COPPER-NICKEL MINING, SMELTING AND REFINING AS AN ENVIRONMENTAL HAZARD TO HUMAN HEALTH

September, 1977

BS-2

Copper-Nickel Mining, Smelting and Refining as an Environmental Hazard to Human Health

A Review of Epidemiologic Literature and Study Recommendations on Sulfur Dioxide and Particulates

Performed Under Contract from the
Minnesota Regional Copper-Nickel Study
Environmental Impact Task Force

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September, 1977

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SUMMARY

Sulfur oxides comprise a vast group of compounds, a few of which are found in the atmosphere as a result of man's industrial processes. These include sulfur dioxide (SO_2), Sulfur trioxide (SO_3), sulfuric acid (H_2SO_4) and various sulfates (XSO_4). Ninety-eight percent of all emitted sulfur oxides consist of sulfur dioxide. This fact, coupled with sulfur dioxide's well known irritant properties, has implicated sulfur dioxide as the pollutant associated with air pollution most likely to cause disease.

A complex series of reactions are associated with sulfur dioxide in the atmosphere. In polluted air, sulfur dioxide is oxidized in appreciable amounts to sulfuric acid and sulfates by photochemical and catalytic processes. Chemical reaction studies within copper smelters have indicated that the presence of sulfates and sulfites are important considerations in the study of health effects of sulfur oxides.

Meteorological factors play an important role in determining which pollutant will be present and in what concentrations. Wind velocity and direction, temperature and rainfall can be directly related to the rate of chemical reactions and the dispersal of the end products of such reactions. Particle sizes of sulfuric acid and sulfates are also affected by the relative humidity which may be important in the consideration of the effect these compounds have on health.

Particulates is an all encompassing term use for all dispersed solid or liquid material in the atmosphere. With this definition, all the various sulfur oxides can be considered also to be particulates. These particulates are of varying size and are capable of being carried over long distances. Some particles are emitted directly from chemical or industrial sources while others are formed by chemical reactions in the atmosphere (as is the case with most sulfuric acid and sulfates found in the atmosphere). The U.S. primary standards for particulates for 24 hours are 75 micrograms/m^3 annual geometric mean and 260 micrograms/m^3 annual maximum.

Sulfur dioxide is a mild respiratory irritant when administered alone. In order to produce death or serious pathological changes in experimental animals, levels far in excess of ambient levels are necessary. Upon inhalation of SO_2, animals have demonstrated an increase in the number of goblet cells found in the lung on autopsy. The lung has been shown to be the major organ of response, but evidence indicates that the stomach and the blood system are also affected. Lesions in the nasomaxillary turbinates have also been demonstrated. At this time there is no evidence to support the carcinogenicity of SO_2 in mammals. At levels far in excess of ambient levels, SO_2 has been shown to reduce ciliary activity and thereby decrease mucociliary clearance. Since this leads to increased residence time of foreign particles within the lungs, this has been proposed as the cause of increased illness during exposure to pollution. The combination of increase numbers of goblet cells and slowed ciliary activity results in excess fluid in the alveoli. It has been suggested that alveolar macrophages are responsible for riddance of the excess mucus, but more study is required. The mode of breathing has been shown to be important in determining the amount of SO_2 reaching the lower airways. Both animal and human studies have shown that more than 99% of all inhaled SO_2 is absorbed in the nose. Mucus flow has also been shwon to be reduced in the nose especially in its anterior part where SO_2 concentrations were the highest. The major physiological mechanism acting to reduce maximum expiratory flow is thought to be a nasobronchial reflex causing bronchoconstriction.

The fate of absorbed SO_2 is still speculative. Results from animal studies have shown that some SO_2 is reabsorbed, some is briefly stored within the body's tissues and some is excreted in the urine. It undergoes chemical reactions within the blood stream to form sulfite and bisulfite. The action of these substances is still unknown.

From animal experiments, sulfuric acid and certain sulfates have been shown to have greater irritant properties than SO_2 alone. Particle size appears to be the determining factor in what effect these substances will have on the health of these animals. At 5 mg/m^3 sulfuric acid mist is detectable by practically all humans, but human responses are quite varied depending on individual susceptibility. Like SO_2, th

main physiological mechanism involved in the inhalation of H_2SO_4 appears to be bronchoconstriction. There exists the possibility of two different mechanisms of action depending on the size of the particle involved. Larger particles deposit in the major bronchi where increased swelling and exudiation of fluid leads to complete obstruction of the airways. Smaller particles act by narrowing airways.

Not all sulfates have been found to potentiate the effect of SO_2. Zinc ammonium sulfate has been found to increase flow resistance the most of all sulfates tested. The physiological response again parallels that produced by histamine. The cations associated with sulfation appears to be related to the amount of histamine released.

A synergistic action exists between SO_2 and H_2SO_4 and zinc ammonium sulfate.

Important in studying health effects of particles is an understanding of where they are deposited and how they are cleared from the lungs. Deposition is dependent on size, shape and density of the particles. The nose is the major site of particle deposition. Deposition in the alveolae has been found to be maximum with particles between 1 and 2 microns. Clearance from the lung depends on where the particle is deposited. Clearance from the alveolar surface is the slowest of all areas.

Studies have shown that respirable particulates may be intrinsically toxic, interfere with clearance of other particles from the lung, or act as carriers of other toxic materials. Animal studies using smoke or carbon black as pollutants have shown that these pollutants by themselves produce little major damage to the respiratory systems at levels even greater than those found in the atmosphere. Studies have found that increased pulmonary flow resistance, the dominant physiological alteration produced by irritant particles is further augmented by small particle size.

Numerous authors have concluded that small particles play an important role in either a synergistic or additive manner on health effects when various gases and particles are mixed.

Exposure of human subjects to SO_2 and NaCl aerosol has not consistently shown the synergistic effect seen in guinea pigs. Synergistic action between SO_2 and dust and SO_2 and ozone has been demonstrated. However, no other studies have investigated the effects of these combined pollutants on man. There is a lack of data on the possible synergistic effects of SO_2 with other substances commonly found in polluted atmospheres such as nitrogen oxides, or hydrocarbons.

A vareity of techniques have been used to measure SO_2 and particulates in the atmosphere. This has made comparison of pollution levels between epidemiological studies difficult . Two common methods for the measurement of SO_2 in the United States has been the West-Gacke method and the conductometric method. European studies have mostly used the hydrogen peroxide method. In the United States, particulates have been measured mostly by the high-volume sampler and in Europe by a method which measures material collected on filter paper. In measuring specific particulates such as sulfates and sulfuric acid, a great deal of work is needed.

Some of the earliest studied on air pollution have centered around acute episodes of high pollution. The majority of these studies utilized mortality data. Results have indicated that excessively high levesl of SO_2 and particulates increased mortality and morbidity, especially among elderly persons and those with chronic lung and respiratory disease.

Attempts have been made to correlate various pollutants with a wide variety of causes of death including arteriosclerosis, rheumatic heart disease and bladder cancer. The causes of death that have received the most attention have been the chronic respiratory diseases (in particular bronchitis) and lung cancer. Most of these studies have adjusted for age and sex differences, but only some have taken into consideration other important confounding variables such as differences in smoking, occupation and socioeconomic class. Few of the studies considered weather and influenza epidemics as possible sources of variation. The combination of different approaches to data collection and interpretation, different statistical analyses and various factors under consideration make any but the most broad conclusions unjustifiable. In general, very high levels of SO_2 and particulates do increase the

the death rate for all causes of death. Bronchitis mortality has been related to air pollution. While the association of lung cancer deaths with air pollution seems to be more related to smoking and some unidentified "urban" factor. Exactly what pollutants are responsible for increased deaths can not be determined by these studies.

Morbidity studies have been concerned mostly with respiratory illness such as chronic bronchitis, emphysema and asthma and with non-disease effects such as decreased lung function. The effects of air pollution have been measured by questionnaire, daily diary reporting, emergency room visits, hospitalization rates, clinic visits, work absences and pulmonary function tests. Some studies deal with well individuals while others look at these already ill with a respiratory disease. It can be concluded that an association exists between the prevalence and incidence of respiratory illness and SO_2 and particulates. Those already affected with disease such as bronchitis have been shown to have exacerbations of their disease upon exposure to these air pollutants. These associations do not necessarily imply a causal relationship. Many authors have also noted a synergistic effect or additive effect between smoking and air pollution, with smoking having a much greater effect than the pollution.

Mortality and morbidity patterns have also been studied during childhood ($\leq$ 15 years) because children are relatively free from the confounding effects resulting from cigarette smoking and occupational exposure and because of the concern over what effect early respiratory disease has on the development of chronic disease later in life. The studies seem to be in agreement that sulfur dioxide and particulates contribute to increased frequency and severity of acute respiratory disease in children. Children appear to be at increased risk to the effects of these air pollutants. Peak expiratory flow and forced expiratory flow in 0.75 second also appear to be influenced by ambient air pollution levels. Exposure to elevated levels of sulfur dioxide has occurred among workers in various industries such as refrigeration and pulp mills. Elevated levels of sulfur dioxide (20-100ppm) promote fits of coughing, sneezing and other discomforts. Recent studies have shown that exposure to levels of SO_2 below the standard for occupational

settings (5ppm TWA) do produce a reduction in forced expiratory volume in 1 second and forced vital capacity and an increase in respiratory symptoms. These effects have been demonstrated after smoking habits have been controlled for. Interaction between SO_2 and respirable particulates apparently is not significant within copper smelters. However, this observation rests solely on one study's findings and should be replicated.

Exposure to elevated levels of sulfuric acid mist is most common in industries producing sulfuric acid or storage batteries. At present the recommended exposure limit of 1.0 mg/m^3 of air as a time weighted average appears to be sufficient to prevent excess respiratory disease. However, no conclusion concerning the prevention of tooth erosion resulting from sulfuric acid mist exposure can be reached.

Most occupational studies on particulates have dealt with a specific kind of particulate such as silica, aluminum or barium dust. A few relevant articles on coal dust exposure and dusty occupation in general were reviewed. Much of the data collected have been either negative or not statistically significant, in regards to pollution effects on health. However, a recent review article concluded that inhalation of most minerals and vegetable dust could lead to increased prevalence of cough and sputum and that some workers show a slight decrease in lung function after prolonged exposure to these materials.

In reviewing all the epidemiological studies, it is difficult to state with any confidence which levels of pollutants cause the effects recorded or even which pollutants are responsible for these effects. Even with these problems, attempts have been made in a number of studies to determine dose-response effects. These authors support the existing primary ambient air quality standards for SO_2 and particulates. Levels of SO_2 at 92-95 micrograms/m^3 with 15 micrograms/m^3 suspended sulfates were found to be associated with excess bronchitis in the CHESS studies. CHESS studies noted other associations with sulfate levels. Suspended sulfates at 24 hour levels of 8-10 micrograms/m^3 significantly aggravated cardiopulmonary symptoms in those already afflicted with the disease. No national standards have been set for suspended sulfates and it is concluded that more data are needed in this area.

I. INTRODUCTION

Sulfur oxides from natural sources have always been present in the atmosphere to some extent. However, industrialization and urbanization have concentrated sulfur oxides emitted from man's industrial processes to levels which have become a threat to human health. Many of the adverse health effects of air pollution have been attributed to sulfur dioxide because of its irritating action upon the nose and eyes. Other sulfur oxides have recently become of great concern as possible etiologic agents.

Sulfur dioxide hasn't always been considered a threat to human health. In fact, sulfur dioxide was used therapeutically in Homer's time and as recently as 1920 (Greenwald, 1954). Dermatoses of dogs and cats were apparently treated with sulfur dioxide in France in the 1920's and the 1930's. It was used for treatment of various ailments in man such as: chronic keratitis of the cornea, diphtheria, tuberculosis and the common cold with varying degrees of success.

Apparently the first report of adverse effects from sulfur dioxide stems from an industrial exposure in 1821. Animal experiments to determine the effects of "low" concentrations of sulfur dioxide were first conducted in 1884 by Ogata who also made the first observations about man's greater sensitivity to sulfur dioxide (Greenwald, 1954). Sulfuric acid became a topic of human studies in 1913 and in animals in 1950. Interest in sulfates and sulfites has been more recent. Likewise, epidemiological studies have concentrated on the effects of sulfur dioxide and particulates with but recent interest in sulfates.

Numerous papers have been published on the effects of sulfur oxides on humans, plants, animals, and materials. This review of the literature will confine itself to human health effects primarily. To understand the effects of various sulfur oxides on man, however, their atmospheric chemistry along with results of experimental exposure of animals and humans must be considered. These latter topics are reviewed fairly briefly here. The major portion of the paper will be concerned with the epidemiologic studies which are the basis for setting national air quality standards for permissible levels of these pollutants in the atmosphere and in occupational settings.

Most of these epidemiologic studies investigating the effects of sulfur oxides (sulfur dioxide) have concurrently looked at the effects of particulates (also called smoke, dust, or fog). The definition of particulate matter overlaps with the various substances considered to be sulfur oxides. That is, sulfates, sulfites, sulfuric acid and even sulfur dioxide are considered to be particulates. For these reasons sulfur oxides and particulates are considered together in this review.

II. Atmospheric Considerations

A. Sulfur Oxides

The classification of sulfur oxides includes a number of different compounds. Among these, sulfur dioxide (SO_2), sulfur trioxide (SO_3) and the corresponding acids, sulfurous acid (H_2SO_3) and sulfuric acid (H_2SO_4) and the salts of these acids constitute the major atmospheric pollutants.

Salts of sulfurous acid (H_2SO_3) are known as sulfites and bisulfites. These generally are not looked for in the atmosphere as it is believed that essentially all sulphur dioxide is eventually oxidized to sulfates, the salts of sulfuric acid (H_2SO_4).

Inorganic sulfates are believed to be the product of the reaction of sulfuric acid with cations or of the oxidation of sulfites.

Other sulfur oxides such as SO, S_2O_3, S_2O_7 and SO_4 have not been found in the atmosphere although they are well known in laboratory studies (Air Quality Criteria -SO_2, 1975).

The major source of sulfur oxides in the atmosphere (other than those occurring naturally) is the combustion of fossil fuels such as petroleum and coal. Other sources include the refining of petroleum, smelting of ores containing sulfur, the manufacture of sulfuric acid, burning of refuse, paper making and the burning or smoldering of coal refuse banks. Approximately 98% of all industrial sulfur released into the air is in the form of sulfur dioxide, 2 - 5% is sulfuric acid (Air Quality and Stationary Emission Control, 1975)

Although almost all sulfur dioxide is believed to be converted eventually to sulfates, not all atmospheric sulfates are a result of industrial pollution. Naturally occurring sulfur dioxide and hydrogen sulfide (H_2S) can also be oxidized to sulfates. In fact it has been estimated that only one-third of the sulfur in the entire global atmosphere is derived from pollution sources (Rall, 1973).

However, this observation does not pertain to local respirable ground levels of sulfur oxides which, in urban areas, is almost entirely due to fossil fuel combustion.

The meteorological and chemical behavior of these sulfur oxides are influenced greatly by the way they are introduced into the

atmosphere. In other words such factors as the type of emitters, whether large or small, and whether they are dispersed or point sources have a role in determining how these pollutants will be found in the atmosphere. The Air Quality Criteria Document for Sulfur Oxides has reported that the trend has been towards large point sources. These contain lower concentrations of polynuclear hydrocarbons and higher concentrations of nitrogen oxides and sulfuric acid. Particulate matter from these large point sources can be better controlled which, therefore, minimizes interaction with sulfur oxides.

A complex series of reactions are associated with sulfur dioxide in the atmosphere. A simplified scheme abstracted from Air Quality and Stationary source emission control is presented below:

$$SO_2 + (O) \text{ --- } SO_3 \qquad (1a)$$

$$SO_3 + H_2O \text{ ----- } H_2SO_4 \qquad (1b)$$

$$H_2SO_4 + X^{++} \text{ ----- } XSO_4 + 2H^+ \qquad (2)$$

$$H_2O + SO_2 \text{ --------} H_2SO_3 \text{ --- } H^+ + HSO_3^- \quad 2H^+ + SO_3^{=} \qquad (3)$$

In reaction (1a) sulfur dioxide is oxidizied to sulfur trioxide which reacts almost immediately with water vapor to form sulfuric acid aerosol (1b). Therefore reactions (1a) and (1b) can be considered one reaction in which sulfur dioxide is oxidized to sulfuric acid. This process occurs in clean air in the presence of sunlight at the low rate of 0.1% per hour.

However, in the presence of other air contaminants the rate is greatly increased by two general mechanisms: 1) Photochemical oxidation which is initiated by light, and 2) catalysis by trace-air ions.

Photochemical oxidation is enhanced by increased sunlight, nitrogen oxides and hydrocarbons. A complex series of reactions involving O_3 atoms and hydrogen leads to the formation of the well known photochemical smog. However, the oxidants responsible for the oxidation of SO_2 in this system are not well established (Cox and Pennett, 1971). Even rates of oxidation vary greatly from study to study; the highest rate reported being 18% an hour (Rall, 1973). Even at 0.65% per hour Coy and Pennett found that significant quantities of sulphate aerosol will be

formed (Coy and Pennett, 1971). One possible factor involved here is that the formation of sulfuric acid aerosol may decrease the amount of sunlight and thereby slow down the reaction rate at which further sulfuric acid may be formed.

Catalytic oxidation of sulfur dioxide occurs in the absence of sunlight. A great deal of interest has been shown in the catalytic role of metal ions in aerosols. Several have been implicated in this process such as manganese, iron, vanadium, aluminum, lead and copper. Judeikis has reviewed briefly the particle-catalyzed oxidation of SO_2. Chemical composition and catalytic reactivity of particles seem to be very important but too little is known about the extent to which natural airborne particles exhibit catalytic activity (Judeikis, 1973). The reactions are very complex with many interrelated variables such as the absorption rate of sulphur dioxide, the size and pH of the aerosol, efficiency of the catalyst, rate of diffusion of reactants within the aerosol and relative humidity (Rall, 1973). Relative humidity seems to be a major consideration as the reaction occurs in water droplets containing absorbed SO_2.

McKay found that the conversion of sulfur dioxide and ammonia to ammonium sulfate in water droplets in the atmosphere is rather rapid and is highly positively correlated with pH (McKay, 1971). There was a tendency for the reaction to slow down as it progressed even when there was no depletion of the gases involved. This was attributed to the steady fall in pH. Alkaline metal compounds and ammonia, therefore, apparently enhance reaction rates by decreasing droplet acidity.

A great deal of research has been conducted on the oxidation rates of SO_2. A summary of these studies abstracted from Rall is presented in Table 1.

Once the sulfuric acid is formed, by one of these mechanisms, it may react further to produce sulphates. This is shown in reaction(2) with X representing metals or ammonium.

