglobin

Given a constant CO concentration in the air, the time involved for the HbCO level to change from level y_1 to level y_2 is given by:

$$\Delta t = -\tau \log \frac{y_1 - \mathrm{HEL} - kC}{y_2 - \mathrm{HEL} - kC}$$

If the atmosphere is unpolluted ($C = 0$) then Δt is the period of time during which the HbCO level decreases from y_1 to y_2. Thus we can determine, for example, the time needed for the HbCO level to fall from 0.200 to 0.010 and from 0.50 to 0.10 for the three standard subjects (male, female and child) and for the previously defined levels of activity A, B and C (Table 3).

If we neglect HEL in the equation for the value of Δt (HEL is always small and is a function of the level of activity of the subject), it then becomes a simple matter to determine the periods of time for the initial HbCO levels to be halved. The times Δt are then independent of the initial and final HbCO levels, and they depend only on the levels of activity of the subjects and the physiological factors involved. Thus we can determine the half-life ($\tau_{1/2} = \tau \log 2$) in each case, this being the period of time for the HbCO level to fall to half of any given value in an unpolluted atmosphere (Table 3). The real half-life is a little lower because we ignore [CO] with regard to [O_2].

The lower the value of $\tau_{1/2}$, the faster will any HbCO level be reduced to one half in an unpolluted atmosphere, and conversely the faster will the new level be doubled in the case of a constant concentration of CO, given that Δt is proportional to τ for such changes in level. The time taken for the HbCO level to double will in fact be proportional to τ (or to $\tau_{1/2}$) the value of this time constant in turn depending essentially on the value of y_2 with respect to the absolute maximum level kC. Thus it would be important to have a good knowledge of half-life. It is interesting to consider what are the population groups (healthy subjects) that are most sensitive to CO pollution in terms of half-life values. The results of the calculations for our sample subjects showed that the standard deviation for the half-life values for either sex amounted to 8%. Thus calculated individual half-life values will deviate appreciable

Table 3. "Standard" values, for 30 year-old men and women and for 6 years-old children, of the constant k, the alveolar ventilation rate $\dot{V}_A$, the rate constant for HbCO formation K, the half-life, the time need for the HbCO level to fall from 0.200 to 0.010 and from 0.050 to 0.010 in unpolluted air, for the levels of physical activity A (at rest-sitting), B (walking 4 km/hour) and C (strenuous or sporting activity).

	Men, k = 0.00183/ppm			Women, k = 0.00202/ppm			Children, k = 0.00223 ppm		
	Activity level A	Activity level B	Activity level C	Activity level A	Activity level B	Activity level C	Activity level A	Activity level B	Activity level C
$\dot{V}_A$, mmole/sec	5.17	10.88	21.77	4.06	8.87	17.74	3.23	5.12	10.25
$K \times 10^{-7}$, fraction/ppm/sec	0.95	1.61	2.35	1.11	1.91	2.75	1.69	2.15	2.81
Half-life $\tau_{1/2}$, min	223	131	90	210	122	85	152	120	92
τ (0.20 → 0.01), min	1030	587	402	973	546	379	706	535	410
τ (0.05 → 0.01), min	575	321	220	543	299	207	494	293	224

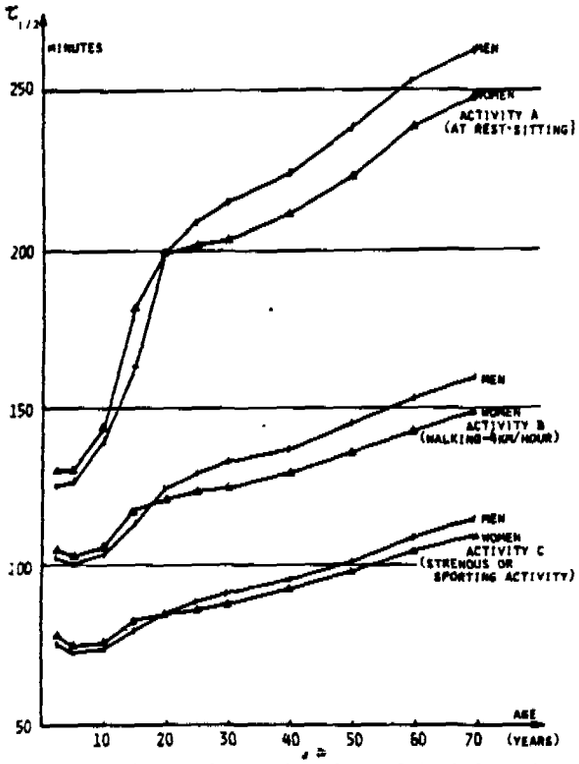

FIGURE 4. Effects of age and the level of physical activity on HbCO half-life.

from the average and the actual deviation will be even greater in the case of the actual population.

The half-life increases with age, the increase being rapid up to the age of 20 years, after which the increase with age slows down (Fig. 4). Age has a greater effect on the half-life than does the sex of the subject. Thus it may be seen from Figure 4 that the half-life for subjects at rest doubles as the age increases from 2 to 70 years, whereas the difference in half-life between male and female subjects does not exceed 6%. The half-life decreases with physical activity, the effect here being about the same for both male and female subjects but less pronounced for children where the muscular power expended is a small proportion of the total power expended. The degree of variation in the half-life with age or the sex of the subject decreases as the level of activity increases. We also studied the effect of the height on the half-life in the case of healthy subjects whose weight was an optimum with respect to height according to the relationship: $m = 75H + 0.25Y - 67.5$ for a male subject, the weight being assumed to be 5 to 10% less for a female (*29*). Height had only a slight effect on half-life in the case of female subjects involved in a low level of activity, when $\tau_{1/2}$ was found to increase with height.

Conclusions

The uptake-elimination of carbon monoxide by hemoglobin, i.e., the variation in the level of carboxyhemoglobin (HbCO) of a subject, can be defined by a fairly complex differential equation which involves a number of physiological parameters. We verified the validity of this equation on a sample of 73 subjects made up of persons of both sexes, and for different levels of physical activity and low carbon monoxide levels. As a result of our tests on these sample subjects we established the validity of two methods of simulating the uptake-elimination of carbon monoxide which take account of the nonpathologic variations for individual subjects. Thus the HbCO levels at each instant of a given period of time (day, week, etc.) can be predicted with reference to initial level and on taking account of the applicable conditions as a result of an analytical method of solving the differential equation (actual calculations in each case or use of an existing set of graphs based on previous calculations). This can be done better by a mathematically based simulation of the periodic variations in HbCO levels without reference to initial level. The HbCO levels depend first of all on the CO concentration in the atmosphere and then on the level of physical activity, the age (the half-life increasing with age) and finally on the sex (the half-life is a little shorter for the female sex) of the subject.

It would appear that the HbCO levels predicted by the periodic simulation are a function of the HbCO half-life (as determined by a fairly simple calculation) but this matter should be the subject of a more systematic statistically based study.

Although we did not study the matter in any detail, it appears that subjects suffering from certain ailments and in particular from respiratory deficiencies for whom certain physiological variables deviate appreciable from the normal values can have carboxyhemoglobin levels that are significantly different from those encountered in the course of this investigation. We need more detailed information for such cases.

It is difficult to reach any conclusion with regard to the short-term and long-term effects of the low carboxyhemoglobin levels that have been observed in a nonsmoking population. With the exception of people who are exposed to the atmospheric pollution due to road vehicle traffic, in particular because of their occupation, it appears however that there are no effects on either the alertness or sensory perception of pedestrians or car passengers making journeys of short duration in the city of Lyon. For the car passengers in our sample, who

were the subjects exposed to the highest level of atmospheric pollution, the HbCO level amounted to 0.027, on the average, at the end of their test journey. The levels of atmospheric pollution normally encountered can however have effects on advent of arteriosclerotic lesions. Thus such levels are sufficient to result in the occurrence or an increase in the seriousness of acute ischaemic incidents in subjects who already suffer from artery deficiencies.

Apart from being useful in establishing carbon monoxide atmospheric pollution indices, the results of this study may also contribute to the establishment of the standards for acceptable carbon monoxide concentrations on the basis of the following approach: establish the carboxyhemoglobin levels that must not be exceeded for both healthy and pathological subjects; determine the CO concentrations that are in agreement with these carboxyhemoglobin levels by simulating the cyclic variations as well as employing other techniques.

In making this approach, it must be understood that there is no such thing as a population of average subjects, but the physiological characteristics and hence the sensitivity to the effects of carbon monoxide vary in accordance with a Gaussian distribution about the mean values that we have considered here for healthy subjects. There is also the fact that there are pathological variations of physiological data for a significant proportion of the population.