Reaction (3) shows the formation of weekly acidic sulfurous acid (H_2SO_3) and its disassocation products the bisulfite (HSO_3^-) and sulfite ion (SO_3^{--}). These reactions might also be important to

Table 1

ESTIMATED SULFUR DIOXIDE OXIDATION RATES IN THE LOWER ATMOSPHERE: TABULATION OF SELECTED STUDIES[1]

Experimental conditions	Presumed atmospheric conditions	Extrapolated SO_2 consumption rate	Reference
Sunlight; High SO_2 concentrations no other impurities present	SO_2; sunlight; clean air	0.5%/hour	Hall, (cited by Urone and Schroeder
Sunlamp in smog chamber; high SO_2 concentrations in pure air	SO_2; sunlight; clean air (reaction unaffected by humidity)	0.1-0.2%/hour	Gerhard and Johnstone
Sunlight; 200-2000 SO; trace impurities	Assuming 300 /m^3 SO_2; bright sunlight for 10 hours would produce 30 of sulfate	0.65%/hour (high rate may be due to trace impurities)	Cox and Penkett
Smog chamber; light SO_2 NO_x, olefins	SO_2, 260 g/^{3} ; ozone 100 olefin, 33 g/m^3 bright sunlight	3%/hour for pentene; 0.4%/ hour for propene	Cox and Penkett
Photochemical reactants SO_2 in ppm concentrations	Sunlight; SO_2, 260 g/m^3 ozone, 200 g/m^3, olefin 33 g/m^3, 40%RH	3%/hour	Cox and Penkett
UV-irradiated gas mixtures; NO_x, hydrocarbons, SO_2, high levels	Noon sun	1-3%/hour	Urone et al
Catalyst droplet exposed to high concentrations of SO_2 in humid air	Natural fog containing 1g crystals of $MnSO_4$ in droplets; 2600 g/m^3 SO_2	1%/min	Johnstone and Coughanowr
Metallic aerosol particles on Teflon beads in flow reactor; SO_2; water vapor	Natural fog (0.2 g H_2O/m^3) in industrial area; SO_2, 260 g/m^3, $MnSO_4$, 50	2%/hour	Cheng et al
Artificial fog in smog chamber; very high levels; SO_2 and metal sulfates	(Levels in smog chamber) 0.6 mg/m^3 SO_2, 2 mg/m^4 Mn SO_4	0.01%/min at 77% RH 2.1%/min at 95% RH	Johnstone and Moll
NH_2SO_4 formation in water droplets exposed to NH, and SO_2	100 g/m^3 SO_2, 10 g/m^3 NH_3, cloud droplet radius of 10	2.5%/min in droplets	Van Den Heuvel and Mason

Table 1
(continued)

Experimental conditions	Presumed atmospheric conditions	Extrapolated SO_2 consumption rate	Reference
Atmospheric study of polluted areas in Japan	- -	11.7%/min	Shirai et al
Atmospheric study of Canadian smelting area	150-4200 g/m^3 SO_2	0.035%/min	Katz
Study of SO_2 oxidation in plume of coal-burning power plant	Found moisture level in plume important, SO_2 6 g/m^3	0.1%/min at 70% RH 0.5%/min at 100% RH	Gartrell et al
Atmospheric study of Rouen (industrial city) in winter	68-242 g/m^3 SO_2	6-25%/hour	Benarie et al

[1]Source: Rall, D.P. Review of the health effects of sulfur oxides, Env. Health Persp. 8: 97-121, 1974

the biochemical reactions occurring in those exposed to SO_2.

Obviously, weather has a marked effect on the atmospheric ch· · al processes. Inversions allow for a buildup of sulfur oxides and other contaminants and provide time for chemical reaction to occur. Wind influences the rate, direction and dispersal of sulfur oxides. Temperature affects the reactivity and solubility of gases (Rall, 1973). Rain is capable of clearing the air of pollutants. Meterological conditions also affect the rate of reactions that these oxides of sulfur undergo. Cloud cover will tend to reduce photochemical oxidation, while high relative humidity and high temperatures will increase photochemical activity. Increased relative humidity will also increase catalytic activity.

The deposition of sulfur dioxide and its oxidation products varies greatly. This can be seen in surveys of these pollutants in the atmosphere. Altshuller, as quoted by Rall, has reported a general build-up of ground level sulfates stretching for many hundreds of miles in the Northeastern United States (Rall, 1973). Rural areas often have high levels of suspended particulate sulfate in spite of having relatively negligible sulfur dioxide levels.

Exact residence times have not been established for any of the sulfur oxides but evidence seems to indicate that fine particulate sulfates reside the longest in the atmosphere. However, even particle size and density depend for a large part on weather conditions. These characteristics will in turn affect the rate that particles settle out of the atmosphere. Of particular interest is a recent report by Smith et al on the chemistry of sulfur and arsenic airborne copper smelter particulates (Smith, 1976). A large copper smelter near Salt Lake City, Utah was the source of a series of air samples. Seven particulate samples collected at three points were analyzed by two methods. It was found that hot water extraction produced higher values for sulfate concentrations than hydrocloric acid extraction. Apparently hot water extraction oxidizes all sulfur compounds so there is an overestimation of sulfates.

Airborne concentrations of sulfate (includes any particulate-

absorbed SO_2 or H_2SO_4 as well as soluble sulfates) and sulfite (includes any particulate absorbed SO_2 as well as sulfites) averaged 109 ± 73 ug$SO_4^=$ /m^3 and 53 ± 39 ug$SO_2^=$/m^3 respectively in the six samples where all data were available. Whereas 85% of all sulfates were found to be respirable, only 43% of the sulfites were found to be. The different size distribution between these two compunds suggest that they are formed by different mechanisms in the smelter environment.

Hansen has postulated that SO_2 is stabilized by chemisorption on metal oxide (ie Fe_2O_4 CuO) to form stable sulfite complexes in the smelter environment (Hansen, 1974). Other evidence is cited to support this hypothesis. The uniform sulfite content with particle size also seems to suggest a mass reaction between SO_2 gas and airborne particulates (Smith, 1976).

However, in the smelter environment the source of sulfate is unknown. It seems likely that it is produced by oxidation of sulfur dioxide within the reverberatory furnaces or convertors. Apparently, the same metals which stabilize SO_2 as sulfite can also catalyze the oxidation of SO_2 to sulfate. Hansen has determined that the two competing processes are controlled by a number of different factors (Smith, 1976). Relative humidity, ambient temperatures, the oxidation potential in the particles, the activities of sulfite complexing metal ions and rates of various reactions producing sulfite or removing it as sulfate are all important in determining which process will predominate. High temperature, high concentration of sulfates, SO_2 and particulates all exist in the smelter environment.

It must be emphasized that the oxidation of sulfur dioxide results in the formation of sulfuric acid and sulfates, which in turn comprise about 5 - 20% of the total suspended particulate matter in urban air. Of these sulfates, 80% are less than 2 microgms in diameter and, therefore, are largely in the respirable fraction of particulate matter (Wagman, 1967).

Sulfates themselves comprise a large group of compounds which, evidently, have different toxicological effects. Accordingly there needs to be not only measurements made on these sulfur oxides but accurate determination of their chemical composition.

B. Particulates

Particulates are any dispersed solid or liquid material in the atmosphere ranging in size from 0.005 to about 500 microns (Fennelly,1976). Particles in this size range have a suspended state varying from seconds to several months. Particulates can be classified as either primary or secondary. Primary particles are usually 1 to 20μ_m in size and are injected directly into the atmosphere by chemical reactions in the atmosphere. They are relatively smaller and classified as sulfates, nitrates and hydrocarbons.

Primary particles are emitted from industrial sources and from natural processes such as forest fires or ocean sprays. Particulate emissions from stationary sources in the U.S. approximate 18×10^6 tons/year (Vandegrift,1971). Table 2 shows the major industrial sources of particulate material.

Particle size is an important factor in any study of particulates. Problems arise in this area because of the many different methods of measuring the size and the fact that size can refer to either the diameter or the radius. Some interpret it to mean the physical or geometrical size, whereas others refer to equivalent sizes based on optical, electrical or aerodynamic properties of the particles (Fennelly,1976, Air Quality Criterion For Particulates,1969).

Most recent data has shown a bimodal rather than normal distribution of size (diameter) for atmospheric particulates, with a peak between 0.1 and 1.0 microns and another peak between 1.0 and 10 microns.

Evidence supporting this has shown that particles larger than 2.0 μ_m are mostly primary particulates and those smaller than 1.0μ_m are mostly secondary particulates. Figure 1 shows some primary particles and their sizes, based on geometric diameter of equivalent spheres.

Particles do not necessarily remain in the area where they are emitted, but can be carried over long distances. Evidence is available showing that particulates produced in an urban area can be carried hundreds of miles to rural areas. Lead particles thought to be from the U.S. have been found in glacial ice in Greenland (Fennelly,1976).

Secondary particulates are the major source of Aitken nuclei or condensation centers necessary for the condensations that take place

Table 2

MAJOR INDUSTRIAL SOURCES OF PARTICULATE POLLUTANTS[1]

Source	Annual tonnage (P)	Emission factor Lb/Ton (e)	Efficiency of control (C_1)	Application of control (C_2)	Net control $C_1 \times C_2$	Emission tons/yr (E)
1. Fuel combustion						
A. Coal						
1. Electric utility						
a. Pulverized	258,400,000 tons of coal	16A = 190 lb/ton of coal	0.92	0.97	0.89	2,710,000
b. Stoker	9,900,000 tons of coal	13A = 146 lb/ton of coal	0.89	0.87	0.70	217,000
c. Cyclone	28,700,000 tons of coal	3A = 35 lb/ton of coal	0.91	0.71	0.64	182,000
Total from electric utility coal						3,109,000
2. Industrial boilers						
a. Pulverized	20,000,000 tons of coal	15A = 170 lb/ton of coal	0.85	0.95	0.81	322,000
b. Stoker	70,000,000 tons of coal	13A = 133 lb/ton of coal	0.85	0.62	0.52	2,234,000
c. Cyclone	10,000,000 tons of coal	3A = 31 lb/ton of coal	0.82	0.91	0.75	39,000
Total from industrial coal						2,595,000
B. Fuel oil						
1. Electric utility	7.18×10^9 gal	0.010 lb/gal	0	0	0	36,000
2. Industrial						
a. Residual	7.51×10^9 gal	0.023 lb/gal	0	0	0	87,000
b. Distillate	2.36×10^9 gal	0.015 lb/gal	0	0	0	18,000
Total from fuel oil						141,000
C. Natural gas and LPG						
1. Electric utility	3.14×10^6 mil. scf	15 lb/mil. scf	0	0	0	24,000
2. Industrial	9.27×10^6 mil. scf	13 lb/mil. scf	0	0	0	84,000
Total from natural gas and LPG						108,000
Total from fuel combustion						5,953,000
2. Crushed stone, sand, and gravel						
A. Crushed stone	631,000,000	17	0.80	0.25	0.20	4,554,000
B. Sand and gravel	918,000,000	0.1	—	—	0	46,000
Total from crushed stone, sand, and gravel						4,600,000
3. Agricultural operations						
A. Grain elevators	177,000,000 tons grain handled	27 lb/ton grain handled	0.70	0.40	0.28	1,700,000
B. Cotton gins	11,000,000 bales	12 lb/bale	0.80	0.40	0.32	45,000
C. Alfalfa dehydrators	1,600,000 tons dry meal	50 lb/ton dry meal	0.85	0.50	0.42	23,000
Total from agricultural operations						1,768,000
4. Iron and steel						
A. Ore crushing	82,000,000 tons of ore	2 lb/ton of ore	0	0	0	82,000
B. Materials handling	131,000,000 tons of steel	10 lb/ton of steel	0.90	0.35	0.32	445,000
C. Pellet plants	—	—	—	—	—	80,000
D. Sinter plants	51,000,000 tons of sinter	42 lb/ton of sinter	0.90	1.0	0.90	107,000
E. Coke manufacture						
1. Beehive	1,300,000 tons of coal	200 lb/ton of coal	0	0	0	130,000
2. By-product	90,000,000 tons of coal	2 lb/ton of coal	0	0	0	90,000
F. Blast furnace	88,800,000 tons of iron	130 lb/ton of iron	0.99	1.0	0.99	58,000
G. Steel furnaces						
1. Open hearth	65,800,000 tons of steel	17 lb/ton of steel	0.97	0.41	0.40	337,000
2. Basic oxygen	48,000,000 tons of steel	40 lb/ton of steel	0.99	1.0	0.99	10,000
3. Electric arc	15,800,000 tons of steel	10 lb/ton of steel	0.99	0.79	0.78	18,000
H. Scarfing	131,000,000 tons of steel	3 lb/ton of steel	0.90	0.75	0.68	63,000
Total from iron and steel						1,421,000
5. Cement						
A. Wet process	43,600,000 tons of cement					
1. Kilns		167 lb/ton of cement	0.94	0.94	0.83	435,000
2. Grinders, dryers, etc.		25 lb/ton of cement	0.94	0.94	0.83	65,000
B. Dry process	31,000,000 tons of cement					
1. Kilns		167 lb/ton of cement	0.94	0.94	0.83	310,000
2. Grinders, dryers, etc.		97 lb/ton of cement	0.94	0.94	0.83	124,000
Total from cement						934,000

Source	Annual tonnage (P)	Emission factor Lb Ton (e_f)	Efficiency[b] of control (C_e)	Application[a] of control (C_t)	Net[c] control $C_e \times C_t$	Emissions tons yr (E)
6. Forest products						
A. Wigwam burners	27,500,000 tons of waste	10 lb/ton of waste	0	0	0	137,000
B. Sawmills	—	—	—	—	—	No est.
C. Pulp mills	37,900,000 tons of pulp					
1. Recovery furnace		150 lb/ton of pulp	0.92	0.99	0.91	256,000
2. Lime kilns		45 lb/ton of pulp	0.95	0.99	0.94	51,000
3. Dissolving tanks		5 lb/ton of pulp	0.90	0.33	0.30	66,000
4. Bark boilers		—	—	—	—	82,000*
D. Particleboard, etc.	—	—	—	—	—	74,000*
Total from forest products						666,000
7. Lime						
A. Crushing, screening	28,000,000 tons of rock	24 lb/ton of rock	0.80	0.25	0.20	264,000
B. Rotary kilns	16,200,000 tons of lime	180 lb/ton of lime	0.93	0.87	0.81	294,000
C. Verticle kilns	1,800,000 tons of lime	7 lb/ton of lime	0.97	0.40	0.39	4,000
D. Materials handling	18,000,000 tons of lime	5 lb/ton of lime	0.95	0.80	0.76	11,000
Total from lime						573,000
8. Clay						
A. Ceramic						
1. Grinding	4,722,000 tons	76 lb/ton	0.80	0.75	0.60	72,000
2. Drying	7,870,000 tons	70 lb/ton	0.80	0.75	0.60	110,000
B. Refractories						
1. Kiln-fired						
a. Calcining	688,000 tons	200 lb/ton	0.80	0.80	0.64	25,000
b. Drying	1,032,000 tons	70 lb/ton	0.80	0.80	0.64	13,000
c. Grinding	3,440,000 tons	76 lb/ton	0.80	0.80	0.64	47,000
2. Castable	550,000 tons	225 lb/ton	0.90	0.85	0.77	14,000
3. Magnesite	120,000 tons	250 lb/ton	0.80	0.70	0.56	7,000
4. Mortars						
a. Grinding	120,000 tons	76 lb/ton	0.80	0.75	0.60	2,000
b. Drying	120,000 tons	70 lb/ton	0.80	0.75	0.60	2,000
5. Mixes	249,000 tons	76 lb/ton	0.80	0.75	0.60	4,000
C. Heavy clay products						
1. Grinding	4,740,000 tons	76 lb/ton	0.80	0.75	0.60	72,000
2. Drying	7,110,000 tons	70 lb/ton	0.80	0.75	0.60	100,000
Total from clay						468,000
9. Primary nonferrous						
A. Aluminum						
1. Grinding of bauxite	13,000,000 tons of bauxite	6 lb/ton of bauxite	—	—	0.80	8,000
2. Calcining of hydroxide	5,840,000 tons of alumina	200 lb/ton of alumina	—	—	0.90	58,000
3. Reduction cells						
a. H. S. Soderberg	800,000 tons of aluminum	144 lb/ton of aluminum	0.40	1.0	0.40	35,000
b. V. S. Soderberg	700,000 tons of aluminum	84 lb/ton of aluminum	0.64	1.0	0.64	10,000
c. Prebake	1,755,000 tons of aluminum	63 lb/ton of aluminum	0.64	1.0	0.64	20,000
4. Materials handling	3,300,000 tons of aluminum	10 lb/ton of aluminum	0.90	0.35	0.32	11,000
Total from primary aluminum						142,000
B. Copper						
1. Ore crushing	170,000,000 tons of ore	2 lb/ton of ore	0	0	0	170,000
2. Roasting	575,000 tons of copper	168 lb/ton of Cu	0.85	1.0	0.85	7,000
3. Reverb. furnace	1,437,000 tons of copper	206 lb/ton of Cu	0.95	0.85	0.81	28,000
4. Converters	1,437,000 tons of copper	235 lb/ton of Cu	0.95	0.85	0.81	32,000
5. Materials handling	1,437,000 tons of copper	10 lb/ton of Cu	0.90	0.35	0.32	5,000
Total from primary copper						242,000

Source	Annual tonnage (P)	Emission factor Lb/Ton (e_f)	Efficiency[b] of control (C_e)	Application[a] of control (C_i)	Net[c] control $C_e \times C_i$	Emission, tons/yr (E)
C. Zinc						
1. Ore crushing	18,000,000 tons of ore	2 lb/ton of ore	0	0	0	18,000
2. Roasting						
a. Fluid-bed	765,000 tons of zinc	2,000 lb/ton of Zn	0.93	1.0	0.98	15,000
b. Ropp, multi-hearth	153,000 tons of zinc	333 lb/ton of Zn	0.85	1.0	0.85	4,000
3. Sintering	612,000 tons of zinc	130 lb/ton of Zn	0.95	1.0	0.95	3,000
4. Distillation	612,000 tons of zinc	—	—	—	—	15,000
5. Materials handling	1,020,000 tons of zinc	7 lb/ton of Zn	0.90	0.36	0.32	2,000
Total from primary zinc						57,000
D. Lead						
1. Ore crushing	4,500,000 tons of ore	2 lb/ton of ore	0	0	0	4,000
2. Sintering	467,000 tons of lead	520 lb/ton of lead	0.95	0.90	0.85	17,000
3. Blast furnace	467,000 tons of lead	250 lb/ton of lead	0.85	0.98	0.83	10,000
4. Dross reverb. furnace	467,000 tons of lead	20 lb/ton of lead	—	—	0.50	2,000
5. Materials handling	467,000 tons of lead	5 lb/ton of lead	0.90	0.35	0.32	1,000
Total from primary lead						34,000
Total from primary nonferrous						475,000
10. Fertilizer and phosphate rock						
A. Phosphate rock	38,000,000 tons of rock	—		—	—	— 53,000
B. Fertilizers						
1. Ammonium nitrate	2,800,000 tons of amm. nitrate	—		—	—	— 28,000
2. Urea	1,000,000 tons of urea	—		—	—	— 10,000
3. Phosphates						
a. Acid manufacture	4,370,000 tons of P_2O_5	—		—	—	— 19,000
b. Granulation	18,000,000 tons of gran. matl.	—		—	—	— 190,000
4. Ammonium sulfate	2,700,000 tons amm. sulfate	—		—	—	— 27,000
Total from fertilizers and phosphate rock						327,000
11. Asphalt						
A. Paving material	251,000,000 tons of mat'l					
1. Dryers		32 lb/ton of mat'l	0.97	0.99	0.96	161,000
2. Secondary sources		8 lb/ton of mat'l	0.97	0.99	0.96	40,000
B. Roofing material	6,264,000 tons of asphalt					
1. Blowing		4 lb/ton of asphalt	—	—	0.50	3,000
2. Saturator		—	—	—	—	14,000
Total from asphalt						218,000
12. Ferroalloys						
A. Blast furnace	591,000 tons of ferro-alloy	410 lb/ton ferroalloy	0.99	1.00	0.99	1,000
B. Electric furnace	2,119,000 tons of ferro-alloy	240 lb/ton ferroalloy	0.80	0.50	0.40	150,000
C. Materials handling	2,710,000 tons of ferro-alloy	10 lb/ton ferroalloy	0.90	0.35	0.32	9,000
Total from ferroalloys						160,000
13. Iron foundries						
A. Furnaces	18,000,000 tons of metal	16 lb/ton of metal	0.80	0.33	0.27	105,000
B. Materials Handling						
1. Coke, limestone, etc.		5 lb/ton of metal	0.80	0.25	0.20	37,000
2. Sand	10,500,000 tons of sand	0.3 lb/ton of sand	0	0	0	1,000
Total from iron foundries						143,000
14. Secondary nonferrous						
A. Copper						
1. Material preparation						
a. Wire burning	300,000 tons insulated wire	275 lb/ton of wire	0	0	0	41,000

Source	Annual tonnage (P)	Emission factor Lb Ton (e_f)	Efficiency[b] of control (C_e)	Application[a] of control (C_f)	Net control $C_e \times C_f$	Emissions tons yr (E)
b. Sweating furnaces	64,000 tons scrap	15 lb/ton of scrap	0.95	0.20	0.19	—
c. Blast furnaces	287,000 tons scrap	50 lb/ton of scrap	0.90	0.75	0.68	2,000
2. Smelting & refining	1,170,000 tons scrap	70 lb/ton of scrap	0.95	0.60	0.57	17,000
Total from secondary copper						60,000
B. Aluminum						
1. Sweating furnaces	500,000 tons scrap	32 lb/ton of scrap	0.95	0.20	0.19	6,000
2. Refining furnaces	1,015,000 tons scrap	4 lb/ton of scrap	0.95	0.60	0.57	1,000
3. Chlorine Fluxing	136,000 tons Cl used	1,000 lb/ton Cl used	—	—	0.25	51,000
Total from secondary aluminum						58,000
C. Lead						
1. Pot furnaces	53,000 tons scrap	0.8 lb/ton of scrap	0.95	0.95	0.90	—
2. Blast furnaces	119,000 tons scrap	190 lb/ton of scrap	0.95	0.95	0.90	1,000
3. Reverb. furnaces	554,000 tons scrap	100 lb/ton of scrap	0.95	0.95	0.90	3,000
Total from secondary lead						4,000
D. Zinc						
1. Sweating furnaces						
a. Metallic scrap	52,000 tons of scrap	12 lb/ton of scrap	0.95	0.20	0.19	—
b. Residual scrap	210,000 tons of scrap	30 lb/ton of scrap	0.95	0.20	0.19	3,000
2. Distillation furnace	233,000 tons Zn recovered	45 lb/ton of zinc	0.95	0.60	0.57	2,000
Total from secondary zinc						5,000
Total from secondary nonferrous						127,000
15. Coal cleaning						
A. Thermal dryers	73,000,000 tons dried	—	—	1.0	—	94,000*
16. Carbon Black						
A. Channel process	71,000	2,300 lb/ton	0	0	0	82,000
B. Furnace process						
1. Gas	156,000	—	—	1.00	—	5,000*
2. Oil	1,189,000	—	—	1.00	—	6,000*
Total from carbon black						93,000
17. Petroleum						
A. FCC units	1.19×10^9 bbl. of feed	—	—	1.0	—	45,000*
18. Acids						
A. Sulfuric						
1. New Acid						
a. Chamber	1,000,000 tons of 100% H_2SO_4	5 lb/ton of 100% H_2SO_4	—	0	0	2,000
b. Contact	27,000,000 tons of 100% H_2SO_4	2 lb/ton of 100% H_2SO_4	0.95	0.90	0.85	4,000
2. Spent-acid concentrators	11,200,000 tons of spent acid	30 lb/ton of spent acid	0.95	0.85	0.80	8,000
B. Phosphoric						
1. Thermal process	1,020,000 tons of P_2O_5	134 lb/ton of P_2O_5	0.97	1.0	0.97	2,000
Total from acids						16,000
TOTAL FROM MAJOR INDUSTRIAL SOURCES						13,081,000

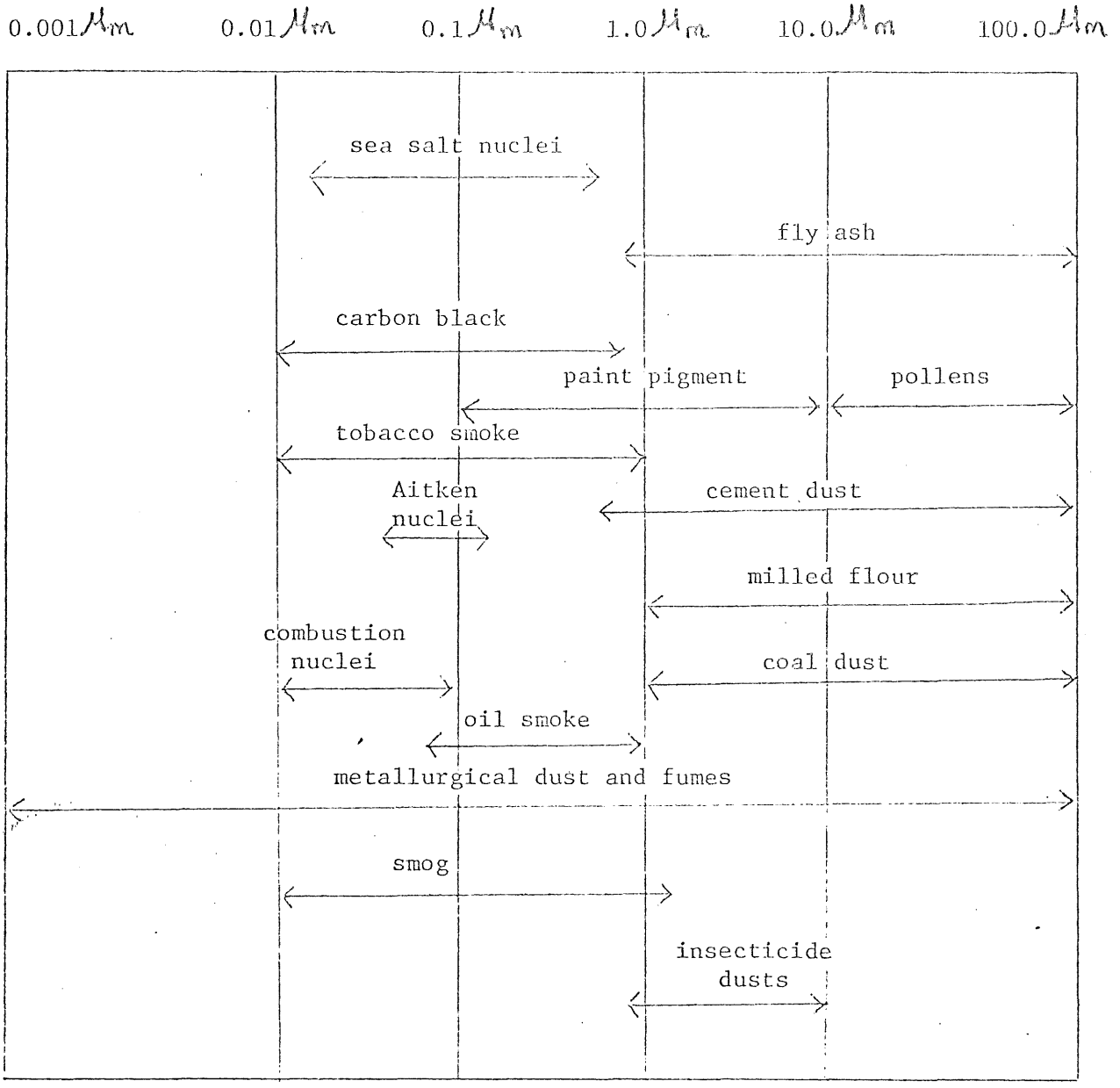
* See specific industry section of Final Report (Contract CPA 22-69-104) for method of calculating quantity emitted.
[a] Application of Control is defined as that fraction of the total production which has controls.
[b] Efficiency of Control is defined as the average fractional efficiency of the control equipment, prorated on the basis of production capacity.
[c] Net Control is defined as the overall level of control, and is the product of the application of control multiplied by the efficiency of control.
[d] Average Ash Content of Coal Used, determined by phone survey:

Type Boiler	(d) Elec. Util.	(e) Industrial
Pulverized	11.9%	10.6%
Stoker	11.2%	10.2%
Cyclone	11.8%	10.3%

[1] Source: Vandegrift, A.E. et al., J. Air Pollution Control Assoc., 21, 321-328, 1971

Figure I

Size Ranges of Some Common Particles



Source: Fennely, P.F. The origin and influence of airborne particulates. Am. Sci., 64, 46-56, 1976.

in the atmosphere. The formation of these particulates is the result of sunlight and atmospheric chemicals such as SO_2, NH_4, NO, H_2O and hydrocarbons (Fennelly,1976). Some specific reactions in the formation of secondary particulates were discussed in the previous section.

Air pollution control regulations on particulates are most often directed toward smoke, dustfall and suspended particulates (Faith,1968). Smoke is defined as a gas-born particle from incomplete combustion and consisting mostly of carbon particles. Dusts are solid particles of natural or industrial origin formed by disintegration processes. Fumes are also solid particles resulting from sublimation, distillation, calcination or chemical reaction processes. Mists are liquid particles.

Suspended particulates consist of any of the above when they are of such a size and density that they remain suspended in the atmosphere. Dustfall refers to particulate matter which settles out of the air in a specific length of time (Faith, 1968).

The standards set for SO_2 and particulates vary from country to country as shown in Table 3 (Biersteker,1976). U.S. primary standards for particulates for 24 hours are $75\mu g/m^3$ annual geometric mean (median, year) and $260\mu g/m^3$ annual maximum (highest day in year). Secondary standards for 24 hours are $60\mu g/m^3$.

There are difficulties in setting ambient air standards because two or three pollutants may be present at the same time and concentrations vary widely due to meteorological and topographical conditions. Also reactions may take place between the various pollutants (Biersteker, 1976

In 1973 Hemeon published a critical review of the regulations established for particulate metter (Hemeon, 1973). He criticized the usage of the term "particulate matter" in that it was too broad to be defined as an air pollutant causing adverse health effects. To be a health hazard an agent should be identified by its chemical composition. Particulate matter is a general designation with no chemical identity and is therefore, a nonentity (Hemeon, 1973).

Also, instead of separate standards for SO_2 and particulate matter, he suggested terms such as "concentrations of soluble sulfate" as a substitute.

Another important area in reviewing atmospheric particles is polycyclic organic matter (POM). This consists of the subcategories: polynuclear aromatic hydrocarbons and polynuclear heterocyclic compounds. POM represents only a very small part of total particulate

matter but it is of importance because of its known health hazard to man and animals. POM is formed in any combustion process involving fossil fuels. It is uncertain whether POM condenses out as discrete particles after cooling or condenses on surfaces of existing particles after formation. According to most investigators POM is bound to particles such as soot. POM is associated largely with particles less than 5 microgms in diameter. These compounds are highly reactive and are degraded in the atmosphere by photooxidation and reactions with SO_2 and other oxidants.

Benzo(a)pyrene (B(a)P) is an important constituent of POM and is usually used to measure the presence of airborne organic pollutants.

TABLE 3

MAIN SO_2 AND PARTICULATES STANDARDS PRESENTLY IN USE

USA 1974	SO_2	80 $\mu g/m^3$ (mean, year), 365 $\mu g/m^3$ (highest day in year) 1300 $\mu g/m^3$ (3 hour maximum, secondary standard to protect against plant damage)
	particulates	75 $\mu g/m^3$ (median, year), 260 $\mu g/m^3$ (highest day in year)
USSR 1973	SO_2	50 $\mu g/m^3$ (24 hrs), 500 $\mu g/m^3$ (20 minutes)
	smoke	50 $\mu g/m^3$ (24 hrs), 150 $\mu g/m^3$ (20 minutes)
Sweden 1965	SO_2	150 $\mu g/m^3$ (highest month), 300 $\mu g/m^3$ (highest day in a month), 750 $\mu g/m^3$ (30 minutes)
Netherlands 1970 proposed	SO_2	75 $\mu g/m^3$ (median, year), 250 $\mu g/m^3$ (98 percentile)
	smoke	30 $\mu g/m^3$ (median, year), 90 $\mu g/m^3$ (98 percentile)
West Germany 1974	SO_2	140 $\mu g/m^3$ (24 hrs), 400 $\mu g/m^3$ (30 minutes)
	particulates	100 $\mu g/m^3$ (24 hrs), 200 $\mu g/m^3$ (30 minutes)
Japan	SO_2	120 $\mu g/m^3$ (24 hrs), 300 $\mu g/m^3$ (1 hr)
	particulates	100 $\mu g/m^3$ (24 hrs), 200 $\mu g/m^3$ (1 hr)

Source: Biersteker, K. Sulfur Dioxide and suspended particulate matter. Where do we stand. Env. Res., 11, 287-304, 1976.

III. Experimental Studies

A. Sulfur Dioxide

1. Introduction

Sulfur dioxide is a weak acid anhydride that is highly soluble in aqueous solution. Absorption of sulfur dioxide into the blood stream leads to the formation of sulfite SO_3 and bisulfite HSO_3 ions at the low pH normally present. These ions are then rapidly oxidized to sulfates by sulfite oxidase. The biochemical mechanism of sulfur dioxide, therefore, can be considered in terms of its weak acidity, the action of sulfite-bisulfite ions; or by the effects of sulfate ions.

An excellent section on the biochemical reactions of inhaled sulfur oxides within the body was presented in Air Quality and Stationary Source Emission Control, 1975. The reader is referred to that publication for greater detail. The author stated that the biochemical mechanisms by which sulfur oxides produce effects in the lung were still unknown. The major physiological response to sulfur dioxide inhalation is bronchoconstriction. Possibly these effects are totally explainable by a decrease in pH. Likewise hyperplasia of mucous secreting cells, which often result from prolonged exposure to sulfur dioxide, may also be due to acidity. The author summits that this explanation is probably an oversimplication of sulfur oxide toxicity. The toxicity of specific sulfur oxides will be discussed in separate sections.

Sulfur dioxide has been implicated as the primary contributing agent in pollution-related diseases. For this reason the effects of sulfur dioxide alone will be discussed in terms of its acute effects, its affect on pulmonary function, histology, and pulmonary defense systems in animals; and its irritative and pulmonary function effects in humans experimentally exposed.

2. Animal Studies

a) Acute Exposure

According to Air Quality Criteria for Sulfur Dioxide the response to sulfur dioxide has been tested in a variety of species including guinea pigs, mice, grasshoppers, and cockroaches. Continuous exposure to SO_2 concentrations of 150 ppm required 847 hours to kill 50% of the mice, while only 154 hours at 130 ppm was required to kill 50% of the guinea pigs (1970). From these data it appeared that mice were more resistant to the effects of SO_2 than were guinea pigs. However, at concentrations of 300 ppm to 1,000 ppm SO_2, guinea pigs were found to be more resistant than mice. At 1,000 ppm SO_2, 50% of the mice died in four hours while it took 20 hours for 50% of the guinea pigs to die. Thus, extrapolations from high to lower concentrations in species sensitivity can be unreliable.

Colucci summarized the available data on acute toxicity of SO_2 as follows: "No significant mortality was observed in animals at SO_2 concentrations ranging from 250 ppm (650 mg/m^3) administered for 40 minutes, to 1180 ppm (3,092 mg/m^3) administered for 90 hours." However, due to great variation among species and among studies this summary statement seems unjustified. Effects that were observed under this exposure (1180 ppm) included "slight eye irritation, excess salivation, coughing, some moderate dyspnea, rhinitis, lachrymation, conjunctivitis, abdominal distention, lethargy, weakness, and paralysis of the hind limbs" (Colucci, 1976).

Studies of this type have varied greatly in the species used, the concentrations of SO_2, and duration of exposure. In spite of these differences, often the same response has been elicited. Therefore, the pathological examination of these acutely exposed

animals is of interest. Generally the lungs have been found to be the critical organ of response (EPRI).

Leong made histological examinations of mice, rats, and guinea pigs which he had exposed to a single lethal exposure of SO_2 ranging from 600 to 5,000 ppm (Leong, 1961). Each species was exposed to three different concentrations of the gas. Several pretreatment procedures were used in order to increase the animals sensitivity to SO_2. These included injection of histamine, injections of albumin, and adrenalectomy. Two mechanisms of death were observed in guinea pigs. Occlusion of the bronchioles and venous congestion with little or no fluid in the alveoli were the distinctive features in those animals which died quickly either after SO_2 exposure or histamine injection. Those that died after 2-3 hours of exposure experienced thickened alveolar walls with 20-30% of the alveoli filled with fluid. The bronchioles were greatly distended. The observations made on these animals were apparently consistent with the hypothesis that animals with brief survival times die of asphyxia produced by the occlusion of the upper respiratory passages. Death after prolonged survival periods resulted from pulmonary failure associated with extensive edema. Leong's study suggested that histamine is involved in the pathological effects brought about by exposure to SO_2.

b) Long Term Exposure

Attempts have been made to assess the tissue damage induced by the inhalation of SO_2 in lower concentrations than those eliciting acute responses.

Alaire has reported minimal alteration of the liver (increased hepatocyte vacuolation) in guinea pigs exposed to 5.72 ppm SO_2 for 52 weeks (Alaire, 1970).

were lost and there was basal cell hyperplasia and transitional hyperplasia; 2-4 weeks of exposure to 200 ppm SO_2 produced squamous metaplasia of the epithelium. Doses of 400 ppm SO_2 for 1 to 2 weeks produced squamous metaplasia. Exposure to SO_2 concentration of 40 ppm for 6 weeks produced no observable changes (Asmundsson, 1973). In order to produce hypersecretion, rats initially received doses of 40 ppm SO_2 for 5 hr/day, 5 days a week. Doses were subsequently raised to 300-400 ppm when no great change was seen in the lungs (Reid, 1963). At this larger dose an increase in the number of mucous secreting cells (goblet cells) were observed both in the main bronchi and in the peripheral airways (which normally lack goblet cells). An excess of mucous cells in man is indicative of chronic bronchitis. The excess goblet cells were still observable 3 months after cessation of exposure; however, the cessation of exposure did seem to end the increase in cells.

An attempt was made to produce chronic bronchitis in male beagles by using an exposure of 500-600 ppm SO_2 for 2-hour periods twice a week for 4-5 months (Chakin, 1974). Upon histological examination of the lungs, the proportion of goblet cells to ciliated cells were found to be decreased at the beginning of the segmental bronchi, while goblets cells were increased at the end of these bronchi and in the bronchioles. Hyperplasia of the bronchial glands occurred. The overall result was excess mucopurulent exudate in the bronchial tree. Since alterations in the quality or quantity of the respiratory mucus is often a major characteristic of obstructive lung diseases in humans these histological changes were significant. It was not suggested that the lesions

This same group showed a lower incidence and severity of spontaneous disease upon examination of the lung and trachea.

Goldring found only minor irritative responses (in the form of focal bronchialization of the alveoli, acute congestion of pulmonary parenchyma, focal emphysema, and epithelial cushioning in the bronchus with the suggestion of hyperplasia) in the lungs of hamsters exposed to 650 ppm SO_2 plus 1% NaCl aerosol for 42 to 63 daily exposures (Goldring, 1967). Goldring also found slight histopathological changes in the lungs of hamsters exposed to SO_2 alone. In animals that were first treated with papain (in order to induce emphysema) and then challenged with chronic exposure to SO_2, a significant number developed a mild form of bronchitis (Goldring, 1970).