More generally, the results of the study can be of use whenever it appears to be necessary to give proper attention to certain periods of time that are being studied out of their normal context (e.g., in the case of industrial medicine studies periods of time, other than the concerned with work high carbon monoxide concentration considered periods, could affect carboxyhemoglobin levels), first for low pollution, because the precision of certain methods is a good as low is HbCO level.

This study has been the subject of an internal report (*30*).

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Noise and Stress: A Comprehensive Approach

by Jack C. Westman* and James R. Walters†

The fundamental purposes of hearing are to alert and to warn. As a result sound directly evokes emotions and actions. The processing of sound by the brain is outlined to provide a biological and psychological basis for understanding the way in which sound can become a human stressor. The auditory orienting response, startle reflex and defensive response translate sound stimuli into action and sometimes into stress induced bodily changes through "fight or flight" neural mechanisms. The literature on the health and mental health effects of noise then is reviewed in the context of an integrated model that offers a holistic approach to noise research and public policy formulation. The thesis of this paper is that research upon, and efforts to prevent or minimize the harmful effects of noise have suffered from the lack of a full appreciation of the ways in which humans process and react to sound.

Introduction

The damaging effects of noise usually are regarded as limited to the structures of the ear through impairing one's ability to hear sounds such as speech and music. Often unappreciated is the fact that noise has more pervasive physiological effects (*1*, *2*).

In the course of evolution, certain fishes developed organs of hearing to orient themselves in space. In amphibians, vision provided the ability to locate prey but was not sufficient in terrestial environments to warn of other predators. Hearing accordingly developed as an organ for perceiving and responding to danger (*3*). Hearing also has played a role in sexual mating behaviors in mammals and even insects. These primitive functions exist in humans as well.

From the outset sound has evoked emotions and actions through the inner ear's direct connections to "fight or flight" neural mechanisms via the autonomic nervous system. Because of this defensive purpose, hearing also cannot be turned off, and sound registers in the brain even during sleep. Only later in primate evolution did the auditory system include higher cerebral centers permitting the appearance of spoken language.

The current usage of the terms "nonauditory" or "extraauditory" is unfortunate. This distinction designates as nonauditory the auditory system's original, primitive influence upon wakefulness and body activity. The auditory system and physiological responses to sound are inseparably connected. Therefore, all of the effects of noise on the body mediated by the ears are "auditory" effects. More precisely, the effects of sound on the body through vibration of structures other than those of the auditory system are "non-auditory" or "extra-auditory."

Another basic consideration in understanding the functioning of the auditory system merits emphasis. The human auditory system was designed to process the frequencies and intensities relevant to survival in the sound environments of nature. The evolutionary process has not allowed humans enough time to adapt hearing to sounds generated by loud modern noise sources. This means that the auditory apparatus is not prepared to cope with commonly encountered urban and industrial noise. Consequently, we find ourselves exposed to sound envi-

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ronments that overload the auditory system. An analogous situation would occur in the visual system if we were forced to look at the sun and thereby damage the retina.

The fundamental relationships of hearing to emotion and action and the auditory system's vulnerability to modern sounds are not appreciated sufficiently by the public. Research also has suffered from a lack of breadth and depth in conception resulting in contradictory findings. For example, laboratory studies of healthy young people have concluded that noise has no harmful psychophysiological effects on humans. At the other extreme are reports that jet aircraft noise increases psychiatric hospital admissions.

We lack a comprehensive model to ensure that research on sound includes the critical variables that make it a significant source of human stress. Much of the research cited in this paper suffers from methodological inadequacies because noise is but one of a number of variables affecting complex human beings. Before delineating the system levels involved in bodily responses to sound, we first will outline the neuroanatomy and physiology of the central processing mechanism of sound.

Neuroanatomy of the Auditory System

An appreciation of the structural basis for physiological and behavioral responses to sound can be gained from knowledge of the neuroanatomy of the auditory system (Fig. 1). The auditory pathways of the central nervous system consist of direct pathways from the inner ear to the auditory cortex and indirect pathways to the reticular activating system which connect to the limbic system and other parts of the brain, the autonomic nervous system and the neuroendocrine system (4).

The direct auditory connections consist of ascending pathways which carry impulses excited by sounds from the receptor cells in the organ of Corti to the auditory centers in the cerebral cortex. These pathways end in the temporal lobe where the sum of incoming impulses are consciously perceived and interpreted. The ascending auditory pathways travel along the auditory nerve via the cochlear nucleus, superior olivary complex, inferior colliculus, nuclei of the lateral lemniscus and geniculate body to a number of areas in the auditory cortex which in turn are connected to other cortical areas that

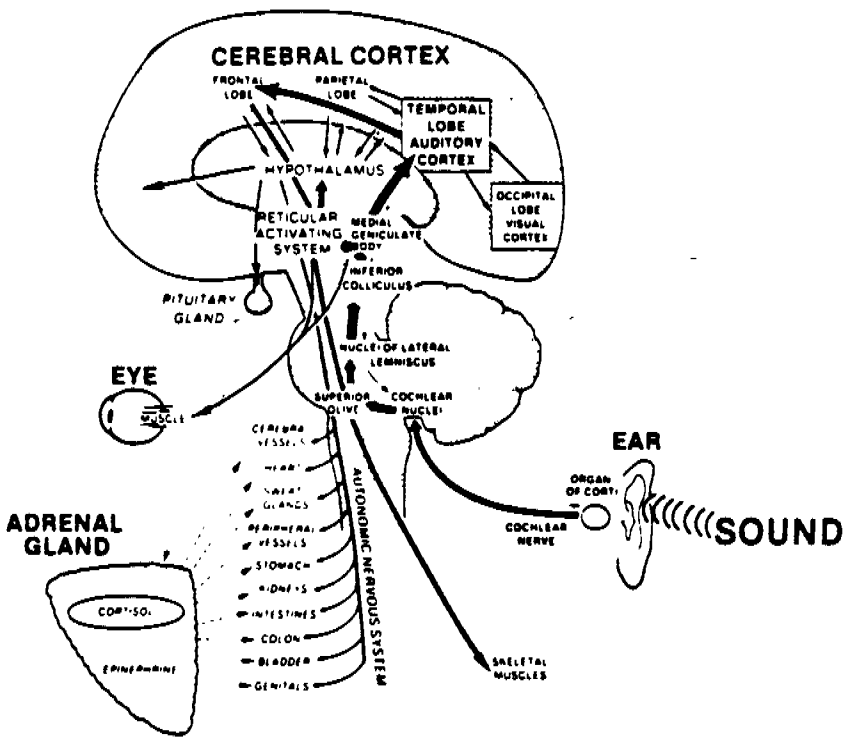

FIGURE 1. Processing of sound by the brain.

receive inputs from the other sensory organs as well.

There also are descending pathways from the temporal cerebral cortex to the dorsal cochlear nucleus via the inferior colliculus and to the organ of Corti via the medial geniculate body, inferior colliculus and lateral lemniscus through the olivocochlear bundle. These descending pathways have inhibitory and, to a minor degree, excitatory influences.

In addition to these direct pathways to and from cerebral cortex, there are a variety of indirect connections from the inner ear to the brain centers that control basic physiological, emotional and behavioral responses of the body. Nerve fibers branch out from the various synaptic junctions along the direct auditory pathways to motor cell nuclei subserving reflexes within the brainstem and to the reticular activating system in the midbrain.

Impulses reaching the reticular activating system excite still other impulses that spread to higher cerebral centers that control alertness, cognition and motor performance. At the same time the reticular activating system conveys impulses to hypothalamic autonomic nervous system centers which are linked to the sympathetic-adrenal neuroendocrine system and thereby regulate the secretion of the catecholamines, adrenaline (epinephrine) and noradrenaline (norepinephrine). Impulses conveyed by the reticular activating system also are transmitted to the pituitary-adrenal neuroendocrine system which secretes corticosteroids (cortisol). The catecholamines play an important role in mobilizing immediate adaptive resources of the body, and the corticosteroids provide for more enduring adaptation to prolonged stress (*5*). Thus, the auditory apparatus is connected to the entire central nervous system and the neuroendocrine system as well.

Physiology of Sound

In conjunction with the other special senses, the auditory system serves to maintain the arousal of the brain projections to the temporal cortex and the reticular activating system via the limbic system and the hypothalamus. In this way cognitive processes and emotions interplay with sound stimuli in influencing the state of consciousness.

The cerebral cortex requires a certain level of arousal to make optimum use of incoming sensory information upon which efficient behavior and physiological functioning depend (*6*). Neither underarousal nor overarousal is conducive to effective performance of physiological functioning (*7*). Sound can improve performance on tasks which are inherently underarousing, repetitive, and monotonous. Conversely, sound can impair performance on tasks demanding concentration and complicated responses (*8*). Sound contributes to the homeostasis of the central nervous system and consequently influences the physiological homeostasis of the body through the autonomic and neuroendocrine centers of the hypothalamus.

The arousal level of the central nervous system depends upon the intensity, complexity, variability, predictability and meaning of sound stimuli. The auditory system responds most to changes in the timing of sound stimuli. Therefore, a transient increase in the firing of auditory neurons may be produced by the termination of a sound as well as by its inception. Some neurons in the auditory system respond to stimulus onset with a high rate of impulse discharge, quickly cease firing, remain silent while the stimulus is continued, and discharge a second burst of impulses when the stimulus stops. However, in a much larger number of neurons, the rate of firing declines to a lower level of activity shortly after the initial high frequency discharge and then is tonically maintained during long periods of continued stimulation. These sound stimulus-induced alterations persist after the stimulation ceases (*9*).

The direct effects of certain sounds on emotions and attitudes is illustrated by the fact that chalk scraping on a blackboard can cause chill sensations in a listener. Musical rhythm, tempo and melody can evoke moods ranging from calmness to excitation or elation. Music also can promote positive attitudes toward work. The further influence of higher cerebral cortical centers on the emotional reaction to sound stimuli is illustrated by a study of sound in hospitals in which one source of annoyance was staff conversations in the halls, not because of undue loudness but because of the discussion of patients (*10*).

Sound stimuli also influence the other sensory systems. For example, sound input overload can induce visual changes in color perception, cause nystagmus and vertigo and even act as an analgesic (*11*).

In summary, sound stimuli play a vital role in maintaining arousal of the brain and thereby influence the basic physiological functioning of the body. Sound may influence the body after cessation of the stimulus through reverberating neural circuits within lower and higher brain centers. In this way sound can produce physiological reactions that develop a momentum of their own independent of the original stimulus.

Fundamental Auditory Responses

Orienting Response (Novelty Reflex)

The basic behavioral response to all sound stimuli is the orientation reflex, which involves ascending and descending auditory cortical pathways and is reflected by an arousal pattern in the electroencephalogram. The response orients the head and eyes toward the source of a sound in order to ready the organism to receive and respond to the sound stimulus situation. There is an associated decrease in auditory threshold and increased attention to the sound stimulus.

The orienting response occurs to sounds of low or moderate intensity and significance. The person's cognitive appraisal of the sound stimulus determines the intensity and duration of the orienting response. It extinguishes, or habituates, after varying repetitions so that the individual can accommodate to familiar and insignificant sounds with relative ease and concentrate on a preferred activity. If an appreciable amount of time passes between repetitions of a specific sound, habituation disappears and repetition of the same sound again evokes an orientation response. Habituation usually does not occur if attention to a sound is voluntarily sustained or if a sound has special significance, either positive or negative. Sounds of close to hearing threshold intensity do not easily habituate, probably because of the auditory system's difficulty in assessing their significance.

Even after behavioral habituation has occurred, sound stimuli continue to activate both cortical and subcortical areas of the brain (*9*). This is in part because excitation transmitted by the reticular activating system continues to arrive in the cerebral cortex after that transmission directly ceases. When the decision is made not to orient to a sound, descending cortical excitation actively restrains, but does not eliminate, the reticular activating system's excitation from spreading to higher areas of the brain. After the orienting response to sound habituates, there may be no change or an increase in the amplitude of the electrical responses evoked in the cerebral cortex and the medial geniculate body. The reticular activating system and the structures that it influences continue to be affected by sound even after behavioral habituation has occurred. This is not surprising because the organism's survival would be threatened by decreased alertness to danger if unattended stimuli were excluded from cognitive appraisal.

Startle Reflex

The second basic auditory response is the startle reflex which is evoked by sounds of sudden, intense, or frightening significance. The reflex has a series of components. First, the middle ear muscle reflexes via the superior olive to the tensor tympani through the fifth cranial nerve and to the stapedius muscle through the seventh cranial nerve provide a small degree of protection against sounds of extremely high intensity. The auropalpebral reflex via the superior olive and the sixth cranial nerve produces eye blinking. There also is opening of the mouth and flexion of the neck via the seventh and eleventh cranial nerves. More generally, there is flexion of most muscle groups in a "freezing" posture with raising of the shoulders, abduction of the arms, flexion of the fingers, contraction of the abdomen, and bending of the knees mediated by the ascending auditory and descending cerebral cortical motor pathways. The typical reflex is completed in less than one second.

Those components of the startle reflex that reflect cerebral cortex activity are subject to habituation or enhancement, however, those involving lower centers in the brainstem are not. The startle reflex accordingly can be decreased by anticipation, increased by background sound levels and exaggerated by emotional states such as fear.

The Defensive Response ("N" Response)

Although usually an extension of the orienting or startle responses, the defensive response merits separate consideration because it can occur independently of them and does not require sounds of high intensity. This response is produced by sounds of sufficient intensity, significance or duration to be perceived as threatening and to mobilize a "fight or flight" reaction. The response includes alerting of the cerebral cortex, emotional arousal, and preparation of the body for action (*12*).

Sounds in the range of 70 to 120 dB can produce the defensive response which appears first in the form of skeletal muscle tension that quickly reaches its peak and decays within a few seconds. Next there is a decrease in skin electrogalvanic resistance which changes more gradually than the skeletal muscle tension. Pupillary dilation occurs as well. A variety of circulatory responses are next in order: first an acceleration of pulse rate and decrease in pulse pressure, then a constriction of the finger and dilation of the chin blood vessels, followed by a slowing of pulse rate and an increase in pulse pressure. Finally in the series comes a shift to slower,

deeper breathing. The defensive response also includes a reduction in salivary and gastric secretions and slowing of digestive processes (*4*).

The defensive response largely involves the sympathetic nervous system but has some parasympathetic aspects. This response is not limited to a single organ system or structural division of the nervous system. It occurs independent of emotional response on the part of the subject. It is altered by sound intensity and band width in a dose-dependent fashion. It does not completely habituate (*13*), although under laboratory experimental conditions, substantial apparent physiological habituation has been reported (*14*). It also may be elicited by low levels of sound with special significance (*15*).

Under actual working conditions, the physiological effects of the defensive response were found in sawyers exposed to bandsaw noise (*16*). Another laboratory study noted a decrease in blood eosinophile level reflecting a stress response after 25 min exposure to 85 dB level noise (*17*).

The defensive response can become the stress that leads to the General Adaptation Syndrome that will be described more fully later with its alarm, resistance, and exhaustion stages if the sound stressor is of sufficient duration, quantity, and quality (*18*). When this takes place the hypothalamic-pituitary-adrenal axis is mobilized with resulting increase in adrenal cortisol and epinephrine output. During prolonged exposure to intense sounds, these endocrine effects may produce gastroduodenal ulcers and renal changes in laboratory animals (*1*).

Next we will enumerate the critical variables that determine whether or not sound stimuli become stressors that produce human stress.

Sound as a Stressor

Modern urbanization, crowding, the mass media, information technology, conditions of work and noise are overloading the human sensory environment (*19*). Of these stimuli our interest is in sound, particularly noise, although sound with meaning, such as speech, also can contribute to overloading an individual's processing capabilities. The progressive increase in noise from industrial, traffic and home sources, both machine and human generated, has reached offensive proportions in the United States (*20*, *21*).

Noise essentially is unwanted sound. As such, subjectively experienced noise is any sound that produces annoyance or communication or task performance interference. The same sound stimulus may be perceived subjectively as noise by some and not by others. For this reason it is useful to define objectively experienced noise as sound that produces harmful bodily effects, which may or may not be subjectively perceived. This point is important because noise can be subjectively or objectively stressful, or both.

In information processing terms, noise is sound that overloads the central nervous system's pro- this state can be detected by changes in the electroencephalogram (*27*). The reception of a stimulus is influenced by two kinds of cognitive state characteristics, current transient influences and enduring qualities of the individual.

The first characteristics are transient influences that are more evident and easily measured than the second type. They include level of mental arousal, from sleep through alertness to anxiety; the context of sensory stimuli arriving through the other special senses; the motor context which includes ongoing task performance, the activities of the individual; the meaning of the stimulus evoked by associations from cerebral cortical memory areas; the degree of perceived control of the stimulus, whether one is able to control the situation is helpless or expects failures (*25*) and social values and attitudes toward the stimulus sources.

The level of mental arousal is influenced whether or not a sound stimulus is consciously perceived as a stressor. During the stage of early sleep, for example, sound can produce orienting and defensive responses and alter the quality of sleep without causing awakening. At the other extreme, an anxious individual can experience heightened sensitivity to a sound stimulus. For example, a study of college age males rated on an anxiety scale disclosed that for subjects rated high on anxiety, household noise levels were stressors as manifested by impaired task performance and subjective frustration (*28*).