Minimal lesions were also observed in rats exposed to 10 ppm SO_2 for up to 3 days. After 24 hours of SO_2 exposure, lesions in the nasomaxillary turbinates were observed. These lesions consisted of edema, necrosis, and desquamation of the respiratory and olfactory epithelium. More severe injury occurred in the nasomaxillary turbinates than in the rest of the respiratory tract. Mice with mild upper-respiratory tract infection had more severe lesions after SO_2 exposure than those mice that were free from disease.

Epithelial changes were observed in the trachea and large bronchi of Syrian hamsters exposed to 100, 200, and 400 ppm SO_2 for periods up to 6 weeks. The sequence of changes were as follows; dilation, vacuolation, and extrusion or exfoliation of ciliated and goblet cells within a few hours of exposure; replacement of ciliated cells by goblet cells 3 or 4 days later; 6-8 days after continuing exposure goblet cells

induced were a precise counterpart of these found in humans, but they were found to be more closely related to those in humans than those lesions produced in rats.

Laskin exposed rats to 10, 51, 105, and 566 ppm SO_2 for various time periods (Colucci, 1976). Pulmonary damage and death occurred at concentrations of 566 ppm SO_2, but no effects were seen at lower exposure levels.

It has been suggested that excess fluid in the alveoli is removed by alveolar macrophages (Barry, 1970). The comparative activity of our lysosomal hydrolytic enzymes were studied histochemically in adult rats exposed to SO_2 to induce hypersecretion of mucus and thereby increase the amount of mucus reaching the alveoli. A marked increase in acid phosphatase was observed throughout the lung parenchyma. Barry suggested that acid phosphatase in alveolar macrophages increased in response to increased mucus reaching the alveoli after respiratory irritation with SO_2 and that it was connected with the break down and removal of the mucupolysaccharide.

Peacock examined three comparable groups of LX mice of both sexes for primary tumors and other lesions after one group was exposed to free radicals and another group was exposed to SO_2 (Peacock, 1967). Incidence of primary lung tumors doubled in those mice (male and female) exposed to 500 ppm SO_2 (only those mice that survived over 300 days were considered) as compared to controls. In females only those exposed to SO_2 experienced any carcinoma of the lung. A slight increase was seen among mice exposed to free radicals. The distribution of tumors could have been a matter of chance as was shown by independent statistical analysis, however, the possibility remains that repeated exposure to SO_2 accelerated the unknown

studies reviewed: "Evidence appears to be emerging to support the pathogenic effects of SO_2 on the nasal mucosa. However, as is characteristic of most animal studies, the levels required to produce these effects are high in relation to that observed in ambient air." Apparently sulfur dioxide does produce epithelial changes in lungs of various animals. The overall results appear to be an excess of mucous exudate in the bronchial tree, due to an hyperplasia of goblet cells. Two studies have implied that SO_2 may act as a carcinogen, but no substantial evidence has been provided to support that hypothesis.

c) Pulmonary Function

For detecing pulmonary irritation, alteration in flow resistance is one of the more sensitive physiological tests.

Increase pulmonary resistance resulted from the administration of SO_2 into the upper and lower airways of anesthetized, paralyzed, artificially ventilated cats. This was prevented by a complete cold block of the cervical vagosympathetic nerves or by injection of atropine intravenously before SO_2 was inhaled. These results seem to establish the reflex nature of bronchoconstriction during inhalation of SO_2 (Nadel, 1965).

Anesthetized dogs were exposed to SO_2 by nose or by tracheal cannula (Frank, 1963). So_2 ranged from 7 to 230 ppm for 15-20 minutes. Breathing through the nose increased nasal flow resistance roughly in proportion to the concentration of SO_2. Nasal flow resistance reverted to control levels 15-40 minutes after exposure ceased. Pulmonary flow resistance underwent smaller changes during exposure to SO_2 through the nose than did nasal flow resistance.

When SO_2 was administered by trachea cannula pulmonary flow resistance rose quickly to a peak in a few minutes and decreased thereafter. The changes in nasal flow resistance were possibly due to mucosal swelling or increased mucus secretions.

Alarie found no adverse changes in pulmonary functions of guinea pigs at exposures of 0.1 to 5 ppm SO_2 for up to one year (Alaire, 1970). Pulmonary function tests included tidal volume, respiratory rate, minute volume, dynamic compliance, pulmonary flow resistance, and carbon monoxide uptake. Body weight, growth,and survival were apparently not adversely affected by exposure to SO_2. Hemotologic variables and clinical measurements were normal.

Lewis found increased pulmonary flow resistance and decreased lung compliance in beagles exposed to 5 ppm SO_2 continuously for 225 days (Lewis, 1968). However, these results were not demonstrated at 650 days in the same animals (Lewis, 1973).

Salem studied the bronchiolar and pulmonary vascular smooth muscles in a group of anesthetized dogs (Salem, 1961). SO_2 concentrations ranging from 200 to 850 ppm administered from 1 to 4 minutes resulted in pulmonary vasoconstriction, bronchoconstriction, with bronchodilation before and after increased pulmonary arterial blood pressure, bradycardia and systemic shock. Pulmonary vessels were determined to be more sensitive than bronchioles to sulfur dioxide exposure. The constriction of these vessles reduced the amount of SO_2 absorbed by the pulmonary circulation and carried to the systemic circulation.

Along slightly different lines, Lee conducted experiments to establish the minimal SO_2 exposure that would consistently affect the respiration and

biochemistry of guinea pigs (Lee, 1966). Exposure to 19 ppm SO_2 for one hour caused an increase in tidal volume, decrease in respiratory rate, along with irregular effects on minute volume. A general decrease in tidal volume and an increase in respiratory rate was observed for SO_2 concentrations of 7 to 17 ppm. Apparently the effect of SO_2 on the tidal volume was dependent on the concentration of SO_2 administered. Below 18 ppm SO_2 tidal volume decreased while above 18 ppm SO_2 tidal volume increased.

SO_2 concentrations of 0.14, 0.64, and 1.28 ppm had no effect on the mechanical properties of the lung, distribtuion of pulmonary ventilation, diffusing capacity, and arterial blood oxygen tension of cynomolgus monkeys exposed continuously for 78 days (Alaire, 1972). A group exposed to 4.69 ppm SO_2 for 30 weeks did show a definite decrease in pulmonary function after an accidental overexposure to concentrations of SO_2 in the range of 200-1,000 ppm for one hour. The lungs and liver were found to be affected upon histological examination.

Alaire conducted a follow-up study exposing cynomolgous monkeys to 5 ppm SO_2 24 hours a day for 78 days (Alaire, 1975). No effects on pulmonary function were observed.

Amdur reported that exposure to as little as 0.15 ppm SO_2 for one hour can induce small reversible increases in pulmonary resistance in guinea pigs (Colucci, 1976).

Apparently some animal species will exhibit a response to low levels of SO_2, but these increases in flow resistance reverse after cessation of exposure.

d) Mucociliary Clearance

Mucociliary clearance is an important pulmonary defense against toxic materials and pathogenic bacteria. Three approaches have been generally undertaken in the study of this mechanism: direct observation of cilia, the clearance of foreign particles, and altered susceptibility to infectious agents.

One of the first studies on mucus flow and ciliary activity in rats was conducted in Scandinavia (Dalhamn, 1956). Two groups of rats were exposed to SO_2, 1 group for 18 days at 11.4 ppm, the other for 67 days at 11.5 ppm. Each group was divided into two subgroups and examined at two different times, immediately after cessation of exposure and 33 days later. A third group comprised of 6 rats were exposed to a continuous stream of air for 62 days. Retardation of the mucus flow was demonstrated in all 4 groups exposed to SO_2. Ciliary activity was significantly reduced in the rats exposed to SO_2 for 18 days, but not in the rats exposed for a longer period. This study indicated that mucus flow can be slowed without a decrease in ciliary activity.

Dalhamn also studied the acute effects of sulfur dioxide on ciliary activity on thd trachea of rabbits in vivo and in vitro (Dalhamn, 1961, 1963). A 5 minute exposure to 20-30 mg/l or 10 ppm SO_2 was required for cessation of the ciliary beat in rabbits during in vitro exposure (SO_2 blown directly over tracheal mucosa). In rabbits spontaneiously breathing through the nose 200-250 ppm SO_2 was required before ciliary beating ceased. The apparent contradiction was explained by absorption of SO_2 in the nasal passages during nose breathing. When 200 ppm SO_2 was inhaled, 6-8 ppm SO_2 was all that was recovered in the trachea.

The effects of inhalation of SO_2 for 30 minutes on the bronchial clearance in three minature donkeys was studied by Spiczelman by means of radioactive monodisperse ferric oxide particles (Spiczelman, 1968). The donkeys exhibited discomfort during all levels of exposure from 0.26 to 713 ppm SO_2, but impaired clearance occurred only at higher concentrations of SO_2 (≥300 ppm). These concentrations also produced coughing and mucous discharge from the nose.

Tracheal mucus velocity was studied in 8 purebred beagle dogs exposed to 1 ppm SO_2 intermittently for 12 months as opposed to 3 dogs not exposed at all (Hirsch, 1975). Teflon discs were used to monitor velocity. Significant slowing of mucus flow as found among SO_2 exposed dogs. Apparently breathing and pulmonary gas exchange were not affected. Long-germ exposure produced impairment of ciliary activity with no alteration in pulmonary function. Slowed mucociliary activity may be one of the first signs of pulmonary dysfunctions.

Four hundred and twenty Long-Evans male rats were exposed to SO_2 concentrations of 0.1, 1, and 20 ppm, for 7 hours a day, 5 days a week for 10 to 25 days (Ferin, 1973). After exposure to SO_2, animals were exposed to TiO_2 aerosol at 15 mg/m^3 for 7 hours (diameter 1.48 microgms). SO_2 was shown to effect the clearance of these "inert" particles. Interestingly, it was observed that short term exposures at higher concentration (20 ppm) were tolerated better than longer lasting exposure to lower levels of SO_2 (1 ppm).

Bacterial elimination in guinea pigs was not impaired by exposure to 10 ppm SO_2 for 4 weeks (Rylander, 1969). Killed, radioactive, and viable E. coli were the organisms used.

The effect of SO_2 alone on the pathogenesis of murine influenza was investigated by Fairchild in male albino mice (Fairchild, 1972). The mean SO_2 concentration ranged

from 2.9 to 34 ppm. Weight loss was used as an indicator of response. At low levels of SO_2 exposure no effect on weight was seen but at 34 ppm, mice lost 15 percent of their weight during the 7 day exposure. At lower SO_2 concentrations the amount of pneumonia that was observed was slightly reduced on the seventh day. However, at 7-10 ppm an increase in pneumonia began to be observed. The underlying mechanisms were not clear. One possible explanation offered was that SO_2 produced inflammatory changes and pulmonary clearance mechanisms were therefore slowed. Possibly alveolar macrophages were impaired. The author pointed out that the concentration of SO_2 that promoted pneumonia in mice was approximately 100 times the concentration commonly observed in New York.

e) Absorption and Distribution

Several animal studies have focused on the amount of absorption that occurs during the breathing of SO_2. Because a large percentage of inhaled sulfur dioxide is absorbed, the fate of this sulfur dioxide is also of interest.

Frank administered 35 SO_2 to anesthetizied dogs by means of a mask with separate connections for the nose and mouth (Frank, 1969). Ninety-nine percent of the gas (1-50 ppm) breathed through the nose was absorbed at a flow of 3.5 liters per minute. When flow was increased 10 fold, the percent absorbed fell several percent. More than 95 percent of all sulfur dioxide (1.10 ppm) inhaled by mouth was absorped at a flow rate of 3.5 liters per minute. However, when flow increased 10 fold, abosrption fell to below 50 percent. The nose was shown to be more effective at removing 35 SO_2 from the airstream. The rate of administration appeared to be quite important in terms of penetration of the upper airways. The mode of breathing, nasal or oral, slow or fast, seems to be more important than the concentration ofSO_2 in the environment in determining how much SO_2 reaches the larynx and the lower airways. To related this finding to man, one would expect

exercise and heavy labor to result in increased exposure of the lower airways to SO_2. Another important finding was the continuous release of SO_2 from the mucus after SO_2 exposure ceased.

The absorption of SO_2 in the respiratory tract of rabbits breathing through the nose has been investigated by Strandberg (Strandberg, 1964). According to Strandberg, several authors have already studied this phenomenon. Gadaskina found that absorption was 63 percent (range 46 percent to 81 percent) rabbits were exposed to 200-2,000 ppm SO_2 Dalhamn and Strandberg found 90-95 percent absorption where rabbits were exposed to 100, 200, and 300 ppm SO_2. In this experiment, rabbits were exposed to concentrations of SO_2 from approximately 0.05 ppm to 700 ppm. Expsure to high concentrations (100 ppm) of SO_2 resulted in absorption in the respiratory tract of approximately 95 percent at inspriation and 98 percent at expiration. However, exposure to low concentrations of SO_2 (.1 ppm) less absorption occurred, approximately 40 percent at inspiration and 80 percent at expiration. Higher concentrations of excess mucus were proposed to occur during higher concentrations of SO_2 thereby increasing absorption.

Amdur using Strandberg's data explained the fact that the presence of a tracheal cannula does not lead to greater response at low concentrations while it does lead to a greater response at high concentrations (Amdur, 1963). Since upper respiratory tract absorption is minimal at low concentrations, it followed that a by pass of the upper respiratory tract with the cannula would not significantly increase the amount of SO_2 reaching the lung.

The absorption and distribution of SO_2 inhaled through the nose and mouth was studied in twelve dogs (Balchum, 1959). A significantly lower percentage of retained 35_S concentration was found in the organs of the dogs breathing through the

nose and mouth than in those breathing via a tracheostomy. Those organs included the trachea, lungs, hilar lymph nodes, liver and spleen. ^{35}S was found to be excreted in urine. Blood levels of ^{35}S and pulmonary resistance were also lower in dogs breathing through their nose and mouth. The various measures seemed to indicate a protective effect of the upper airways in that less sulfur dioxide reached the lungs when breathed through the nose. Labelled $^{35}SO_2$ was only slowly removed from the trachea and lung, being detected in these tissues a week after exposure (Balchum, 1960). According to Balchum, Bystrova found radioactive sulfur in the tissues of mice three weeks after exposure.

Yokayama exposed 5 mongrel dogs to 22$\pm$ 2 ppm $^{35}SO_2$ while they were anesthetized (Yokayama, 1971). Expsosures lasted from 30-60 minutes. Blood ^{35}S levels rose progressively during exposure and decreased slightly hours after exposure. More ^{35}S was found in the plasma than in the red blood cells. Of the ^{35}S associated with red blood cells, two thirds appeared to be intracellular. What affect the sulfur that enters the RBC may have is not known. Again, ^{35}S was found to be excreted in urine.

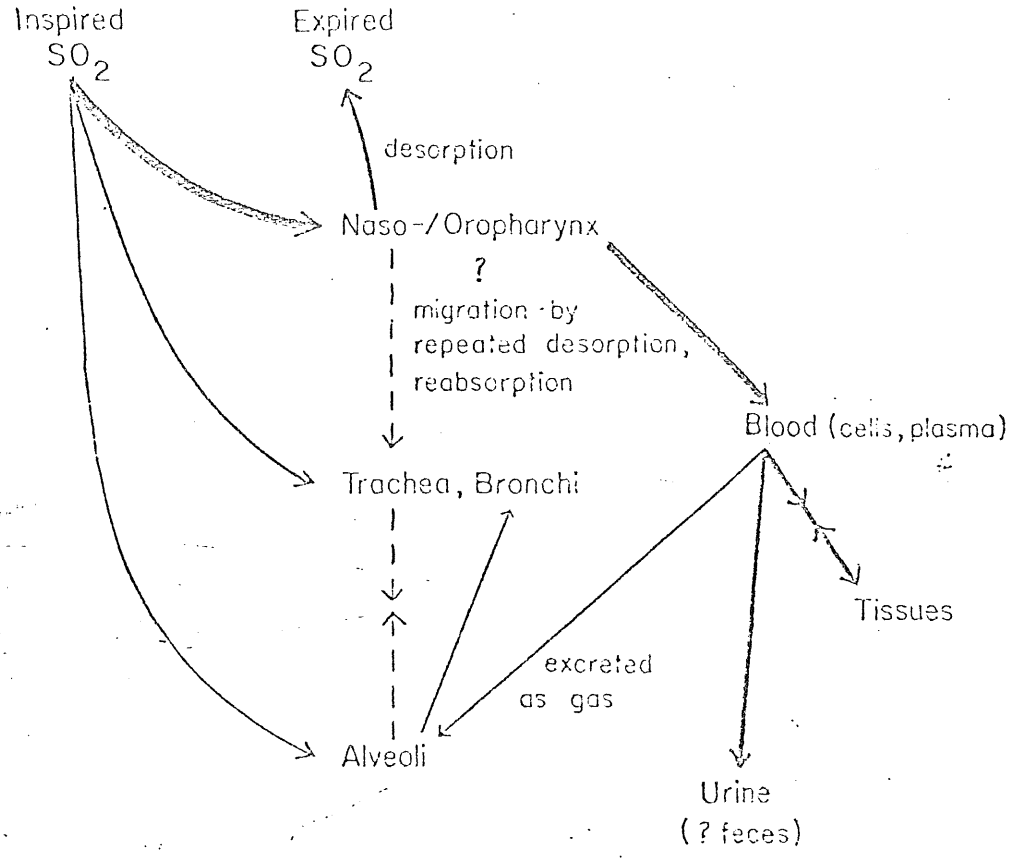
Figure 2 presents the possible paths that SO_2 follows after its removal from inspired air (Frank, 1969).

At high exposure levels the upper airway absorbs a large percentage of inhaled sulfur dioxide and thereby minimize exposure of the lungs and lower airways. The absorption of SO_2 is not a rapidly reversible process, but rather leads to biochemical reactions within the body such as the formation of sulfite which apparently is reversible.

3. Human Studies

Sulfur dioxide is a mild respiratory irritant that can cause irritation and inflammation of the eye conjunctiva. According to Sax, 0.3-1 ppm can be detected by taste rather than smell in the average individual (Sax, 1963). Sax has

Figure 2 . Different Paths Taken by SO_2 After its Removal from Inspired Air[1]



[1]Source: Frank, N.R. et al, Arch. Environ. Health, 18, 315-322, 1969

also stated that 3 ppm has an easily detectable odor, although other studies have found wide variability in the level at which SO_2 is detected. Twenty ppm is the level at which SO_2 becomes irritating to the eyes and 10,000 ppm is irritating to moist areas of the skin within minutes of exposure. The upper respiratory tract and the bronchi are the organs primarily affected by SO_2 inhalation. Edema of the lung or glottis may result with possible respiratory paralysis at very high concentrations. Concentrations of 400-500 ppm is immediately dangerous to life. These findings have come mostly from industrial exposures to SO_2. The toxicity of SO_2 at much lower concentrations has also been studied under controlled conditions with healthy human volunteers.

Melville compared the effects of SO_2 inhaled by mouth and nose in 49 healthy volunteers (Melville, 1970). Specific airway conductance (SO_{aw}) decreased after inhalation of SO_2 in low concentrations (below 5 ppm) during both nose and mouth breathing. However, the decrease was greater with mouth breathing. No difference in SO_{aw} between nose and mouth breathing was observed after inhalation of 5 ppm SO_2. No further decreases in SO_{aw} could be found after exposure to 5 ppm SO_2 for 5 minutes even when exposure lasted up to 1 hour. The authors suggested that this indicated acclimatization to SO_2.

Speizer and Frank using 7 human subjects found that with exposures up to 25 ppm for 30 minutes less than 1 percent of SO_2 entering the nose reaches the oropharynx. It was implied that these low concentrations were sufficient to initiate reflex changes in bronchomotor tone (Speizer and Frank, 1966).

Anderson confirmed this finding in testing pharyngeal air samples in 15 young healthy men during 6-hour exposures to 1.5 and 25 ppm SO_2 (Anderson, 1974). Significant decreases in nasal mucus flow rates were observed during the 5 and 25 ppm exposure particularly in the anterior nose and in subjects with initially slow mucus flow rates. Increased nasal airflow resistance and decreased forced expiratory volume in 1 second

(FEV_{1sec}) and forced expiratory flow during the middle half expired volume was found at all exposure levels. This study seemed to indicate that nosobronchial reflex bronchoconstriction was occurring.

According to Colucci, W ir failed to find any dose-related changes in males exposed to 0.3-1.0 ppm SO_2 for 120 hours. At 3 ppm significant but minimal reversible decreases in small airway conductance occurred.

It has been concluded from this and other evidence that "the experimental threshold concentrations for the demonstration of the bronchoconstrictor effects of SO_2 for brief expsosure is something close to 1. ppm (ca 2.5 mg/m^3) in healthy adults" (Colucci, 1976).

Pulmonary resistance was measured in 10 healthy males in Kawaski after inhalation of about 10 mg/m^3 of dust with deep breaths (Toyama, 1964). The mean diameter of the dust was 2 microgms. The degree of increased airway resistance depended mostly on individual sensitivity. The results suggested that fine particles produce increased flow resistance by phsical rather than chemical means.

Wolff failed to find any changes in tracheobronchial clearance in 9 healthy adults exposed to 5 ppm SO_2 (Wolff, 1975). He suggested that clearance results from the local action of absorbed gas. The observed decreases in MMEF appeared to be caused by reflex bronchoconstriction.

A series of experiments on a total of 25 healthy human volunteers extending over a period of 4 years found a great deal of individual variation both between and within subjects (Lawther, 1975). However, increases in airway resistance were seen at low concentrations (1-3 ppm) of SO_2 when inhaled deeply. Higher concentrations (5-30 ppm) of SO_2 caused changes in resistance when inhaled normally.

Stokinger after reviewing several papers on the affect of pure SO_2 on man concluded that concentrations above 1 ppm

pure SO_2 were required before serious or even significant effects would be expected on the health of healthy individuals (Stokinger, 1968).

The effect of SO_2 on individuals with impaired respiratory systems would be expected to be greater, but no such studies would be conducted for ethical considerations.

B. Sulfuric Acid and Sulfates

1. Introduction

Since sulfuric acid and acid sulfates may be responsible for much of the aggravation of respiratory illness associated with SO_2 levels im many epidemiologic studies, toxicologic effects of these compounds are of great interest (Utidjian, 1975).

2. Animal Studies

a. Acute Exposure

Exposure of various animals to high concentrations of sulfuric acid has been used to estalish its relative toxicity and its affect on tissues in the respiratory tract. Sulphates seemingly have not been studied in this manner.

In 1948 Mather and Olmstead first established that sulfuric acid aerosol was highly toxic (Bushtueva, 1961c).

Treon et. al. established that guinea pigs were the most sensitive to H_2SO_4 aerosol, dying after 2.75 hours inhalation of 22 ppm sulfuric acid (Treon, 1954).

Amdur determined that the eight hour lethal concentration 50 percent probable (LC_{50}) of sulfuric acid having a mass median diameter (MMD) of microgms 18mg/m^3 for guinea pigs 1-2 months old and 50 mg/m^3 for guinea pigs 18 months old (Amdur, 1971).

Pattle et. al. also determined an eight hour LC_{50} for guinea pigs. Exposure was with sulfuric acid with a MMD of 2.7 microgms and 0.8 microgms. LC_{50} for the 2.7 microgms particles was 27 mg/m^3 while the LC_{50} for the 0.8 microgms particles was 60 mg/m^3 (Amdur, 1971). An important finding showed that the presence of ammonium carbonate in quantities sufficient to provide an excess of ammonia gave protection from levels of sulfuric acid which in the absence of ammonia would have caused 50 percent mortality. From this study it appeared that sulfuric acid was more toxic than ammonium sulfate.

Amdur and Pattle both reported pathological findings that suggested that animals dying after exposures of less than 2 hours to H_2SO died of asphyxia caused by bronchostenosis and laryngeal spasm (Amdur, 1971). Those that died after longer exposure also exhibited capillary engorgement and hemorrhage. These changes might be related to the combined effects of anoxia and increased intrathoracid pressure caused by bronchostenosis and laryngeal spasm. This action seems to be related to concentration and to individual sensitivity. Apparently sulfuric acid can also produce parenchymal lung damge depending on total dosage received.

Bushteuva exposed guinea pigs continuously for 5 days to SO_2 and sulfuric acid alone and in combination (Bushteuva, 1960). Edema and thickening of alveolar walls occurred in animals exposed to 2 mg/m^3 of H_2SO_4. Pathomorphological changes in the lungs and upper respiratory tract were evident in those exposed to 3 mg/m^3 SO_2 and 1 mg/m^3 H_2SO_4. Combined concentrations of SO_2 at 1 mg/m^3 and H_2SO_4 at 0.5 mg/m^3 produced similar but only slight changes.

Three groups of 15 male albino rats were exposed to 703 ppm of "fuming" sulfuric acid; one group for 5 hours, one group for 5 hours/day for 6 days and the last group for 5 hours/day for 5 weeks, in order to study the affects it had on lung surfactant (Krishman, 1974). The rats showed an increase in response with increasing length of exposure. The first group was comparable to the control while the group exposed for 5 weeks showed a definite decrease in surfactant activity. This was determined by the increased minimum and maximum surface tension and decreased phospholipid content. Histopathological changes in this group were indicative of emphysema in 10 out of the 15 rats. The effects of H_2SO_4 were likened to the effects of alcohol in the stomach, with small amounts tending to increase secretion and large amounts inhibiting

production. Possibly prolonged exposure to H_2SO_4 fumes can alter surfactant in the lung and lead to emphysema.

In a study with beagles exposed to SO_2 (0.5 ppm) and H_2SO_4 (0.9 mg/m^3) alone and in combination for 620 days of continuous exposure, SO_2 alone produced no specific effects (Lewis, 1973). H_2SO_4 decreased the animals' lung and heart weights, along with a decrease in lung capacity. Lung parenchyma was also seriously affected.

Regardless of particle size , 1 microgms, 1 microgms-4 microgms, concentrations of sulfuric acid beteen 0.1 and 1 mg/m^3 were usually able to produce slight but definite histopathological changes in cynomolgus monkeys (Alaire, 1975). Concentrations above 1 mg/m^3 induced definite histopathological changes, while concentrations above 2.5 mg/m^3 also induced pulmonary function impairment. The authors concluded that deleterious effects detected from exposure to mixtures of SO_2, fly ash,and H_2SO_4 mist were attributable to the acid mist alone.

b. Pulmonary Function

Pulmonary function tests are useful in studying effects of exposure to levels of pollutants that do not end in death or do not tend to produce pathological effects. The studies that have been done on the health effects of sulfates in animals fall mostly into this category.

Amdur exposed guinea pigs for 1 hour to concentrations of sulfuric acid mist ranging from 2-40 mg/m^3 (Amdur, 1958). The size of the particles seemed important in determining the response. Particles of 7 microgms did not penetrate beyond the upper respiratory tract and produced only a slight (though significant) response in flow resistance. The effects caused by the 2.5 microgms particles and the 0.8 microgms particles were dependent upon concentration. At higher concentrations (40 mg/m^3) the 2.5 microgms particles produced a greater effect. At lower levels of 2 mg/m^3, which seem to be a more realistic concentration,

the 0.8 microgms particles caused a greater response. Bronchial constriction was suggested as the physiological mechanism involved. Interestingly, this is the same manner in which irritant acid gases behave (Amdur, 1958). The response to 0.8 microgms particles was immediate while the initial response to larger particles was quite slow. Due to differences of response time, different mechanisms of action between the sizes of particles has been suggested (Amdur, 1971). Pathological findings seemingly bear this out. Lungs in the rats exposed to 2.5 microgms were edematous with extensive areas of atelectasis. This suggested that larger particles were deposited in the major bronchi. Local irritation then caused swelling and increased exudation of fluid, leading to complete obstruction. Smaller particles seemed to be responsible for narrowing the airways rather than complete obstruction. Once exposure had ceased, these animals demonstrated a slow return to normal. Apparently particles deposited in the respiratory tract continue to exert their effect after cessation of exposure while whole irritant gases are cleared from the lung as soon as exposure ceases.

According to Lee, there was an increase in mucus production in rats exposed to H_2SO_4 for 14 days (Lee, 1977).

The ability of donkeys to clear radiolabelled Fe_2O_3 particles upon exposure to H_2SO_4 was studied at the New York University Institure for Environmental Medicine. One hour exposures to H_2SO_4 significantly slowed clearance, but $(NH_4)_2SO_4$ had not such effect. Apparently some of the animals developed a persistent slowing of clearance after repeated short-term exposures. Normal clearance did not return for several months.

The Environmental Protection Agency conducted studies on the effects of H_2SO_4 on the immune system and certain hematological parameters (Lee, 1977). Rabbits exposed for 4 hours on two successive days exhibited an increase in thymidine incorporation of lymphocytes with or without

T cell nitrogen. Immunized mice exposed to H_2SO_4 showed no change in number of antibody producing spleen cells. A significant reduction in hematocrit, an increase in polymorphonuclear leucocytes and a decrease in lymphocytes were observed in rabbits exposed to H_2SO_4 for 2 hours.

A study at the University of Washington has addressed the question of whether or not H_2SO_4 may be neutralized in the lung by NH_3 which is naturally secreted by the body (Lee, 1977). Enough ammonia is present to convert 13 to 520 microgms/m^3 of inhaled H_2SO_4 to $(NH)_{42}SO_4$ or $(NH_4)_2HSO_3$. The site of reaction or when this reaction takes place is unknown.

Amdur and Corn studied the irritant effect of zinc ammonium sulfate, zinc sulfate, and ammonium sulfate in guinea pigs (Amdur and Corn, 1963). At first, concentrations of approximately 1 mg/m^3 and size of 0.29 microgms were used. Zinc ammonium sulfate was determined to be the most irritant in terms of increased flow resistance. Ammonium sulfate was the least irritant producing one-third to one-fourth the response looked by zinc ammonium sulfate. Particle sizes 0.28 microgms, 0.51 microgms, 0.74 microgms and 1.4 microgms at concentrations of 0.25-3.6 mg/m^3 for 1 hour were then investigated as far as the irritation potential of zinc ammonium sulfate was concerned. As particle size decreased, the response to a given concentration increased and the dose-response curves became steeper. A small increase in concentration produced a greater effect at smaller particles sizes. Particle size and particle concentration appear intrinsically related. When zinc ammonium sulfate and SO_2 were administered together, the effect was more than additive.

The effect of zinc ammonium sulfate was also examined by Nadel, in anesthetized artificially ventilated cats (Amdur, 1971). At a concentration of 40-50 mg/m^3 the effect of zinc ammonium sulfate was found to be similar to the physiological response produced by histamine, but

to a lesser extent. This finding is particularly interesting in light of Charles' study of guinea pig lungs subjected to 10-200 mm concentrations of ammonium and various anions (Charles, 1975). His study suggests that the inhalation irritation associated with certain sulfates may be related to their ability to release histamine in the presence of ammonium ion.

The affects of various aerosols on the respiratory response of guinea pigs exposed to SO_2 and several sulfates were investigated (Amdur and Underhill, 1968). Ferric sulfate was classified as an irritant, but ferrous sulfate and menganous sulfate produced no detectable changes in flow resistance. This study determined that all sulfates did not potentiate the effect of SO_2. These experiements indicated that the key to the role of SO_2 in air pollution toxicity lie not in SO_2 itself but in its atmospheric chemistry.

In the presence of 1.3 mg/m^3, SO_2 flow resistance was increased by 15 percent. If atmospheric reactions completely oxidized this SO_2 to 7 microgms H_2SO_4, then flow resistance would be increased 60 percent. A complete conversion to 0.30 microgms zinc ammonium sulfate would increase flow resistance 300 percent. Since complete conversion is highly unlikely, Amdur chose a 10 percent conversion rate, which is very likely. Even with this conversion rate, 0.3 microgms zinc ammonium sulfate produced would increase flow resistance 45 percent.

Cations associated with sulfates can increase susceptibility to infection (Coffin and Knelson, 1976). Charles found that "there was a gradation of histamine release according to the specific salt and the concentrations." Sulfate removal from the lung was also found to be associated with specific cations. It would appear that the action by the cations occurs on the cell membrane and leads to penetration or absorption of the anion into the cell. The anion then binds to mast cell granules and

histamine is released. The histamine and related substances initiate the bronchoconstrictive reaction. With the increasing evidence that sulfates and their associated cations are important in health effects, more attention should be given to cationic substances polluting the air.

Combinations of sulfur dioxide with sulfuric acid or with various sulfates, might increase pulmonary flow resistance more than the expected from the addition of the two compounds alone. Amdur presented evidence that the effect may be more than additive with H_2SO_4 at submicron particle size (Amdur, 1953). Particles of 2.5 microgms did not show that effect. The combined effect of zinc ammonium sulfate and sulfur dioxide was also found to be more than additive (Amdur, 1963).

Amdur executed a series of studies with guinea pigs to test the validity of the proposed threshold value of 1 mg/m^3 for sulfuric acid (Colucci, 1976). Percent change in pulmonary resistance was studied as a function of H_2SO_4 concentration and particle size and as a function of post-exposure time. The results showed that:

1) The percent changes in resistance increased with increasing H_2SO_4 concentration from 0.07 to 0.86 microgms/m^3 at a particle size of 1 microgm, but it is not a strictly linear relationship;

2) There was a five-fold increase in irritant potency between H_2SO_4 aerosol particle sizes ranging from 2.5 to 0.1 microgms, all within the "respirable range," with Amdur further stating that the concentrations of SO_4/m^3 utilized in the study fell within the range of hourly maximum values in urban communities;

3) The irritant potency of sulfuric acid, based on percent increase in resistance, far exceeds the irritant potency of eight other commonly occurring sulfates;

4) Sulfuric acid concentrations of 0.1 and 1.0 mg/m^3 induce an increase in resistance that does not return to zero 30 minutes post-exposure;

5) In general, resistance and compliance values did not return to control levels by the end of the exposure period when the exposure to H_2SO_4 had exceeded 0.4 to 0.6 mg/m^3. (Note: equivalent resistance and compliance values would have returned to control values if SO_2 had been administered instead of H_2SO_4);

6) The effects of sulfuric acid administered with SO_2 are more than additive at very high concentrations, but not at those likely to occur in the ambient air.

Tables 4-7 provide information on the irritant potency of sulfuric acid (4) and sulfates (5), the ranking of sulfates for irritant potency (6) and the interaction of sulfates and SO_2 (7).

3. Human Studies

Little information exists on the effects of sulfuric acid in man. No data exist on the affect of various sulfates on human health. It is known that direct contact with sulfuric acid results in the rapid destruction of tissue with severe burning. Effects of inhalation of sulfuric acid mist are a bit more difficult to quantify. Sulfuric acid mist in concentrations of 0.125-0.5 ppm is mildly annoying, 1.5-2.5 ppm is unpleasant, while 10-20 ppm is unbearable with severe coughing and irritation of mucous membranes of the eyes and nose. These concentrations occur only in occupational settings (Sax, 1963). The exposures that humans are subjected to under experimental conditions are much lower.

Amdur exposed 15 normal human subjects to concentrations of sulphuric acid mist from 0.35 to 5 mg/m^3 for 5 to 15 minutes (Amdur, 1952). Percent retention of sulfuric

Table 5

IRRITANT POTENCY OF SULFATE SALTS[1]

Compound		μM	Number of Animals	μg SO_4/m^3	% Increase Resistance	% Increase Resistance μg SO_4/m^3
Zn $(NH_4)_2(SO_4)_2$	+	0.29	12	163	22*	0.135
"		0.51	9	981	43*	0.044
"		0.74	10	914	21*	0.023
"		1.4	6	718	5	0.007
$(NH_4)_2$ SO_4	+	0.19	10	363	23*	0.063
"		0.20	10	1553	-4	-0.003
"		0.29	6	729	28*	0.038
"		0.81	10	6926	0	0
NH_4 HSO_4		0.13	19	775	15*	0.019
"		0.52	10	2168	28*	0.013
"		0.77	10	9157	23*	0.002
$CuSO_4$		0.11	23	257	9	0.035
		0.13	30	1232	25*	0.020
		0.33	35	1448	14*	0.009

+ Data from Amdur and Corn

* Change statistically significant

[1]Source: Colucci, A.V. Sulfur Oxides: Current status of knowledge EPRI EA-316 Prepared for Elect Power Research Institute, December, 1976

Table 6

RANKING OF SULFATES FOR IRRITANT POTENCY[1]

Compound	% Increase/Resistance g SO_4/m^3
H_2SO_4	0.410
$Zn(NH_4)_2(SO_4)_2$	0.135
$Fe_2(SO_4)_3$	0.106
$ZnSO_4$	0.079
$(NH_4)_2SO_4$	0.038
NH_4HSO_4	0.013
$CuSO_4$	0.009
$FeSO_4$	0.003
$MnSO_4$	-0.004

[1] Source: Colucci, A.V. Sulfur oxides: Current status of knowledge EPRI EA-316 prepared for Electric Power Research Institute, December, 1976

Table 7

INTERACTION OF SULFATES AND SO_2 [1]

Compound	More than Additive
H_2SO_4	No
$Zn(NH_4)_2(SO_4)_2$	Yes
$Fe_2(SO_4)_3$	Not tested
$ZnSO_4$	Not tested
$(NH_4)_2SO_4$	No
$CuSO_4$	Yes
NH_4HSO_4	No
$FeSO_4$	Yes
$MnSO_4$	Yes

Combination of SO_2 and $CuSO_4$

SO_2 PPM	$CuSO_4$ gSO_4/m^3	Number of Animals	% Increase Resistance	Total Sulfur g/m^3
0.5	-	18	13	1310
-	257	23	9	86
0.4	333	10	59	1159

[1] Source: Colucci, A.V. Sulfur Oxides: Current status of knowledge EPRI EA-316 Prepared for Electric Power Research Institute December, 1976

acid was determined by measuring total volume of air breathed, the concentration in the mixing chamber and the concentration in the exhaled air. An average of 77 percent of the sulfuric acid was retained. The mist particle size averaged 1 microgm. The inhalation of sulfuric acid caused changes in respiration at all concentrations, with shallower and more rapid breathing. The subjects could not detect the acid by odor, taste or irritation below 1 mg/m^3 (the maximum allowable range). At 5 mg/m^3 the acid mist was detectable to all subjects, but the response was quite varied among the subjects. The main response was a decrease in minute volume.

Sim and Pattle studied the response to sulfuric acid mist during different relative humidities in healthy males (Sim and Pattle, 1957). Concentrations of 20.8 mg/m^3 for 30 minutes during high humidity produced "intense coughing." Exposure to 39 mg/m^3 for 60 minutes at low humidity was "well-tolerated." They found that exposure to sulfuric acid under high humidity increased mean particle size and produced more irritation. The addition of ammonia gas abolished the irritant effects of acid. Two of the subjects exposed to sulfuric acid developed long-lasting bronchitis symptoms.