The interaction of sound stimuli with other sensory stimuli may be significant. For example, related visual stimuli enhance the effect of sound. Clinically, sound can have an analgesic effect when certain intensities and frequencies occur in the presence of pain as is known in the practice of dentistry.

The ongoing motor activity of an individual influences cognitive state with higher levels of arousal by sound stimuli occurring while complex tasks are being performed and lower levels of arousal occurring when routine, monotonous activities are taking place.

For obvious reasons related to survival at a primitive level the meaning of sound is one of the most important factors that determines an organism's response. Threatening sounds of any kind portend potential danger, however, certain sounds acquire particular significance because of their symbolic meaning to the individual. Conversely, familiar,

repetitive sounds of moderate intensity cease to attract attention. Meaning connoting potential danger, then is related to unfamiliarity, rapid changes in intensity, or learned associations. For example, a study of evoked auditory potentials in the brain demonstrated that quickly changing acoustical events produce prominent cerebral excitation. The study also showed that sounds with symbolic meaning were perceived as more annoying than meaningless sounds of the same intensity and also produced larger evoked cerebral potentials (*29*).

Of particular importance is the fact that habituation does not occur to repeated novel laboratory stimuli that imply conflict or are coupled with an instruction to pay attention to that stimulus. Even covert associations with sound stimuli, such as a subject's attitude toward the experimenter, may decrease habituation (*8*). In addition, the symbolic meaning of a sound stimulus can evoke irrational responses, adding unconscious determinants of meaning (*30*, *31*).

In addition to the meaning of the sound stimulus, a sound's predictability is an important determinant of response. In one study, unpredictable noise resulted in lower tolerance for frustration and greater impairment of performance efficiency than predictable noise (*32*). Furthermore, those investigators found that an individual's ability to control the noise source, and even the belief that one could, reduced the adverse impact of unpredictable noise (*8*). They postulated that the deleterious effects of noise were a function of unpredictability and the belief that one cessing capacity because it is too great in quantity, appears too rapidly or is dissonant in meaning or pattern. Noise is a commonly used standardized stressor in laboratory testing designed to evaluate human responses to stress (*5*, *22*). In laboratory animals, for example, it is used as a stressor to produce lesions in the renal, reproductive and cardiovascular systems (*23*).

Another illustration of the use of sound is in stress studies such as the one by Cantrell, who exposed healthy young male volunteers to intermittent noise for several weeks (*24*). He found significant increases in plasma cortisol and blood cholesterol levels in addition to associated annoyance and sleep disturbance effects during prolonged exposure to bursts of 85 to 90 decibel noise.

We can use current approaches in stress research to facilitate our understanding of sound as a stressor (*22*, *25*). In stress research the environmental conditions and the intervening bodily structures and processes that determine when and in what forms stress reactions occur are taken into account (*26*).

The work of Rahe, although encompassing life change in addition to sensory stressors, is particularly useful in identifying specific variables that should be taken into account in research on the human effects of noise. Rahe developed a life stress and illness model which identifies the key steps along a pathway extending from a person's exposure to a stressor to the eventual reporting of an illness (*25*). Rahe's model (Fig. 2) utilizes the analogy of a series of optical lenses and filters in which stressors are depicted by a series of "light rays" of different stimulus characteristics.

The influence of a person's perceptual state in altering the experience of a stressor is represented by a "polarizing filter" shown in step 1. Possible sensitization, or desensitization, of a person to a stressor is indicated by changes in the "light rays" as they pass through the filter. The psychological defense mechanisms which appear to be capable of "diffracting away" a stressor's impact are depicted

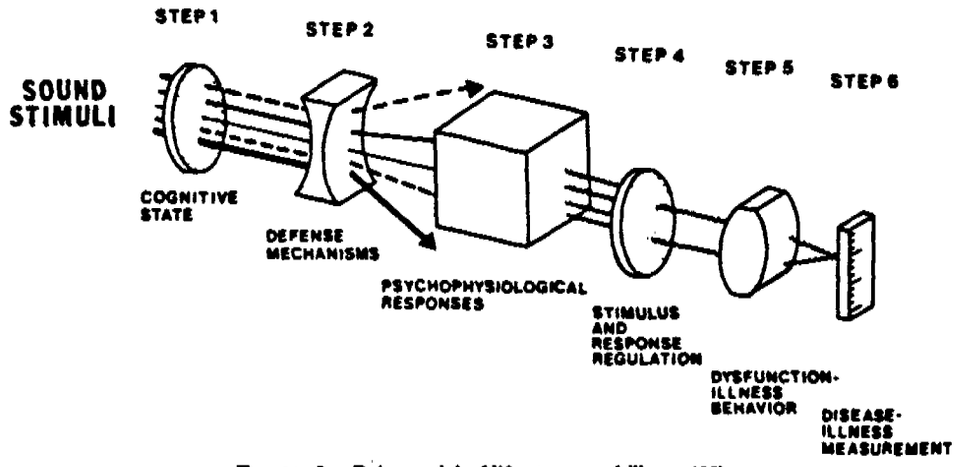

FIGURE 2. Rahe model of life stress and illness (*25*).

by the negative lens in step 2. Stimuli not so diffracted pass on to produce a variety of physiological reactions represented by the "black box" in Step 3. The wavy lines emerging from the black box cease to represent specific stressors and begin to indicate various psychophysiological responses to perceived and "undefended" stressors. Next a "color filter" shown in step 4 depicts how a person may cope with or absorb certain of these physiological reactions. Prolonged psychophysiological activations, if unabsorbed, lead to organ dysfunction and eventually to psychological and bodily symptoms. Symptomatic individuals may then seek medical care. A person's "focusing" of attention on symptoms is indicated by the illness behavior "positive lens" in step 5. If these symptoms are reported to health personnel, the person receives a medical diagnosis which then can be used as a measure of illness as represented in Step 6.

The value of Rahe's model is that it incorporates pertinent system levels in conceptualizing human responses to stressors, ranging from organ system to societal levels. It permits inclusion of both subjective and objective data as well. Furthermore, the model reflects clinical realities by recognizing the social factors that influence whether or not experienced dysfunctions become labeled as manifestations of illness. For these reasons, we will use Rahe's model to elucidate key variables in the human experience of sound as a stressor.

Cognitive State

Bearing in mind the preceding discussion of the characteristics of sound experienced as noise, the first step in processing a sound stimulus is the cognitive state of the individual. Some variations in this state can be detected by changes in the electroencephalogram (*27*). The reception of a stimulus is influenced by two kinds of cognitive state characteristics, current transient influences and enduring qualities of the individual.

The first characteristics are transient influences that are more evident and easily measured than the second type. They include level of mental arousal, from sleep through alertness to anxiety; the context of sensory stimuli arriving through the other special senses; the motor context which includes ongoing task performance, the activities of the individual; the meaning of the stimulus evoked by associations from cerebral cortical memory areas; the degree of perceived control of the stimulus, whether one is able to control the situation is helpless or expects failures (*25*) and social values and attitudes toward the stimulus sources.

The level of mental arousal is influenced whether or not a sound stimulus is consciously perceived as a stressor. During the stage of early sleep, for example, sound can produce orienting and defensive responses and alter the quality of sleep without causing awakening. At the other extreme, an anxious individual can experience heightened sensitivity to a sound stimulus. For example, a study of college age males rated on an anxiety scale disclosed that for subjects rated high on anxiety, household noise levels were stressors as manifested by impaired task performance and subjective frustration (*28*).

The interaction of sound stimuli with other sensory stimuli may be significant. For example, related visual stimuli enhance the effect of sound. Clinically, sound can have an analgesic effect when certain intensities and frequencies occur in the presence of pain as is known in the practice of dentistry.

The ongoing motor activity of an individual influences cognitive state with higher levels of arousal by sound stimuli occurring while complex tasks are being performed and lower levels of arousal occurring when routine, monotonous activities are taking place.

For obvious reasons related to survival at a primitive level the meaning of sound is one of the most important factors that determines an organism's response. Threatening sounds of any kind portend potential danger, however, certain sounds acquire particular significance because of their symbolic meaning to the individual. Conversely, familiar, repetitive sounds of moderate intensity cease to attract attention. Meaning connoting potential danger, then is related to unfamiliarity, rapid changes in intensity, or learned associations. For example, a study of evoked auditory potentials in the brain demonstrated that quickly changing acoustical events produce prominent cerebral excitation. The study also showed that sounds with symbolic meaning were perceived as more annoying than meaningless sounds of the same intensity and also produced larger evoked cerebral potentials (*29*).

Of particular importance is the fact that habituation does not occur to repeated novel laboratory stimuli that imply conflict or are coupled with an instruction to pay attention to that stimulus. Even covert associations with sound stimuli, such as a subject's attitude toward the experimenter, may decrease habituation (*8*). In addition, the symbolic meaning of a sound stimulus can evoke irrational responses, adding unconscious determinants of meaning (*30*, *31*).

In addition to the meaning of the sound stimulus, a sound's predictability is an important determi-

nant of response. In one study, unpredictable noise resulted in lower tolerance for frustration and greater impairment of performance efficiency than predictable noise (*32*). Furthermore, those investigators found that an individual's ability to control the noise source, and even the belief that one could, reduced the adverse impact of unpredictable noise (*8*). They postulated that the deleterious effects of noise were a function of unpredictability and the belief that one had little or no control over the noise source. A laboratory study of rhesus monkeys exposed to noise disclosed that plasma cortisol levels were significantly higher in animals with no control over the noise source than in those with control (*33*). Similar findings resulted from an experimental study of humans performing mental arithmetic problems under noise exposure (*34*).

The importance of attitude toward the noise source is illustrated by another study in which a positive or negative attitude toward all aspects of one's community consistently influenced the reporting of perceived annoyance by noise positively or negatively (*35*). In the same vein, a Swedish study disclosed that propaganda promoting the importance of the air force diminished the reported annoyance levels in a community exposed to military aircraft noise (*36*).

The second kind of variables that influence the cognitive state of an individual are enduring background characteristics in the form of individual differences in temperament and cognitive styles, organic disease processes and mental illness.

Individual variations have been demonstrated in the ways that sensory stimuli are processed. Some individuals reduce and some augment the intensity of stimuli, leading to low or high sensitivity to a particular stimulus (*19*). Sensitivity to noise also is correlated with empathic, creative, intellectually oriented personality traits, confirming Schopenhauer's comment that "noise is a torture to people of great intellect" (*37*). Extraverted children may have a higher level of noise tolerance than introverted children (*38*). Moreover, individuals who express criticism tend to report annoyance by noise (*35*). Further evidence of individual differences in sensitivity to noise is reflected by the finding that some people thrive on noise which tends to synchronize their electroencephalograms while most people show electroencephalographic desynchronization (*39*, *40*). At the other extreme, it is likely that 4 to 6 % of the normal population is "noise sensitive," in the sense that they do not adapt to noise at all (*8*). For all of these types of individuals, noise has implications detrimental to their mental health.

As an illustration of other background illness characteristics, one study showed that cardiac infarction and schizophrenic patients showed greater stress responses to noise as measured by cortisol and urinary catecholamine levels than did normal subjects (*41*). Similarly, persons with cerebral vascular disease were found to be more susceptible to the detrimental effects of noise than normal subjects (*42*). Another unique group of patients harmed by sound are those susceptible to audiogenic seizures. Some are affected by sounds that produce the startle response and others by sounds such as music (*43*).

The role of psychiatric status in sensitivity to sound was suggested in a study in which normal subjects and patients with specific phobias showed habituation of physiological responses to noise while hysterical patients did not. Moreover, patients with diffuse phobias, anxiety neuroses and agitated depressions all habituated more slowly than normals (*44*). In a general sense, another survey found that psychiatric patients were more annoyed by noise than normal subjects (*45*).

Defense Mechanisms

The next cluster of variables that influence an individual's response to sound stressors are internal defense mechanisms noted in step 2 of Rahe's model. In contrast with coping techniques which are directed toward changing the stimulus environment, the defense mechanisms are devoted to maintaining homeostasis or internal equilibria, within the person.

The defense mechanisms operate automatically and unconsciously. The most primitive is the acoustic reflect which offers a small degree of protection from high intensity sounds. Another example of a physiological defense is cerebral cortical inhibition such as was demonstrated in a study of laboratory animals exposed to extreme sound which ultimately produced convulsive seizures and lethal cerebral hemorrhages. This study found that a seizure producing epileptogenic focus of excitation arising in the medulla was actively inhibited by the cerebral cortex. When this inhibitory process was exhausted, seizures occurred (*46*).

In addition to these physiological defenses, psychological defenses shield the individual from physiological arousal and also play a significant role in reducing sensitivity to sound. For example, the psychological defenses of repression and denial can minimize physiological responses as was found in a study of patients in a coronary intensive care unit (*25*).

Psychophysiological Responses

The next level, step 3 in the model, comprises psychophysiological responses to sound stressors. The psychophysiological responses can be divided into two categories. First are responses within the awareness of the individual, such as sweating, change in heart rate and muscle tension. Second are those responses which occur outside of one's direct awareness, such as changes in serum lipids, cortisol, blood pressure and blood sugar levels.

The psychophysiological responses are manifestations of the defensive response to sound, can be immediate or delayed, and occur in interactional patterns. Thus, studies of single physiological responses oversimplify the mixture of responses. An example of an immediate psychophysiological response to noise is the finding of elevated diastolic and systolic blood pressures and urinary excretion of norepinephrine metabolites in brewery workers on days in which they deliberately did not wear hearing protective devices (*48*).

Genetic and constitutional individual differences may increase the likelihood that a particular organ system will respond to stressors more than others and over time lead to disease. There also may be a critical period during infancy in which visceral learning takes place, adding conditioning of an individual's disposition to the physiological responsiveness through a specific "target" organ system (*49*). For example, in certain predisposed individuals, the target organ is the cardiovascular system, and sound stimuli produce intermittent increases in blood pressure which may eventually cause structural changes in blood vessels leading to permanent hypertension (*50*).

Stimulus and Response Regulation

The next cluster of variables are stimulus and response reduction mechanisms. These coping techniques may deal with the stressor itself or with the physiological and emotional responses to it (*51*, *52*). Using ear protective devices is an example of dealing with the stressor itself by reducing the reception of the sound stimulus.

If one becomes aware of the psychophysiological responses, particularly if they are seen as threats to health, deliberate response management techniques can be employed. For example, muscle relaxation may "absorb" the muscle tension that contributes to elevation in blood pressure.

In a broader social sense, stimulus regulation can be achieved through an individual's participation in community, industrial and consumer efforts to acoustically condition home and working environments and manufactured products.

Dysfunction: Illness Behavior

In step 5 in the model, the lack or failure of defense mechanisms and regulation techniques play important roles in producing dysfunction. The concept of sensory and information input overload is useful in understanding how the central nervous system responds when defense mechanisms and regulation techniques fail to adequately screen incoming stimuli. In this conception sensory inputs are the sound stimuli and information inputs are sounds with symbolic, message containing meaning. Overload results from an excess of the number or rate of sensory or symbolic stimuli or both.

Human experiments have shown the disorganizing and psychotogenic effects of sensory overload. Experimental exposure to intense visual and auditory sensory overload produces dramatic effects in the form of heightened and sustained arousal, mood changes, illusions, hallucinations, and body image distortions (*19*).

Sensory and informational sound overload also are commonplace in modern, urban living (*53*). Jets, air compressors, sirens, rock and roll music and road traffic are generally unpredictable and often uncontrollable sources of stimulation that contribute to making the sound of our environment inimical to mental well being. Low frequency noises have effects similar to the more familiar piercing high frequency sounds (*54*, *55*).

A typical household vignette illustrates the unrecognized importance of sound sensory and informational overload in our lives. The washing machine provides a steady hum, the clothes dryer suddenly begins to vibrate; then the telephone jangles while the delivery boy rings the doorbell; a jet aircraft rumbles overhead and automobile horns are heard, a television set blares in the background; and amidst this confusion, children begin to fight, cry and scream. The overall noise level is not high by hearing damage risk criteria, but a homemaker can attest to the resulting frustration, irritability and even anger. Over time, one manages to adapt to this noise routine. However, one makes errors in balancing the checkbooks, screams at the children for minor transgressions, is irritable with one's spouse, and generally shows symptoms of stress by the end of the day. Furthermore, when one becomes resigned to a lack of control over one's environment, the resulting "learned helplessness" itself may become a stressor and contribute to additional symptoms of depression (*10*, *56*).

Selye's classic work on stress provides a framework for understanding the body's responses to sensory and information input overload (*18*). His terms stressor and stress are comparable to stress and strain in physics. In his view stressors produce two types of changes in the body. The first is a primary nonspecific change in an organ system called the "Local Adaptation Syndrome." This local adaptation occurs repeatedly in normal living. For example, running produces stress in the musculoskeletal and cardiovascular systems. The resulting exhaustion is reversible through rest.