The sensitivity to light on exposure to sulfuric acid was tested in 2 human subjects for time periods of 60, 90, 120 minutes by (Bushtueva, 1957). Determinations of sensitivity were made every 5 minutes the first half hour and every 10 minutes thereafter. The normal curve of dark adaptation for both subjects was used as a control. Sulfuric acid aerosol at a concentration of 2.4 mg/m^3 caused a sharp reduction in light sensitivity. However, concentrations of 0.7-0.96 mg/m^3 produced a rise in optical sensitivity. Concentrations of 1.1-1.3 mg/m^3 first brought some increase, then a reduction. The significance of these findings is difficult to interpret. Threshold irritation effects of H_2SO_4 aerosol were determined by questioning 10 subjects

exposed to different levels of H_2SO_4. The range of concentrations was from 0.6-0.86 mg/m^3. Highly sensitive individuals had an average threshold value of 0.55 mg/m^3 (Bushteuva, 1957).

The Environmental Protection Agency plans to study the effects on human health of exposure of 100 microgms/m^3 H_2SO_4 (Lee, 1977). Particle sizes of 0.3-0.09 microgms diameter will be considered initially. The first set of experiments should have begun in the Spring of 1977.

The toxicology of sulfuric acid may be summarized, in part, as follows (Colucci, 1976):

1) "particle size is an essential determinant of the irritant potency of H_2SO_4"

2) "sulfuric acid elicits the greatest irritant response among all sulfur oxides tested."

This appears to be true in animals and possibly in humans. Colucci draws two more conclusions which require some comment; the first being that "H_2SO_4 induced increase in pulmonary resistance does not return to normal 30 minutes post-exposure, which suggests that exposure to sulfuric acid can induce irreversible deleterious effects at concentrations less than 1 mg/m^3."

This conclusion is inconsistent with that of Amdur, who found that a slow return to normal has been a consistent feature of exposure to irritant aerosols. No mention has been made that this latter effect is indicative of "irreversible deleterious effects." The second conclusion which Colucci draws from these studies and which requires comment is that "Under ambient circumstances, the mechanics of emitted H_2SO_4 make it an infeasbile component of the group of harmful air pollutants." Though it is true that H_2SO_4 seems to be rapidly neutralized in ambient air, the fact that its distribution and concentration in ambient air is unknown coupled with the fact that it is so toxic warrants its consideration as a potentially dangerous component of ambient air.

The role of particle size and concentration of sulfuric acid and particularly various sulfates seem to warrant further animal and human study.

C. Sulfites

1. Introduction

Typically, sulfites have not been considered a major constituent of sulfur oxide pollution, mainly because it was believed that sulfites were rapidly oxidized to sulfates under ambient atmospheric conditions. Therefore, few experiemental and human studies have been performed in this area and no epidemiologic study to date has assessed sulfites specifically.

It has recently been postulated by Eatough that sulfites and bisulfites "May be an important component in the initiation or exacerbation of respiratory disease by sulfur oxides" (Colucci, 1976).

In a study conducted by Eatough and Colucci, appreciable levels of sulfites were detected downwind from and in the vicinity of a copper smelter (Colucci, 1976). The large volumes of sulfite species collected suggested that sulfite does not deteriorate rapidly in the atmosphere as was believed. It has been postulated that "Upon contact with metal oxides in particulates, SO_2 forms sulfite complexes. Furthermore our data suggest that these complexes are stable against air oxidation of the sulfite moiety."

Metal sulfites may be involved in causing adverse health effects in exposed individuals. The mechanism hypothesized involves the release of sulfite, stored in the metal complex, upon contact with the moist surfaces of the respiratory tract. This released sulfite could then cause damage to surrounding tissue.

The formation of sulfite within blood has been associated with exposure to sulfur dioxide and might play a role in biochemical mechanisms of SO_2 toxicity.

2. Animal Studies

Gunnison investigated the reactivity of sulfite or bisulfite within mammalian plasma in vitro and vivo (Gunnison, 1971).

Sulfite added to serum was monitored by determinations of sulfite concentration in the reaction mixture. The evidence provided seemed to indicate that sulfite reacts with disulfide bonds found in plasma to form S-sulfonates. This reaction was supposedly reversible. It was proposed that the reactivity of sulfite with plasma might also facilitate the maintenance of low concentrations of sulfites in the body during very low level exposure to sulfites. Four rabbits were exposed to 23 ± 5 ppm SO_2 and their plasma was analyzed for the presence of cyanalytic sulfite before and after exposure. No free sulfite was detected, but plasma and serum S-sulfonate content seemed to increase substantially. Unfortunately very few studies have been conducted on the inhalation of various sulfites.

Mice were exposed to sulfur dioxide, sodium sulfite, and sodium metabisulfate (Alarie 1973). At 1 ppm metabisulfate had a greater effect than SO_2 on the respiratory rate. Alarie concluded that "bisulfite anion was responsible for respiratory irritation."

Exposure of guinea pigs to SO_2 plus sodium bisulfite aerosol increased their pulmonary flow resistance at 80% relative humidity. Chemical analysis of that aerosol revealed the presence of SO_2 and bisulfite (McIlton 1973).

Alarie exposed animals to mixtures of transition metal sulfite aerosols similar to those found in amibent air (Colucci, 1976). The results of these studies should be informative as to whether sulfites in the ambient air do pose a potential threat to human health.

3. Human Studies

Gunnison and Palmes measured the plasma S-sulfonate in human subjects exposed to 0.3, 1.0, 3.0, 4.2 and 6.0ppm SO_2 for periods up to 120 hours (Gunnison and Palmes, 1974). Plasma levels of S-sulfonate were positively correlated with atmospheric sulfur dioxide. From the regression line an estimated increase of 1.1 n moles of S-sulfonate per ml. of

plasma resulted from each ppm of SO_2 increase within the exposure chamber. The health effects of these S-sulfonates within the blood stream are apparently still unknown. However, these changes in protein structure may be irreversible, and may result in tissue damage. Until the effects of S-sulfonates can be determined, metal sulfites should be classified as a potential respiratory irritant.

Recently there has been some concern over the health effects of sulfur dioxide and dietary sulfites in sulfite oxidase-deficient individuals on the grounds that these individuals might be unusually vulnerable to mutagenic and other effects of sulfites and bisulfates (Hickey 1976). However, this concern does not seem to be well founded at this time. As Alarie pointed out in his rebuttal of that paper, "there is no evidence for wide-spread sulfite-oxidase deficiency in humans." Possibly the sulfite oxidizing capability in human populations should be surveyed to determine whether a significant susceptible population exists. According to Alarie if a large susceptible population existed, the dangers of sulfites are not sufficiently well-documented to be of too much concern (Alarie 1973).

More work in the area of sulfite toxicity is needed before definitive conclusions can be reached.

D. Particulates

1. Introduction

Particles, on entering the respiratory tract, follow the moving airstreams but particles also have a mobility of their own independent of air flow. This can cause them to come into contact with the walls of the airway. The motion of the particles which results in depositions is dependent on their size, shape, and density (Muir 1972).

Three mechanisms are important in the deposition of particulate matter. These are gravitational settling, diffusion, and inertia. The gravitational settling of particles is important in the deposition of large particles or particles of high density such as dusts of heavy metals on the lower surface of the airways or alveoli.

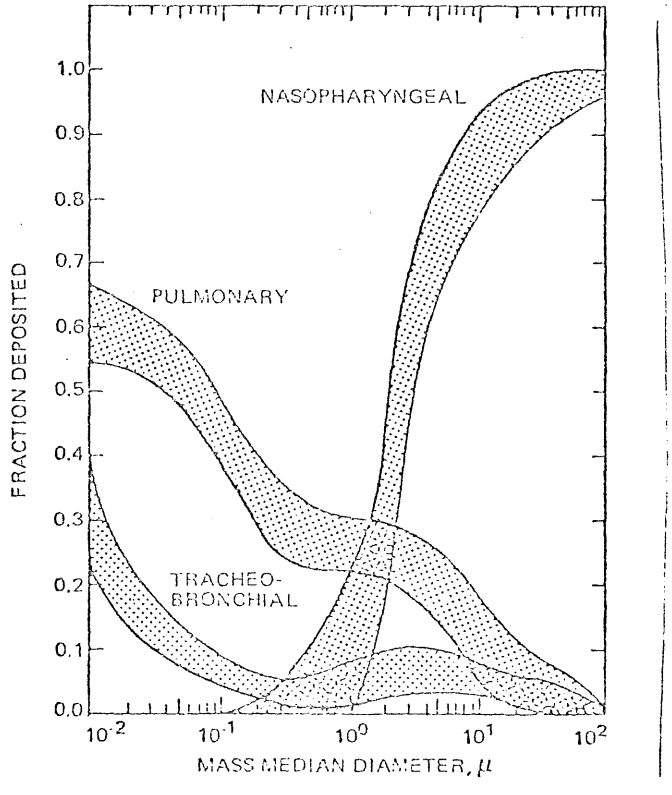
Diffusion or Brownian movement is the result of the random bobardment of the particles by air molecules. This may be a major mechanism for the deposition of small particles ($\leq$ 0.1microgms) in the lower pulmonary tract.

The third mechanism, inertia is important when the direction of the airflow changes and the particles continue to move in the original direction for a short period. Inertia is of greatest importance in the deposition of particles which are large and of high density at points in the respiratory systems where the direction of airflow changes (Air Quality Criteria, 1969)

Flow rates and gas mixing also need to be considered in the deposition of particles. Some studies have found that the inhalation of particulate matter such as sulfuric acid mist can cause a decrease in expiratory flow rates in humans Gas mixing is the exchange of new air inhaled with the residual air left in the lungs. Altshula found that nondiffusible particles greater than 0.5 microgms will move only to the depth of the new air, but smaller particles will move independently into the static lung air (Air Quality Criteria, 1969).

Figure 2 shows the relationship between particles of various mass diameters and the percent deposited in various sections of the respiratory tract.

Figure 3. Fraction of Particles Deposited in the Three Respiratory Tract Compartments as a Function of Particle Diameter.[1]



[1]Source: Air Quality Criteria, 1969

Landahl found that the nose is the major site of particle deposition. During breathing few particles greater than 20 microgms in diameter and only 50% of those 5 microgms in diameter are able to penetrate the nose (Muir, 1972). Even particles as small as one micron have been found deposited in the nose.

A very important aspect of deposition is the proportion of particles which reach the alveoli. This portion, called respirable dust, is associated with the development of pneumoconiosis. Although there has been wide disagreement on the size of particles at which alveolar deposition is at a maximum, the most frequently quoted size has been 1 micron. Some investigators have calculated the size as between 2 and 4 microns (Muir 1972). In general, particles between 1 and 2 micron have maximum efficiency of deposition whereas particles of 0.1 micron have a minimal efficiency. However if a large number of particles of this size are present they may be as important as smaller or larger particles in terms of toxicity. Furthermore, the percentage of deposition of particles less than 0.1 micron is as great as for sizes more than 1 micron. Since different clearance mechanisms of particles from the lung operate in the different areas of the respiratory tract, the area of deposition affects the rate of clearance.

Substances which are soluble are rapidly absorbed from all areas of the tract. Insoluble substances on ciliated epithelium are moved to the pharnyx and then swallowed or expectorated.

In the tracheobronchial system ciliary transport rates seem to be unaffected by the size, weight or shape of the particles. Studies of clearance in the human lung have shown that the healthy mucosa is essentially cleared in less than 24 hours.

Some studies have used aerosols tagged with a dye to follow the course of the clearance. Brieger and LaBelle showed that 24 hours after exposure 50% of the total dye in the body was found in the intestinal tract. This indicates the possible consequences of air pollutants on organs other than the lungs.

Clearance of particles from the alveolar surface is slow. After a few hours of deposition, particles are encased by macrophages. Non-toxic dusts are carried in this way to the ciliated epithelium. Experiments on humans have shown that alveolar clearance is exponential with respect to time and has a 60-120 day half life (Muir 1972).

Figure 4 presents a schematic diagram of all deposition sites and clearance processes.

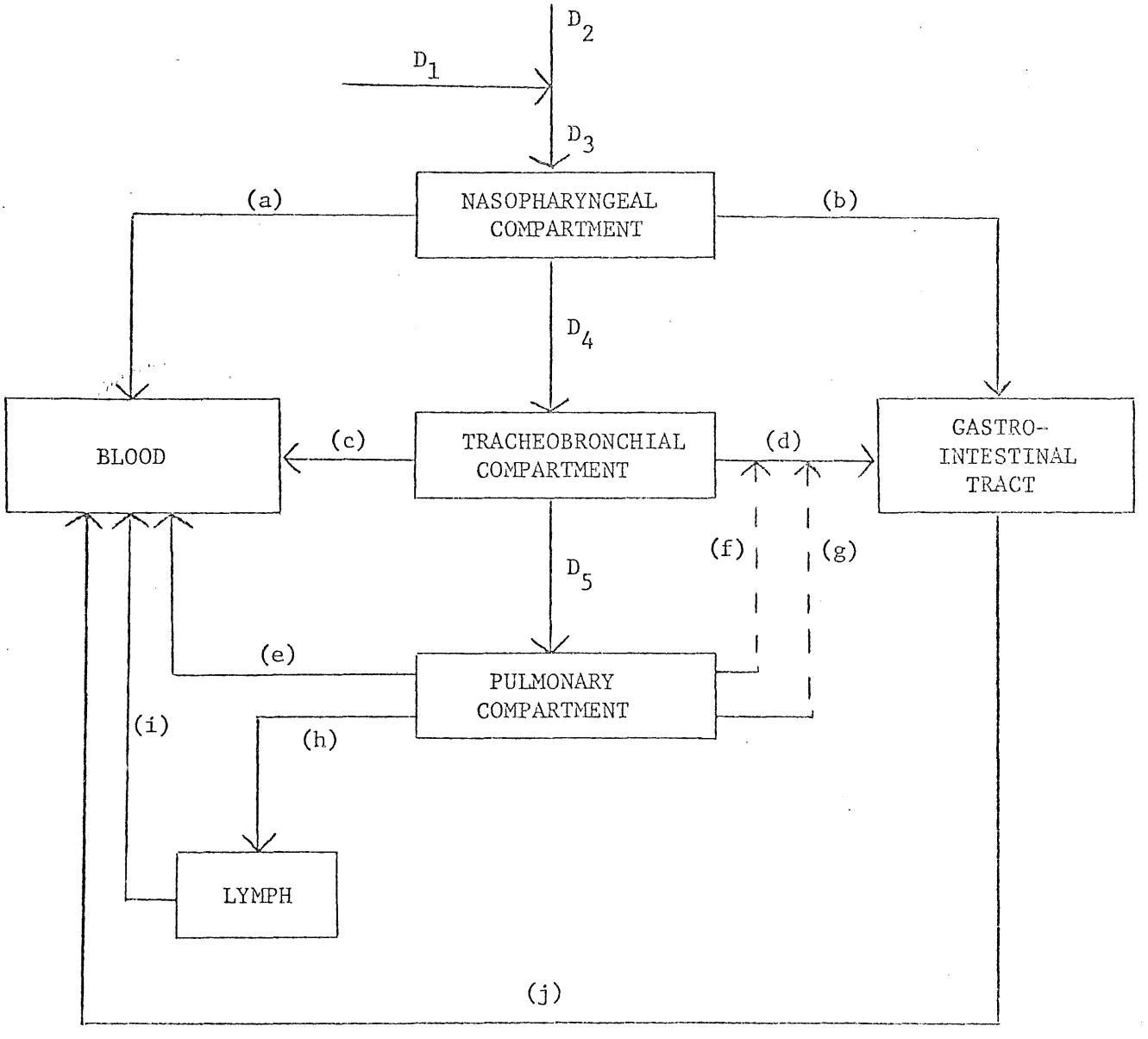
The three main areas of the respiratory system are shown. D_1 refers to inhaled particulate matter, D_2 to material in the exhaled air and D_3, D_4, and D_5 are particles deposited at the three sites. The other letters refer to the following: a.) the uptake of material from the nasopharynx directly into the bloodstream, b.) rapid movement of particulate matter from the nasopharynx by ciliary transport of mucus, c.) the rapid absorption of particles from the tracheobronchial system into the blood stream, d.) the rapid ciliary movement of tracheobronchial mucus with particles being carried to the gastrointestinal tract, e.) movement of material from the pulmonary region to the circulatory system, f.) the rapid movement of particles again dependent on macrophages and ciliary movement, g.) a second slower movement dependent on ciliary movement and phagocytic action but rate limited by the nature of the particles, h) the slow removal of particles by the lymphatic systems, i.) a continuation of pathway where particles are carried into the blood stream and j.) the absorbtion of material from the gastrointestinal tract into the blood. The models presented by the Task Group on Lung Dynamics have been shown to yield predictions which have been substantiated by experimental findings.

2. Animal Studies

a. Introduction

A vast amount of data is available from animal studies on the pathological and physiological effects of various kinds of particulates. Most of these studies centered around one specific kind of particulate such as lead, arsenic or asbestos.

Figure 4. Schematic Portrayal of Dust Deposition Sites and Clearance Processes[1]



[1]Source: Air Quality Criteria, 1969

Toxicological studies have shown that particles may be intrinsically toxic (such as lead, beryllium, and asbestos) their presence may interfere with clearance of other particles from the lungs, or they may act as a carrier of toxic materials.

Carbon, a common particulate, is an efficient adsorber of many organic and inorganic compounds. The deposition of a particle carrying a high concentration of a chemical may be more highly toxic than the absorbed chemical alone.

Some studies have dealt with the pathological effects of smoke and carbon alone on animals.

Schnurer exposed rabbits and rats to bituminous coal smoke for 80 days (Schnurer, 1937). The smoke contained an average of 125 million particles per cubic foot, 0.4 million of these were free sulfur dioxide. All the lungs examined were deeply pigmented.

These animals were shown to have developed fibrous reactions about the carbon deposits with the formation of collagen fibers. These lung changes were analagous to those found in a mild grade of bituminous pneumoconiosis of soft coal miners.

Vintinnes studied the effects of bituminous coal dust and coal smoke on the resistance of rats to lobar pneumonia (Vintinnes, 1951). The concentration of coal dust in the exposure chambers varied between 400 and 850 million dust particles per cubic foot of air. Duration of exposure to dust or smoke before injection of pneumococcus culture varied from 5 to 165 days for dust and from 2 to 154 for smoke.

The coal dust exposed animals were found to have a significantly lower infection and mortality rate than controls. In the smoke exposed group there was no consistent difference in mortality. It was concluded that the exposure to coal dust or smoke did not increase susceptibility to lobar pneumonia.

Naw studied inhallation of carbon black dust in hamsters, mice, guinea pigs, and monkeys (Naw, 1962). No significant effects were found other than the accumulation of dust in the pulmonary system.

Mice and guinea pigs exposed to smoke from a kerosene lamp survived exposures as high as 664 mg/m^3 of smoke for six hours (Salem and Cullumbine, 1961). Autopsy studies revealed no obvious damage to the lungs of these animals.

A similar study but at a lower exposure ($50mg/m^3$) found no signs of edema, hemorrhage or emphysema (Pattle and Burgess, 1963). However, pathological examination of the lungs showed soot particles spread over the lining of the bronchiolis and alveoli.

From these studies it appears that smoke or carbon black by itself produces little major damage to the respiratory system of animals at levels even greater than those found in the atmosphere.

b. Pulmonary Function

A pattern of pulmonary impairment consistent with peripheral airway obstruction was found in monkeys exposed to bituminous coal dust (Meorman, 1975). Some reduction in forced expiratory volume and maximum expiratory flow were also observed. Specific lung volumes did not differ significantly from the controls.

Aerosols of zinc ammonium sulfate caused an increase in pulmonary flow resistance in guinea pigs (Amdur and Corn, 1963). This aerosol was known to have been present at the Donora fog episode of 1948. Smaller particles were found to have greater irritant action at any given mass concentration.

Incubation of lung fragments of guinea pigs with 10 to 200 mm concentrations of ammonium ion produced the release of substantial amounts of histamine (Charles and Menzel, 1975). Sulfate ions when tested with ammonium were found most potent. An osmotic effect was discounted. The studies suggested that the irritation associated with inhalation of certain sulfate and other salts may be a function of their

ability to release histamine when ammonium ions are present.

Amdur and Underhill observed the effects of various aerosols ($Na_3UO_4MnO_2NaCL$, KCL, MnCL, NH_4SCN, Fe_2O_3, carbon, and open hearths dust) on pulmonary flow resistance in guinea pigs (Amdur and Underhill, 1968). All the aerosols studied when administered alone produced no alteration in pulmonary flow resistance. A "fly ash" mixture from an oil burner was also tested and proved to be inert. Ferric sulfate was found to be an irritant, however. A concentration of 1 mg/m^3 produced a 77% increase in flow resistance in 15 animals which was statistically significant.

In contrast to these findings Dautrebande found increased airway resistance in guinea pigs and humans with exposure to many different "inert" particulate matter (Air Quality Criteria,1969).The differences between the studies have been attributed to the much higher concentration used by Dautrebande.

Particle size may have an important role in determining the toxic effects of an irritant. In the study by Amdur and Corn as the particle size decreased from 1.4 to 0.29 microns the response to an equal mass concentration increased. A concentration of 1.4 $mg./m^3$ of zinc ammonium sulfate 0.74 microns in size resulted in a 21% increase in resistance. A concentration of 1.8 mg/m^3 at particle size of 0.3 microns produced a resistance increase of 130%.

The Air Quality Criteria for Particulate matter concluded that the main physiological effect of irritants is to increase pulmonary flow resistance, and that this response may be increased with a decrease in particle size. Furthermore, it appears that heavy amounts of inert particles can cause an increase in flow resistance.

E. Sulfur Oxides and Particulates

1. Introduction

Of importance in the toxicology of particulates is their relationship to mixtures of irritant gases. Two major factors, particle size and their inherent chemical nature, are important in determining the health effects of observed gases and particulates (Severs, 1975). Many studies have been conducted on the influence of particulate material on the toxicity of gases.

2. Animal Studies

The first experiment relating such an effect of particulates was in 1939 when it was found that mustard gas alone was harmless to rats, but could produce pulmonary edema and death when administered along with sodium chloride.

Studies since then have observed particulates with ammonia, formaldehyde, and oxides of nitrogen to mention a few. Probably the most work has been done with mixtures of particulates and SO_2.

The effect of a mixture of SO_2 and smoke on mice and guinea pigs was found to be greater than the effect of SO_2 alone (Pattle and Burgess, 1957). This was felt to be the result of an addictive effect rather than absorption of the gas on the smoke.

Salem and Cullumbine studied the effect of kerosene smoke on the toxicity of sulfuric acid, SO_2, acrolein, and acetaldehyde in guinea pigs, mice, and rabbits (Salem and Cullembine, 1961). In guinea pigs smoke was found to increase the toxicity of sulfuric acid. The toxicity of acetaldehyde and SO_2 was decreased. In mice the toxicity of SO_2 was increased. The experiment indicated that guinea pigs were more susceptible to sulfuric acid mist and that mice and rats had a higher resistance to it.

SO_2 was readily absorbed when active carbon was exposed to a concentration of 3% of the gas, thus demonstrating the physicochemical basis for a synergistic effect between SO_2 and carbon particles (Dalhamn, 1963).

In rabbits , carbon alone was not found to effect ciliary movements but the velocity of movement was significantly lower when exposure was to carbon and SO_2 at 100 ppm. This reduction was, however, similar to that found after exposure to the same concentration of SO_2 alone. A conclusion was reached that no gas-aerosol synergistic effect on ciliary movement could be demonstrated for SO_2 and aerosols at levels approximately those in urban atmospheres.

Animals exposed to low concentration of SO_2 and high concentrations of inert dust showed no difference in ciliary frequency of the tracheal mucosa when compared to control animals exposed to dust alone or clean air (Fraser, 1968).

Amdur found that NaCl, KCl, and NH_4SCN (ammonium thiocyanate) with SO_2 potentiated an increase in air flow resistance (Amdur, 1968). Insoluble aerosols were ineffective in potentiating a response. It was proposed that the potentiation effect of SO_2 was mediated by the solubility of the gas in a liquid and its oxidation to sulfuric acid. Aerosols of NaCl and of KCl would absorb water to become liquid droplets. Dry particles of carbon fly ash or manganese dioxide showed no potentiating effect.

In a study of combinations of SO_2 and open hearth dust in guinea pigs, open hearth dust alone produced no respiratory effects with concentrations as high as 7 mg/m^3 (Amdur, 1970 SO_2 at several concentrations also did not have an increased effect when combined with the dust or iron oxide fume. These results are consistent with the proposed mechanism explained above.

Alarie studied monkeys and giunea pigs exposed to mixtures of SO_2, fly ash and sulfuric acid mist (Alarie, 1973, 1975). Pulmonary function tests and hematologic and chemical analysis were also conducted. No detrimental effects could be found for long time exposures to 0.1 to 5 ppm of SO_2 alone or to 0.1 to 0.5 mg/m^3 exposures to fly ash. Also no detrimental effects were found with mixtures of SO_2 and fly ash. Exposure to

sulfuric acid mist at concentrations above 1 mg/m^3 regardless of particle size resulted in definite histopathological effects in monkeys. At concentrations of 0.1 and 1 mg/m^3 definite changes were found but to a lesser degree. The effects, mostly changes in the bronchial mucosa, noticed with exposure to mixtures of SO_2, fly ash and sulfuric acid mist were attributed to the acid mist alone.

Hamsters exposed to 40 ppm SO_2 for four hours per day for six weeks produced no histopathological changes (Asmundsson, 1973). A four hour exposure to 40 ppm SO_2 along with 0.74 g/m^3 of carbon dust produced neutrophils in the airway epithelium. The author suggested that the synergistic effect is due to the SO_2 being absorbed on carbon particles and later released, attracting leukocytes to the area.

Beagle dogs were used in an experiment to test pulmonary function after exposure to NO_2 (Lewis, 1969,1973). A 1967 study related NO_2 and particulate matter (iron oxide) to pulmonary function. A lung exposed previously to an irritant was more difficult to alter physiologically than one never exposed to toxic concentrations of pollutants. Also relatively low levels of H_2SO_4 aerosol, H_2SO_4 had the greatest toxic implications in human health. Also dogs exposed to NO_2 and iron oxide particulates were found to have significant increase in total pulmonary resistance from a control value of 1.6 to 4.0 cm H_2O/liter/second.

A study of the effects of SO_2 and dust on the microflora of the respiratory system used rats exposed to 1 ppm SO_2 and 1 mg/m^3 of dust for 12 hours a day for four consecutive months (Battigelli, 1969). A second group was exposed to graphite dust alone. Monitoring of the surface microflora from the turbinates, stem bronchi and from lung homogenates was carried out. No meaningful differences could be distinguished between the two exposed groups and the control group. There were no trends which were consistent with an effect of SO_2.

Mice exposed to carbon alone (500 - 600 mg/m^3) or with SO_2 were found to have a decrease in the antibody formation ability (Zarhower, 1972). Exposure to 2.00 ppm SO_2 for 192 days was associated with decreased antibody formation.

At 135 days of exposure an inrease in antibody production occurred in the spleen after exposure to SO_2 alone. This activity decreased by 192 days but it supported the idea that SO_2 under certain exposure conditions can have an adjuvant effect.

In a study of the effects of corn dust, corn starch, and SO_2 on swine, no clinical or pathological changes were found in piglets exposed to corn starch alone (Martin, 1973). However, the combination of the dust with SO_2 produced symptoms similar to those found with SO_2 alone. Clinical changes included ocular or nasal irritation and increased salivation. Histologically the changes in the epithelium of the turbinates and bronchi included loss of cilia, disappearance of goblet cells and alteration of cell type. There were no changes in the respiratory area of the lung attributable to SO_2 or dust.

McFilton conducted an experiment on the role of relative humidity on the synergistic effect of SO_2 and aerosols (McFilton, 1973). Relative humidity was found to be an important variable for aerosols capable of absorbing water at relative humidities below 95%.

The various animal studies have shown that there is a wide variation of response in different animals of the same species. This therefore is an important factor in interpreting the various studies.

From the animal studies cited it can be concluded that small particles probably do play an important part in either a synergistic or additive manner on the effects noted from various mixtures of gases and particles.

The role of POM in producing human skin cancer from occupational exposure is well established. However, POM do not appear to significantly influence the pathogenesis of

non-neoplastic lung diseases like emphysema and chronic bronchitis.

Stenbach observed the carcinogenic effects on hamsters of benzo(a)pyrene alone or in combination with dusts of titanium dioxide, aluminum oxide, carbon or ferric oxide (Stenback, 1976). Dusts administered alone resulted in interstitial cell proliferation, bronchial epithelial alterations, and a few granulomatous changes but no tumors. B(a)P alone induced two tracheal papillomas but in combination with dusts a number of tumors were induced depending on the dust.

Asahima injected mice with suspensions of an organic extract of particulate atmospheric pollutants as well as oxyneutral subfraction and acidic, basic, neutral, aliphatic, aromatic, and insoluble fractions (Asahima, 1972). Results showed wide variations in carcinogenicity and the incidence of tumors in various organs in different test groups.

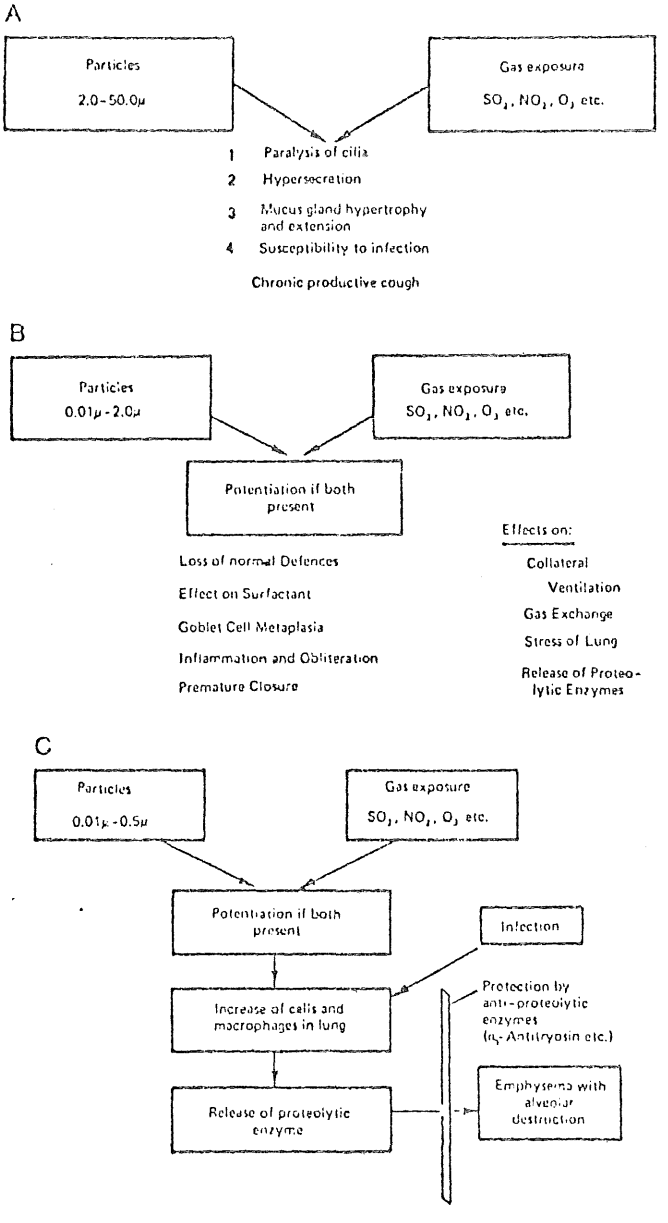
Saffiotti produced malignant tumors in hamsters by intratracheal instillation of a suspension of B(a)P with hematite as a carrier. These lung tumors were similar to those found in human cancers. (Air Quality Criteria, 1969)

There was an increase in the action of the carcinogen which resulted from its adherence to fine particulate matter. In this form it is carried deep into the lung and released.

A study by Kuschner demonstrated that inhalation of B(a)P in the presence of SO_2 caused the development of bronchogenic squamous cell carcinoma. However neither B(a)P or SO_2 alone caused the development of tumors. (Air Quality Criteria, 1969)

The effects of various gases and particles on major lung areas are shown in Figure 5 .

Figure 5. (A) Effect of irritants in major bronchi; (B) effects of irritants in terminal bronchioles; (C) effect of irritants in alveoli.



3. Human Studies

Few experiments have been conducted on the effect of combined pollutants on man.

Toyama in a study of 13 healthy male adults exposed to SO_2 and NaCl separately and in combination found that NaCl aerosol had no effect on pulmonary flow resistance when administered for five minutes (Yoyama, 1964). SO_2 alone caused changes in resistance proportional to the exposure concentration. Resistance increased 5% at 1.6-5 ppm SO_2 and 50% at 56 ppm SO_2. SO_2 and NaCl were administered together five minutes after pulmonary flow returned to control values. Pulmonary flow resistance was found to increase 20% above that observed for SO_2alone.

Healthy males in Japan inhaled SO_2 and dust in order to measure airway resistance. Recovery times were quite variable ranging from 30 minutes to two hours. Upon recovery, subjects were exposed to 3-40 ppm SO_2 for five minutes. Finally, upon recovery from that exposure, subjects were exposed to a mixture of the two pollutants in the same concentrations for an unspecified amount of time. Results indicated that bronchial response was largely dependent on individual susceptibility. However, synergistic action between the dust and sulfur dioxide increased resistance.

Snell exposed nine subjects to SO_2, NaCl aerosol, distilled water aerosol, and to SO_2 aerosol mixtures (Snell, 1969). When subjects received SO_2 and saline aerosol no significant decreases in flow rates occurred at any of the levels of SO_2. A combination of SO_2 and distilled water aerosol significantly decreased flow rates only at 5 ppm SO_2. Examination of the particle sizes revealed that sonic generation of the distilled water produced particles in the area of 0.3 mm. Saline aerosol on the other hand had the greatest number of particles between 6 and 8 mm. This would apparently account for the discrepency between this study and Amdur's, where a synergistic effect of

SO_2 and saline aerosol was found at a particle size of 0.04 mm but not at 2.5 mm.

The ability of the two aerosols to produce changes in pulmonary resistance seemed to be related more to particle size than to chemical reaction. A comparison of nasal and mouth inhalation of SO_2 showed that a drop in MEF 50% VC occurred virtually only during inhalation of the dry gas through the mouth. The inhalation of SO_2 water aerosol combination through the nose, resulted in an increase in total respirtory conductance and a drop in flow rates only slightly less than that observed during inhalation through the mouth.

Burton, studied 10 healthy male volunteers ages 25-34 with no previous history of significant cardiopulmonary disease (Burton, 1969.) Pulmonary flow resistance, airway resistance and thoracic gas volume were measured. The subjects were used as their own controls by obtaining baseline data after breathing warmed, humidified, medical grade air. The subjects were exposed to SO_2 - NaCl aerosol mixture. The concentration of SO_2 was 3.0 ppm. No significant increases were found for the measured pulmonary function factors after exposure to SO_2 alone or SO_2 aerosol mixtures when compared to individual or mean group controls. These findings confirmed those of Frank. Toyama's use of industrial dusts may have been more irritant than the NaCl aerosol accounting for the response found between SO_2 and dust in that study. No gas-aerosol synergism could be demonstrated for SO_2 and NaCl aerosol at levels approximating those in urban atmospheres. These findings are in contrast to those in animal studies (Amdur, 1968, 1970.)

Hazucha studied the effect of SO_2, O_3, and a SO_2 - O_3 mixture on light 18 - 25 year old normal non-smoking males during light exercise (Hazucha, 1975). Pulmonary function tests were made at 30 minute intervals, consisting of 15 minute exercise periods on a bicycle ergometer and 15 minutes of rest, over a two hour period. A concentration of 0.37 ppm ozone produced a barely significant decrease in maximal mid-expiratory flow

rate (MMFR) at the end of two hours. SO_2 alone at a concentration of 0.37 ppm produced no significant effect on pulmonary function. The SO_2 - ozone mixture produced a greater decrease in pulmonary function than either gas alone.

In an attempt to discover the source of eye irritation caused by Los Angeles smog, Cadle exposed 25 staff members of the Stanford Research Institute to an artificial smog containing all the major constituents of that smog (Cadle, 1951). It was found that removal of all the gaseous components eliminated the eye irritating action of the artificial smog, while removal of all particulate constitutents had no such effect. No single constituent of the artificial smog was found to be responsible for all irritating action. These results are only suggestive of what might be true in the smog of Los Angeles.

Epidemiologic Studies

A. Introduction

Epidemiologic studies have been used to set the primary air standards for levels of sulfur dioxide and particulates permissible in the atmosphere and within occupational settings. Unfortunately these studies are often difficult to interpret due to differences in aerometric measurements and meteorological aspects that have not been considered. The main difficulties are briefly outlined in the next two sections.

B. Problems in Interpretation

1. Meteorologic Effects

The relationship between pollutants and health may be confounded by various meteorologic factors. Goldstein in a review paper emphasized the significant effect of weather on health (Goldstein, 1972). Oechi and Buechley demonstrated that periods of hot weather can have a marked effect on mortality in the absence of high levels of pollution (Goldstein, 1972). Tromp separated the effects of weather and pollution (allergens) and found that strong atmospheric cooling was the major triggering factor in the causation of asthma attacks. (Tromp, 1968).

Because of the strong correlation between air pollution and meteorologic factors it is difficult to separate their effects. The level of pollution depends on the amount of pollutants emitted and the rate of dissemination of these pollutants through the atmosphere. Both of these are greatly influenced by weather. In nonindustrial areas the weather influences the need for coal consumption for heating homes and businesses. Thus, in a rather complex way the amount emitted depends to some extent on the prevailing weather. The rate of dissemination of pollutants is more readily apparent since weather influences atmospheric reactions. In addition, wind velocity, barometric pressure, precipitation, and atmospheric stability affect the length of time pollutants remain in an area.

There is great need to consider meteorologic factors in epidemiologic studies investigating the health effects of air pollution. Unfortunately few studies have considered these factors and those that have generally had a difficult time separating the effects of weather from air pollution.

2. Aerometric Effects

Reliable interpretation of epidemiologic studies is impeded by the fact that few of these are based on accurate aerometric data. Often they rely on parameters such as dustfall, smoke shade, coal consumption or, at best, simply sulfur dioxide and particulates. Only in fairly recent studies conducted by CHESS has any attempt been made to measure sulfates (CHESS, 1974). Since other pollutants are often associated with sulfur dioxide in the atmosphere, it is possible that health effects attributed to SO_2 may be due to exposure to some other agents. Particulate matter has often been considered in regard to interaction that may occur with sulfur dioxide. However, particulate matter is not a single entity, but rather a potpourri of several agents including sulfur oxides such as sulfates and sulfuric acid. Sulfates alone can comprise 5 to 20 per cent of suspended particulate matter. In addition, different cations are associated with the "sulfate" complex. Another factor that must be considered is that SO_2 is a precursor to these chemical substances that contribute to the particulate loading of the atmosphere. Therefore, it is important in epidemiologic studies to measure carefully these various sulfur oxides.