The second change is the "General Adaptation Syndrome" which is activated by intense and persistent stressors that produce a specific effect on the adrenal glands, thymus and stomach. The fully developed general adaptation syndrome consists of three stages: an alarm reaction, a stage of resistance and an ultimate stage of exhaustion. Extremely severe stress can lead rapidly to exhaustion and death.

Stressors, then, set in motion adaptive responses which maintain biological and psychological homeostasis. In addition to specific organ system responses, a relatively stereotyped set of neuroendocrine reactions contribute to the development of the general adaptation syndrome. Most prominent are increased secretion of the adrenal cortical hormone, cortisol, and increased activity of the sympathetic nervous system, including increased secretion of epinephrine by the adrenal medulla. The increase in sympathetic nervous system activity prepares the individual for "fight or flight." The net effect of these responses is to mobilize nutrients, such as glucose from the liver and fatty acids from fat tissue, to "arouse" the central nervous system, to provide more oxygen and nutrients to skeletal muscles, to increase contractibility of skeletal muscles and to increase coagulability of the blood. When these responses are persistent, the sustained effects of cortisol may appear in the form of gastric ulceration, inhibition of immune responses, hypertension, atherosclerosis, sterility and personality changes (*57*). Most stressors act for a limited time and produce changes corresponding to the first and second stages of Selye's syndrome. The complete general adaptation syndrome results in a specific set of physical changes: enlargement of the adrenals, shrinkage of the thymus and lymph nodes and ulceration of the stomach.

Selye's conception helps to explain that subjective experience and physiological responses to stressors can appear to have returned to normal or pre-stressor levels during the second stage of resistance. This point is essential in understanding the phenomenon of habituation which has been repeatedly observed in experimental studies of human responses to sound as a stressor (*8, 14*). Habituation may reflect the completion of a local adaptation syndrome cycle with restoration of normal bodily functioning. On the other hand, it may reflect a stage of resistance during which the body is moving into the full general adaptation syndrome which gains a momentum of its own and exacts a physiological cost through the development of dysfunction of the various organ systems.

A stimulus appraised as threatening gradually loses its capacity to arouse an emotional response if it is reappraised on repetition as less harmful and results in adaptation (*26*). This surface adaptation may be deceptive, however, and continued exposure to the stressor may produce cumulative effects that appear after stimulation is terminated. This may be in the form of strain induced by the adaptive responses themselves. In spite of adaptation, then, stressors may cause biological and behavioral aftereffects following cessation of the stimulus (*8*).

Laboratory studies of the physiological and behavioral reactions to noise indicate that adaptation (habituation) generally takes place in healthy subjects. There is laboratory evidence, however, which suggests that some components of physiological responses to noise do not habituate completely (*58*), although this work has been questioned (*14*). It is important to distinguish between the tension response of an organism to stressors and stress which is a dangerous condition resulting from failure to manage tension effectively (*59*).

Another factor should be taken into account. More than lower animals, human reactions to stressors not only depend upon the direct impact of stimuli themselves but also on associated cues that signify the meaning and consequences of the stimuli. Human stress, therefore, must be defined in terms of transactions between a stimulus and an individual's reaction to the situation.

The fact that sound stimuli are processed cognitively, therefore, introduces the important conception that psychological stressors, such as the anticipation of harm, can strongly influence human responses to sound stressors (*52*). Activation of the neuroendocrine system usually depends upon the individual's recognition of a stressor as a threat. The auditory system, however, like heat or cold stressors, automatically activate the reticular activating system and thence can evoke autonomic-neuroendocrine responses.

Dysfunction resulting from sound stressors, then, may be the direct result of the sound stressor situation or may indirectly result from the activation and progress of the general adaptation syndrome. Dysfunction may be subjectively experienced

as symptoms, for example, annoyance and tinnitus, or be objectively demonstrable as physical signs, for example, elevated blood pressure and hearing loss. At the same time subjective reports of interference with task performance and speech communication also can be accompanied by objective changes in cerebral responses on the electroencephalogram (*27*).

Human dysfunction can be categorized according to the influence of noise on five basic, interrelated functions that influence the well being, or mental health, of an individual: (1) hearing, (2) sleep, (3) task performance, (4) speech communication and (5) emotional state.

Hearing. The effects of noise on hearing in the form of temporary and permanent threshold shifts and progressive deafness are well documented (*60-62*). There are three levels of hearing at which loss of acuity can occur: the primitive, warning, and symbolic (*63*).

The primitive level includes the familiar background sounds of one's every day environment. Loss at this level constitutes a form of sensory deprivation and may lead to a sense of isolation. Loss of hearing at the warning level contributes to a sense of insecurity and physical vulnerability in the environment. Loss at the symbolic level interferes with interpersonal communication and may result in social isolation, withdrawal and depression. Overlap between levels of hearing loss magnifies the psychological impact on the affected individual.

In addition the need to wear a hearing aid in itself may cause self-consciousness and undermine self-esteem. The emotional and psychological reactions to hearing loss accordingly are threats to an individual's mental health (*13, 64, 65*).

In a more general vein, the loss of hearing with aging (prebycusis) has been related in part to noise exposure in urbanized societies (*66, 67*).

Sleep. Chronic sleep disorders detrimentally affect health and well-being. A major portion of complaints about noise arise from disturbance of rest and sleep (*31*). The Environmental Protection Agency Urban Noise survey found that 28% of the sampled population experienced sleep disturbance which also was rated as the most annoying effect of noise (*20*). Similar findings have been reported by other surveys (*68-71*).

The electrophysiological response to noise tends to decrease during exposure to noise during sleep, however, autonomic responses do not (*31, 72*). This has been shown in a study in which cardiovascular responses did not habituate to traffic noise experienced by sleeping subjects (*73*). In sleep, noise evokes the same orienting response in the form of EEG arousal and changes in heart rate, GSR and finger vasoconstriction as during waking without its voluntary motor component (*31*).

The evidence also is clear that noise exposure during sleep lightens the level of sleep, especially for subjects of an anxiety-introversion personality type (*27, 70, 74*). Sleep disturbances have been reported in response to low frequency noise in the 20-1000 Hz range (*55*). Intermittant noise above the mean background level has a greater effect than louder, more continuous noise on vegetative functions (*75*). Age and sex in addition to sleep stage are critical factors in determining the physiological responses of noise sensitive individuals. Older subjects and women are more sensitive than younger subjects and men. Moreover, sounds with meaning tend to awaken subjects at lower intensities than those without meaning (*76*).

A study devoted to the next day effects of noise-exposed interrupted sleep showed impaired performance of tasks affected by the lack of sleep. There also is suggestive evidence that noise experienced during the waking hours may reduce the duration of sleep of susceptible persons (*77*).

All of these findings suggest that susceptible persons may be affected by noise occurring during sleep as well as during the waking state. For night workers, mothers with babies and elderly persons, day and nighttime noise can be a significant problem (*31*).

Task Performance. There is little evidence that significant performance impairment on simple tasks occurs under continuous noise below 80 to 90 dB (*77*). Unpredictable or intermittent noise, however, does affect performance at even lower levels (*78*). It is well established that noise has a negative effect on work tasks that involve listening or conversing (*79*). Adverse effects occur with complex, multicomponent tasks that require prolonged vigilence or continuous performance and those in which information content is high. Under these circumstances, impairment of task performance persisting after exposure to noisy environments has been reported (*80, 81*).

Evidence has accumulated regarding noise interference in the school performance of children When children are involved in complex activities requiring precise movements and intense concentration, noise produces inattention and impaired task performance (*82, 83*).

A study of the effects of noise generated by expressway traffic in homes showed higher reading achievement for children exposed to lower ambient noise levels (*84*). Another study suggests poorer task performance by young children from noisy than quiet homes (*85*).

A study compared children from schools and

homes with noise levels of 87-99 dBA with those of 48-65 dBA levels. The children in the noisy environments showed increased distractibility and impaired achievement in school. Over a period of four years they became more distractible, indicating increased sensitivity to noise with the passage of time (*86*, *87*). Children exposed to high noise levels in schools also attain lower reading achievement than those with low noise levels (*88-90*).

One study of preschool children found that reflex motor reactions to sound and light stimuli were delayed in those exposed to moderate background levels. The children with the higher noise level required more time in task performance as well (*91*).

All of these performance effects influence an individual's attitude toward work and may constitute additional stressors in themselves, contributing to frustration and stress reactions.

Speech Communication. Interference with communication through speech not only creates personal frustration but has consequences in social interaction. Individuals react to noise levels that do not completely interfere with intelligibility. Noise accordingly may reduce efforts to converse, lead to repeated speech, and ultimately to withdrawal (*92*). The hearing impaired are particularly susceptible to these reactions (*93*). Interference with communication between teachers and children in air traffic exposed schools also has been found (*94*).

Children's speech acquisition and language development may be impaired since the repetition of speech needed to develop these skills is reduced as background noise level increases. Noise accordingly may interfere with the perception of speech by young children and affect the acquisition of language. More than adults, children depend upon the clear perception and repetition of speech sounds during early learning periods (*61*).

Emotional State. The most prominent subjective emotional response to noise is annoyance, a commonly reported but difficult to describe and quantify emotional state. Research on annoyance is hampered by the ambiguity of the term and the fact that one can be annoyed by noise itself or by its symptomatic and behavioral consequences. Arhlin relates annoyance to the direct effects, such as hearing loss, sleep, task performance and speech interference, and the indirect effects of noise, such as blood pressure elevation, headaches, fatigability, anxiety, depression and accident risk (*95*).

A standardized definition of annoyance is needed because each study tends to report annoyance in a different way. In its most specific sense annoyance is an emotion with a protective function. It motivates an individual to try to avoid or influence the sound stressor. Like discomforts such as pain, chill and warmth, annoyance serves to warn an individual of unpleasant or harmful environmental conditions. Annoyance also can be produced by interference with task performance sleep and somatic symptoms. The direct experience of annoyance by noise itself differs from indirect annoyance because of a headache.

Annoyance directly related to noise, then, is an unpleasant emotion experienced as irritability and is a form of anger or hostility related to the state of the individual in a particular social and environmental context. For example, the sound of the barking of one's own dog may be less annoying than the barking of a neighbor's dog. In another vein, some experimental subjects refused to continue in a noise study because they perceived it as unpleasant (*8*). There also is a tendency to regard sound as noise at work more than at home (*96*). Because of this relationship to the peculiarities of the context, annoyance can be expected to vary in its occurrence and reporting.

Annoyance is heightened when noise is perceived as unnecessary; when those responsible for the noise are perceived as unconcerned about the exposed population's welfare; when other aspects of the environment are disliked; when noise is believed to be harmful to health, and when noise is associated with fear (*10*).

Although defined differently from study to study, annoyance is a commonly used concept in surveys of community responses to noise. The tendency is to define annoyance of the respondents in terms of physiological responses, although a scale has been developed that excludes somatic symptoms (*45*). It can be inferred then that the more annoyed a respondent the greater the physiological reactions the person is experiencing. Direct physiological measurements would be preferable to subjective reports, however, the stage of this research is not sufficiently advanced to permit the specific measurement of noise induced stress isolated from other environmental stressors.

The evaluation of annoyance is further complicated. Not only is it an ambiguous concept, but respondents are influenced by the questions they are asked. For example, more positive responses were obtained when people were asked if aircraft noise produced specific symptoms than if asked about symptoms without suggesting a connection to aircraft noise (*97*, *98*). When annoyance was analyzed according to attitude, activity interference and symptoms, McKennel found that 65% of his sample reported feeling annoyed, 35% reported interference with activities and 5% reported symptoms (*99*).

Although methodological problems are important in assessing studies of reported annoyance due to noise, a number of surveys suggest that between 30% and 40% of urban dwellers are regularly annoyed by noise (*20, 21, 31, 96, 100*). In the flight pattern of Heathrow airport in London, 65% reported annoyance (*99*).

Noise in industrial situations also may induce what has been described as an "astheno-vegetative syndrome" in the form of increased fatigability, decreased capacity for focusing attention and slowing of motor reactions (*101*).

Disease: Illness Measurement

In step 6 of the model, whether or not people define themselves as ill depends upon individual and cultural attitudes toward assuming the patient role. These personal and social factors influence whether or not an individual minimizes or exaggerates symptoms and adopts "sick" behaviors such as missing work and seeking health care. The critical step for defining illness, then, occurs when health care is sought and a diagnosis is established. This point is the entree for measuring illness resulting from sound induced stress.

There is an inevitable gap between laboratory studies of the immediate and delayed effects of noise on health. Still, some investigators regard noise pollution in densely populated areas as a social danger comparable to that of known ingested carcinogens and air pollutants (*102*). Imposing problems, however, stand in the way of proving this thesis as illustrated by methodological criticisms of a study which found that people residing near the Los Angeles International Airport had a higher death rate from stress related diseases than a control population (*103*).

More specifically, European research on industrial noise has identified a cluster of symptoms encountered by physicians and referred to as "noise sickness" (*31, 104*). This syndrome is manifested by tinnitus, increased sensitivity to noise, fatigability, lowering of general resistance to illness, headaches, irritability, sleep interference, "heart pains," weight loss, tremors, digestive disorders and ultimately hearing loss. These symptoms are based upon the stress responses of the auditory, autonomic, cardiovascular, endocrine, and gastrointestinal systems and precede the actual loss of hearing.

Although short-term studies show that work performance can be maintained under noisy conditions, the more important consideration is the long-range effect of noise on health. The European data appear to show that complete physiological and psychological adaptation to prolonged noise exposure does not occur. The person reacts unfavorably to noise from the beginning, and adverse reactions progressively increase with the passage of time. This is most evident in work requiring complex task performance. Because of the cumulative negative effect on one's state of health, the adaptation of many individuals working in noisy environments exacts a health cost (*101*).

For convenience we will briefly summarize the relationship between noise exposure and (1) mental illness, (2) cardiovascular disorders, (3) gastrointestinal disorders, (4) neurological disorders and (5) fetal abnormalities.

Noise and Mental Illness. The role of noise in mental illness is most difficult to assess. Several studies of mental hospitals in the vicinity of Heathrow Airport in London disclosed a small but significantly higher admission rate than those in less noisy areas (*105-107*).

Another piece of evidence relating a form of mental illness to noise is through an indirect relationship between noise induced hearing loss and mental illness. Acquired deafness forces a change in life style toward greater social isolation and leads to an over-representation of mental illness in deaf people of all ages. One study found that 46% of a group of elderly deaf persons were paranoid and 21% had affective disorders (*65*).

On the other hand, noise-related annoyance in itself probably is not a cause of mental illness, although psychiatric patients do constitute a vulnerable group to the adverse effects of noise. Somatic and emotional symptoms associated with annoyance by noise are significant, however (*45*). The consumption of tranquilizers and sedatives has been used as an index of these symptoms resulting from noise exposure. Greater usage of these medications have been found in air and road traffic areas exposed to high levels of noise (*69, 99, 108, 109*).

Noise and Cardiovascular Disorders. There is a consistent correlation between prolonged exposure to high intensity industrial noise and an increased prevalance of hypertension, as demonstrated by over 40 studies (*110*). The risk increases with advancing age and increasing years of employment for both men and women. The risk also is greater under circumstances of intermittent impulse or impact sound than continuous or relatively steady sound. There is significant confirmation under actual living and laboratory conditions of the association between high intensity sound and cardiovascular disorders in children and adults (*10, 69, 111, 112*.

More specifically, prolonged noise exposure produced sustained elevations in blood pressure in a controlled experimental study of Rhesus monkeys. A carefully designed and monitored study of mon-

keys exposed for nine months to a continuous noise environment simulating that of urban factory workers disclosed significant, sustained elevations in blood pressure levels and alterations in diurnal blood pressure rhythms (*113*). These changes persisted after discontinuing exposure to the noise environment, suggesting a basis for long-term noise effects on the cardiovascular system in humans. Since Borg's study disclosed that lifelong exposure to high noise levels did not produce hypertension in rats (*114*), this study of primates is important because it bears a closer relationship to the human situation.

The fact that all persons exposed to noise do not show cardiovascular disorders is consistent with the likelihood that noise affects the health of susceptible individuals when combined with other stressors, such as work pressure and population density. Furthermore, environmental stressors are most likely to affect people who are unable to control them. Thus, people in institutions, with low incomes and low levels of education and children are especially likely to show adverse reactions from noise exposure (*10*).

Noise and Gastrointestinal Disorders. The data presently available are insufficient to justify judgments about the role of long term noise exposure in gastrointestinal disorders (*110*). The European literature on industrial noise, however, strongly suggests such a relationship (*10, 101*).

Noise and Neurological Disorders. A number of investigators report neurological changes associated with long-term occupational noise exposure (*110*). The principal signs include: autonomic imbalance such as dematographism, hyperreflexia, hyperhydrosis, and hand and eyelid tremors; an altered sense of balance; decreased tactile sensitivity of the hands and feet; decreased stimulus reaction time; a decreased reactivity to visual stimuli; and obscuring of regional activity in the electroencephalogram.

An uncommon neurological disorder that is directly affected by auditory stimulation is the audiogenic seizure syndrome (*43*). In individuals with this disorder seizures are precipitated by certain sounds.

Noise and Fetal Abnormalities. The human fetus perceives and responds to environmental sound in utero as reflected in motor activity and heart rate change. In the last trimester of pregnancy, the fetus can be conditioned by external sound stimuli. Maternal anxiety related to noise can produce increased fetal activity. A possible subtle prenatal effect of maternal anxiety induced by noise exposure could be infants who are hyperactive and have dysrhythmic temperaments (*115*).

In experimental animals, maternal and fetal abnormalities have been linked to noise (*116*). At this time, however, the evidence of the adverse effect of noise on the human fetus is suggestive but not established (*117, 118*).

In summary, the data on the health effects of noise indicate that sound exposure of more than 3 to 5 years with intensity levels of 85 dBA to 90 dBA is associated with increased health risk. Furthermore, the adverse physiological effects of noise surface before damage to hearing appears suggesting that attention to the physiological effects of noise may well enhance the prevention of noise induced hearing loss.

The effects of noise on children deserve special attention because children do not spontaneously report them, have little awareness of their significance and cannot significantly influence their environments. The evidence is that children may be particularly susceptible to noise-induced developmental and learning impairment which have long-range implications for later life (*10*).

For those who choose to question the health implications of noise, we must recognize that positive proof of cause and effect between a stimulus and human disease can never be established in the strictest experimental sense because of the multitude of intervening variables. Research in the health sciences differs fundamentally from that of the physical sciences. In even the most sophisticated epidemiological survey, a correlation remains a correlation. Species differences always exist and must be considered in even the most convincing animal study. For ethical reasons these are the only kinds of research evidence we are likely to have. We need further research to illuminate specifics but not to prove that noise is a significant threat to human health.

Implications

Our thesis is that research on, and efforts to prevent or minimize, the harmful effects of noise have suffered from the lack of a full appreciation of the ways in which humans process and react to sound. In an effort to stimulate more comprehensive approaches, we have described an integrated model of the auditory processing of sound based upon current knowledge of neuroanatomy, neurophysiology, neuroendocrinology and human stress.

Piecemeal research on narrow aspects of noise-related problems has led to conflicting conclusions that either minimize or exaggerate the significance of noise for physical and mental health. The designation of the general physiological effects of sound as "nonauditory" has been particularly misleading

to the general public. Because of this fragmentation and ambiguity, definitive action has been stymied by misunderstanding of the economic, social, and personal costs of noise control efforts. Underlying the confusion is the failure to appreciate that, beyond human communication, sound plays a vital role in the physiological functioning of the body.

As is true with other human problems, additional inevitable resistances to facing and remediating the untoward effects of noise have been encountered. This is particularly because the root causes of noise pollution are the imposition of modern technology and population pressures on natural human living conditions. Solutions accordingly require adjustments in styles of behavior and living. Even though short range inconveniences may lead to long range benefits, the human tendency is to resist change and maintain the status quo. Workers fail to wear protective hearing devices, manufacturers do not acoustically condition products and government does not adequately enforce standards. Moreover, the human capacity to adapt to noisy environments masks the magnitude of the problem. Hearing loss in itself further may reduce awareness of noxious sounds. These resistances are important determinants of ambiguities in the measurement of community responses to noise (*119*).

We believe that the paralysis of effective action is not a result of lack of knowledge but of a failure to integrate and articulate existing knowledge so that compelling reasons can stimulate the motivation needed to implement changes. For this reason, education of the public and workers in the field is the most important need today.

The compelling reasons for action are the facts that substantial groups of the population are vulnerable to adverse health effects from noise, that the quality of life is generally eroded by annoyance from noise, that sleep is disrupted, that productivity is reduced, and that the education of children is affected by noisy environments.

Without question noise can be a stressor and consequently an important underestimated pollutant of modern society as are chemicals and particulate matter that pollute the air, water, and food. Moreover, noise significantly affects the human nervous and endocrine systems. Because these systems are capable of sophisticated short range adaptive maneuvers, the harmful effects of noise, like other pollutants, usually become evident at later points in time. Noise is one of the main sources of sensory overload for city dwellers and industrial workers (*19*).

More than other pollutants noise interacts with other sensory stressors, population density, life change and life circumstances. Thus, noise plays an aggravating role in addition to stress generated by environmental conditions and attitudes toward them. These complex interactions have led to despair in ferreting out the exact role of noise in stress induced dysfunctions. When seen in the context of all of these factors, however, noise often emerges as the one most accessible to preventive and remedial action. This is reflected in the already existing federal, state, and local noise control measures. Actually, there is little more that needs to be known. The problem lies in the lack of coordination between acoustical engineering, urban planning, health, architecture, audiology, and other related professional disciplines.

There are essentially three points of intervention in noise control: reducing sound emission from the source, blocking sound transmission from the source to the ear, and protecting the ear itself from receiving the sound. Practical considerations limit the reduction of sound emission from industrial, traffic and aircraft sources. Still, acoustical conditioning of working and living environments can effectively reduce transmitted sound. Finally, sound can be effectively blocked at the level of the ear through protective hearing devices. By intervening at any or all of these levels there are few noise problems that cannot be effectively managed today. Thus, the problem is not that remedies are unavailable or too costly, but that the least expensive ones are not being used.

The multifaceted nature of solutions to the noise problem involves the cooperation of those who generate and those who are affected by noise. We cannot realistically expect dramatic reductions in the sources of noise pollution (*120*). Unlike other forms of environmental pollution, however, individuals can minimize the adverse effects of noise upon them. To the extent of economic feasibility industry should more actively reduce noise emission at the source by machines, vehicles, and appliances. Beyond that point, individuals can and should protect themselves from harmful sounds through acoustical conditioning and sound occluding ear devices.

The fundamental problem is one of attitude at the levels of government, industry, consumers, and health care workers. Noise already has been identified as a national hazard by Congress in the form of the Noise Control Act of 1972 and the Quiet Communities Act of 1978. Federal standards for new product noise emission, labeling requirements, and state and local regulations are being promulgated (*121-123*). Yet unachieved, however, is public awareness of the significance of noise pollution. An attitude of helplessness prevails leading to either resignation to the existence of noise or escape from it by

moving out the urban areas or changing jobs. Unappreciated is the fact that citizen initiatives, community organization, labor union bargaining, consumer demand, and personal efforts can create a climate in which an attitude of mastery over noise rather than helplessness can be achieved.

The basis now exists for public, consumer and labor expectations that acoustical conditioning be given priority equivalent to air conditioning in housing and industrial construction and in machine and appliance manufacturing. The problem lies simply in a lack of awareness of the importance of these factors. People have become accustomed to accommodating to noise through bodily defense mechanisms and lack an understanding of the personal and governmental resources available to them. Citizens do not fully appreciate that, negative research findings and preoccupation with the details of measuring community annoyance notwithstanding, they have the right to determine the quality of their lives and to be free from the harrassment of noise generated by industrial, vehicular, office, airport, and household appliance sources.

Summary

The fundamental purposes of hearing are to alert and to warn. The auditory orienting response, startle reflex and defensive response translate sound stimuli into action and sometimes into stress induced bodily changes. In the course of human evolution the additional purposes of communication and entertainment developed as sound assumed symbolic meaning.

The brain's processing of sound has been outlined as the biological and psychological basis for the effects of sound on the body. An integrated model then was presented for analyzing the impact of sound as a stressor on the body and for identifying key variables for research on the health effects of noise. In addition to the characteristics of the sound stimulus, a variety of personal and social factors determine whether or not noise becomes a stressor. The cognitive state, defense mechanisms, psychophysiological responses and stimulus and response regulation techniques of the individual person play vital roles. When the tension induced by sound persistently alters the homeostasis of the neuroendocrine system, a state of stress results with accompanying dysfunction in hearing, sleep, task performance, speech communication, and emotional state. When dysfunction leads to the assumption of the patient role, stress induced illness can be identified in the form of the suggested syndrome of "noise sickness;" cardiovascular, neurological, and gastrointestinal disorders; and possibly aggravated mental illness and fetal abnormalities.

Noise is a stressor and an important, largely unrecognized, pollutant of our environment. Our quality of life generally is eroded by annoyance from noise, and substantial segments of the population are vulnerable to its adverse health effects. More specifically, sleep is disrupted, productivity is reduced and the education and development of children is affected by noisy environments.

The prevention and reduction of noise pollution need not await further knowledge. The technology for reducing noise emission, acoustically conditioning environments and protecting hearing now exists. The problem is the lack of public awareness of the significance of noise pollution and solutions to it. The challenge is to convert through education a public attitude of helplessness to one of mastery through citizen initiatives, labor union bargaining, consumer demands and personal efforts to adopt the most feasible noise and noise response control measures.

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