In epidemiologic studies investigating the effects of air pollution on health some determination of pollutant exposure is always made. In earlier studies a simple index of "clean vs. dirty" was often all that was given. As measurement of specific pollutants became more important, a variety of techniques were implemented. The pollutants that first became of any interest were sulfur dioxide and smoke. Accordingly these were the only pollutants for which measuring techniques were developed. Recent concern for other sulfur oxides has sparked interest in developing more accurate techniques for the measurement of other sulfur oxides and particulates. Since the technique used affects the concentration of pollutant obtained, the measurement techniques that have been employed will be discussed briefly in terms of those commonly used and their comparative reliability.

The measurement of sulfur oxides in the atmosphere appears to be almost as challenging as atmospheric chemistry itself. Of the three sulfur oxides generally implicated in producing effects on health (sulfur dioxide, sulfates and sulfuric acid) only sulfur dioxide seems to be measured with very reliable methods. An in-depth discussion of various

methods used can be found in Air Quality Criteria for Sulfur Oxides (1968). Since different methods are used with various sampling techniques among the countries and sometimes within countries, comparisons of actual sulfur dioxide levels are virtually impossible.

In the United States the two methods most commonly used to measure SO_2 are the West-Gaeke (colormetric: pererosaniline) and the conductometric methods. The former method is specific for sulfur dioxide and sulfite salts. This method has also been reported to be the most satisfactory for intermittent and continuous sampling (Air Quality Criteria 1975). Apparently, conductometric methods are affected by other pollutants present in the atmosphere; therefore, the results are sometimes very approximate.

In Europe, the method most often used in the hydrogen peroxide approach; however, the presence of other gases in the sample may give erroneous results.

A widely used technique, called the lead peroxide candle, measures "sulfation rate." The measurements are given in milligrams of sulfur trioxide per 100 cm^2 of exposed lead peroxide candle surface per day (mg SO_2/100 cm^2/day). This method has a great many difficulties associated with it and, therefore, is only a rough indication of sulfur dioxide concentration.

Other techniques for measuring sulfur dioxide are being devised and warrant careful consideration.

Most epidemiologic studies on the health effects of air pollution have used one of two methods to measure particulates. In the United States a high-volume sampler has been the preferred method. Europeans, on the other hand, have generally used a procedure which depends on the darkness of the material on the filter paper, referred to as smoke. Although both are reported in micrograms per cubic meter ($\mu g/m^3$) of air, total suspended particle concentrations tend to be about 1.5 - 2.5 times higher than smoke shade concentrations when the same air is tested (Commins and Weller, 1967).

Of the two methods, measurement of the total-suspended particles appears to be more accurate as it does not depend on the color of the particles. In terms of determining health effects, both methods have serious limitations. These methods measure all particulates, while

only those about 1 - 2 μ in diameter can penetrate deeply into the lung (Air Quality Particulates 1969). Furthermore, exact composition of the particles might be important in the production of respiratory tract damage but these methods fail to give any indication of these possible effects. Basically, these procedures only indirectly measure particles in polluted air which are injurious to health.

The method of measuring particulates often determines how particle size is reported. At the present time there are no standardized techniques for sizing and sampling of particulates, so that much data on particulate size is difficult to assess (Fennelly, 1976). In the Air Quality Criteria for Particulate Matter (1969) size refers to particulat diameter or Stokes diameter.

One important group of particulates (sulfates) provides a good example of the difficulties which arise in measuring specific compounds. First of all, there is the possibility that a portion of the sulfates detected in particle traps actually result from the reaction of sulfur dioxide with the trapping material. The concentration of sulfates obtained also may depend on the sampling volume.

The operational definition of sulfates is "material collected on a high volume sample filter and analyzed as water soluble sulfates". Measurement of sulfates with this method not only may be inaccurate, but factors that appear important in the biological activity of sulfates such as chemical structure, acidity, and particle size cannot be measured by this method. Although sulfates are principally derived from sulfur dioxide, the sulfate concentration is not always correlated with sulfur dioxide. Other factors such as long range transport seem to be involved and need to be considered. There appears to be considerable controversy on whether "water soluble sulfates" is even a worthwhile group of compounds to measure. The Environmental Protection Agency is in the process of finalizing a 5 year research plan on sulfates, investigating the health effects, ecological effects, atmospheric chemistry and transport, and measurement methodology and instrumentation. The primary objective of this research will be to determine whether regulatory action on selected sulfates is warranted (Lee, 1976).

A great deal of work needs to be done in the area of standardizing sulfate measurements. This is particularly true now that sulfates are believed to play an important role in effects on health once attributed only to sulfur dioxide.

As far as communitity studies on air pollution are concerned, sulfuric acid has never been measured. As Rall stated, "sampling and analysis of atmospheric sulfuric acid can most optimistically be described as in the development stage" (Rall, 1974).

To sum up briefly what needs to be done in the area of determining the concentration of various sulfur oxides in the atmosphere for epidemiologic studies, 3 areas require attention of researchers: 1) standardization of sulfate measurements, 2) analysis of various sulfates present, and 3) analysis of atmospheric sulfuric acid. In order to understand fully the relationship of ambient sulfate levels to health effects, the processes by which they are produced and their relationship to sulfur dioxide sources also need consideration (Rall, 1974).

C. Acute Exposures

Several acute exposures have focused attention on the effects of air pollution on human health. The first well-studied episode occurred during a fog on December 1, 1930 along the valley of the Meuse River in Belgium (Goldsmith, 1968). Several hundred people became ill and 63 died over a five-day period. It was estimated that sufficient quantities of SO_2 and sulferic acid were present to cause the incident, although no measurements were made during the episode. Roholm suggested that fluorides might be the cause of the episode, but it is generally felt that a combination of pollutants was involved (Roholm, 1937).

Two other episodes are also widely discussed in the literature, on in Donora in 1948 and the other in London in 1952.

The fog which occurred in Donora, Pennsylvania caused 43% of the population (14,000) to become ill and resulted in 20 deaths (Schrenk, 1949). No single substance was found responsible, but SO_2 along with its oxidation products and particulate matter were considered significant contaminants.

Then in December 1952, a 4-day fog caused over 4,000 excess deaths in the Greater London area (Logan, 1953). Air pollution measurements had been made during the episode. The highest values reached were 4.46 $\mu g/m^3$ for smoke and 1.34 ppm for sulfur dioxide (Scott, 1953). The Greater London area experienced several air pollution episodes before and after 1952 but none has come close to causing 4,000 excess deaths (Ministry of Health, 1956).

These three episodes have certain characteristics in common. Each occurred during anticyclonic weather accompanied by fog and a temperature inversion, which led to a buildup of pollutants (particulates, mostly carbon and iron dust, and various gases) and an increase in morbidity and mortality particularly from cardiac and respiratory causes.

Ashe compared these three episodes and also considered episodes in Cincinnati (1949), Poza Rica, Mexico (1950), Gallipolis Ferry, West Virginia (1955-56), and Los Angeles smogs (Ashe, 1959). He concluded that the weather made air pollution particularly hazardous.

Before 1952, other fogs in London: 1873, 1880, 1882, 1891, and 1892, had been associated with increases in mortality (Ministry of Health, 1954). These were all associated with cool temperatures, but no pollution measurements had been made. It was the episode in 1952 that stimulated the interest in looking at air pollution and its possible effects on health. Therefore, during subsequent though less severe episodes, pollution data were collected for analysis. Gore and Shaddick and Burgess and Shaddick described investigations using daily mortality figures for the county of London for a series of "fogs" episodes during 1954-1957 (Gore and Shaddick, 1958; Burgess and Shaddick, 1959). To reduce the effects of chance fluctuations, seven-day moving averages of the number of deaths were used. Seven recording stations furnished the necessary pollution data. Critical levels of 2,000$\mu g/m^3$ of smoke and 0.4 ppm (1,144$\mu g/m^3$) SO_2 or about 4 times the customary winter level of pollution were determined above which a marked number of excess deaths would occur. Scott observed a similar relationship during subsequent fogs in London (Scott, 1958, 1959, 1963).

Waller noted that patients with chronic bronchitis and emphysema in London were adversely affected by high levels of pollution during a fog episode in the winter of 1954-55 (Waller, 1955; 1957). No specific pollutant was held responsible.

Bradley, et. al. investigated a fog in December, 1957 which was estimated to have caused between 800 and 1,000 deaths (Bradley, 1958). They noticed increases in deaths and cases of sickness before the atmospheric pollution had reached levels considered to be seriously high. These results seemed to indicate that lower levels of pollution were causing deaths.

In an attempt to determine to what degree relatively minor fog incidents were accompanied by increases in mortality, Martin and Bradley investigated the fogs during the winter of 1958-1959 (Martin and Bradley, 1960). A considerable number of fogs occurred where small increases in pollution were found to be accompanied by increases in daily deaths. A significant positive association between black suspended matter and daily number of deaths was found. A slightly less significant association was found between SO_2 concentrations and deaths. This was in keeping with evidence that black suspended matter had played a more prominent role in increasing mortality (Scott, 1958, 1959; Burgess and Shaddick, 1959).

When these data were considered along with data from the winter of 1959-1960, Martin concluded that it would be too difficult to determine a "threshold value below which levels of air pollution would be considered safe" (Martin, 1966). The lowest levels considered were $500 \mu g/m^3$ of smoke and $409 \mu g/m^3$ of SO_2.

Greenburg studied mortality during an episode in New York City in November, 1953, in which excess deaths were related to concentrations of sulfer dioxide and suspended particulates (Greenburg, 1962a). An analysis of clinic visits of children and adults during this episode revealed an increase in upper respiratory illness and cardiac visits. However, no effects of air pollution on the number of asthma clinic visits were observed in the 4 hospitals studied (Greenburg, 1962b).

During a later episode in 1962, Greenburg did not detect any excess deaths or increases in visits to emergency clinics for upper respiratory complaints, asthma, or cardiac conditions (Greenburg, 1963). A significant increase in visits for upper respiratory infections did occur at four homes for the aged during this period.

However, in McCarroll and Bradley's study of this same episode, a comparison of 24-hour average levels of pollutants with New York City mortality figures (using a 15-day moving average) showed excess deaths occurring on December 1 (McCarroll and Bradley, 1966). These deaths followed a daily average sulfer dioxide concentration of 0.72 ppm and smoke shade in excess of 6coh units during a period of atmospheric inversion and low ground-wind speed.

McCarroll followed daily deaths in New York City for a three year period and found periodic peaks in mortality associated with periods of high pollution (McCarroll, 1966, 1967a). Characteristically these episodes had an effect on death rates in ages 45-64 and in those over 65. McCarroll concluded, "If these excess deaths are related to air pollution the mechanism is probably protean and pervasive, affecting the course of a variety of different diseases through a basic physiologic effect" (McCarroll, 1967b).

In 1967 Glasser published a study on the New York City air pollution episode of November 23-25, 1966 (Glasser, 1967). Unusually high levels of SO_2 and smoke were present during this period. The highest level of SO_2 (1.02 ppm) and smoke (8.2 CLHS/1000 ft.) were found on the third day of the episode. Four different control periods were used to compare mortality data: 1) the 2½ weeks preceding the episode, 2) the five day period following the episode, 3) the previous five years corresponding to the period preceding the episode and 4) the previous five years corresponding to the week of the episode. For the control periods the average number of daily deaths ranged from 233.9 to 238.3 with the episode week having a range of 257.3 to 266.0. The average number of daily deaths during the week of the episode for those under 45 years was 3.9 more than all control periods combined. For ages 45-64 and 65 and over the excess was 5.0 and 15.2 respectively. The temperature during the episode was 18°F above normal but it was concluded that with the exception of mortality due to vascular lesions of the central nervous system temperature could not account for the increased deaths. Emergency visits to hospitals for bronchitis and asthma were increased on the third day of the episode in three of seven hospitals studied.

Greenburg studied another acute air pollution incident in New York City from January 29 to February 12, 1963 (Greenburg, 1967). On 73% of these days the SO_2 level was 0.40 ppm or higher with an average hourly reading on one day of 1.50 ppm which remained for four hours. During January and February 1963 there was widespread infection of the population with Asian influenza. This time period was also among the coldest of the decade. Eight hundred and nine

excess deaths occurred during the study period compared to control periods. Chi square calculation revealed a statistically significant increase ($p \leq 0.01$) in deaths due to influenza-pneumonia, vascular lesions of the central nervous system, diseases of the heart, and "all others" in age groups 45-64 and over 65 compared to control years. Three estimates were obtained of the number of excess deaths due to air pollution alone after controlling for temperatures and the effects of influenza. These were 195, 345 and 405 and were obtained by using three different control periods in the comparison.

Other acute episodes have been studied in terms of mortality and morbidity. These are reviewed by Goldberg and the Air Quality Criteria Reports (Goldberg, 1962; Air Quality Criteria, 1969).

Overall there appears to be ample evidence to conclude that usually high levels of pollution increases mortality and morbidity, especially among the elderly and those people with obstructive lung disease or cardiac disease.

A summary of these studies is presented in Table 8.

TABLE 8

EPIDEMIOLOGIC STUDIES ON THE EFFECT OF ACUTE POLLUTION EPISODES ON MORTALITY[1]

Mortality Increases Due to Acute Episodes (hourly or peak):

Date	Authors	Location/Episode Date	Substance and Concentration	Deaths Attributed to Episode	Observations/Comments
1962	Greenburg, et al	New York City Nov. 1955	Maximum ½ hour value: .86 ppm SO_2, average daily value: probably .15 - .2 ppm SO_2		Excess deaths related to elevated concentrations of SO_2 abd TSP.
1960	U.S. and Canada Joint Commission	Detroit Sept. 1952	TSP: rose above 200 $\mu g/m^3$. Maximum (instantaneous) SO_2: 1 ppm		Rise in infant mortality and deaths in cancer patients during 3-day period
1954	Wilkins, E.T.	London, smog 1952	Maximum daily concentration (in 2 successive days): 1.34 ppm SO_2, 36 cohs smoke.**	4,000 excess deaths (some among infants <1 yr.)	Elderly and people with preexisting pulmonary an cardiac diseases were mo susceptible.
1931	Firket, J.	Meuse Valley, Belgium Dec. 1-5, 1930	SO_2: peaked at 9 ppm, and H_2SO_4	63 deaths	Many people ill with respiratory symptoms.

Mortality Increases Due to Acute Episodes (Maximum 24-hour or daily mean):

1973	Lebowitz, et al	Tokyo 1968-69	SO_2 and particulates	Excess mortalities	SO_2 contributes to exces mortalities independent of weather
1967	Glasser, et al	New York City Nov. 23-25, 1966	SO_2: 0.41-0.41 ppm (24 hour), 1.02 ppm (peak hourly)		
1967	Brasser, et al	Rotterdam, Netherlands	SO_2: 0.11 - 0.19 ppm (24 hr.)	Excess deaths	Only some indication tha excess mortalities occur beyond this mean 24-hour SO_2 value
1965	Watanabe, H.	Osaka, Japan Dec. 1962	SO_2>0.1 ppm, TSP: 1,000 $\mu g/m^3$	Excess deaths	
1963	Lawther, P.J.	London 1958-59	SO_2: 0.25 ppm. Smoke: 6 cohs (750 $\mu g/m^3$)	Excess deaths	

1963	Greenburg, et al	New York City Dec. 1, 1962	SO_2: 0.72 ppm. Heavy smoke	Excess mortalities	Assumed a 3-day time la between pollution episo and observed increased mortality. Was a stati tically significant relationship between increased air pollution and mortality
1963	Greenburg, et al	New York City Jan 7, 1963	SO_2: 0.6 ppm. Heavy smoke	No increased mortality	
1962	Greenburg, et al	New York City 1953	SO_2: 0.15 - 0.2 ppm. Heavy smoke		
1960	Martin, Bradley	London 1958-60	SO_2: 0.14 ppm, Smoke: 4 cohs (500 $\mu g/m^3$)		Lowest SO_2, and smoke levels which elicited a response
1958, 1959, 1963	Gore, Burgess, Shaddick, Scott	London, acute fog 1954-59	SO_2: 4 ppm. Black suspended matter: 16 cohs (2,000 $\mu g/m^3$). (100) Smoke (1956, 1959): 9.6 cohs (1,200 $\mu g/m^3$). SO_2 (1959): 0.3 ppm	Excess mortalities	(120) For London incide SO_2 concentrations corr late with excess mortal ties

**125 $\mu g/m^3$ = 1 coh (coefficient of haze)

[1]Source: Colucci, A.V., Sulfur Oxides: Current Status of Knowledge, EPRI EA-316, Dec. 1976

ADDITIONAL EPIDEMIOLOGIC STUDIES ON THE EFFECTS OF ACUTE POLLUTION EPISODES ON MORTALITY

Source	Population	Method	Suspended Particulates	Smoke	SO_2	Other	Conclusions
Glasser 1967	Avg. daily mortality all ages, male and female Control periods 233.9-238.3/day week of episode 257.3-266.0/day	Examined both mortality and morbidity in relation to air pollution episode in New York City Nov. 23-25, 1966 Also used as controls: 1) 2½ week period before episode 2) 5 day period following episode 3) 5 year period previous to episode corresponding to week of episode 4) previous 5 years corresponding to week before episode	not stated	Range of mean levels 1.3-6.1 COHS 1000 ft. min. level range 0.5-4.0 COHS 1000 ft. max. level Range 2.3-8.2 COHS 1000 ft. measured bi-hourly	Range of mean levels 0.10-0.51 ppm min. level range 0.02-0.30 ppm max. level range 0.28-1.02 ppm hourly measurements	None	Mortality increased to higher than expected leve and remained for seven days. Average of 24 more deaths per day found in comparison to control periods with a total of 168 excess deaths. The excess mortality increase with increasing age. Morbidity was measured by clinic emergency visit for bronchitis and asthma There was an increased number of visits on the 3rd day of the episode in patients age 45 and over in three of the seve hospitals checked.
Green-burg 1967	4,596 deaths during period studied (306 per day) All causes	Jan. - Feb. 1963 High air pollution episode New York City reviewed and compared with control years prior and following episode in relation to mortality. Other stresses such as cold and epidemic diseases also present. Controls used were: 1) days before & after episode 2) similar period during 1958 3) days prior & subsequent to	not stated	Jan. 29 - Feb. 12 47% of days had level of 4COH units or more daily avg.	Jan. 29 - Feb. 12 73% of daily levels were 0.40 ppm or higher daily avg.	none	An estimated 200 - 400 excess deaths attributed to air pollution alone after controlling for temperature and influenza. Increase in mortality for older age groups (45 and over) and fo the causes influenza - pneumoni vascular lesions, cardiac & "all others". No significant increase in deat of early infancy (<28 days) and no excess deaths in childre

D. Chronic Exposures

1. Mortality Studies

Mortality studies have most frequently been utilized in examining the effects of air pollution on human populations. As previously mentioned, it was the observation that increased numbers of deaths occurred during air pollution episodes that brought attention to the fact that air pollution posed a threat to health. The continued use of mortality data is due, in part, to their easy accessibility. Mortality studies also tend to be relatively inexpensive and less time consuming than morbidity studies.

Along with these advantages come certain problems inherent in all mortality studies. First and foremost is the fact that mortality data provide rather crude measurements as they represent the final results of ill health. Furthermore, certifications of death, upon which most mortality studies are based, are not always reliable particularly for selected entities and may not reflect the contribution of air pollution. The extent to which chronic respiratory diseases are listed as the cause of death, or as an underlying cause, depends to some extent on the familiarity of the physician with the patient's medical history and the local medical usage. Death certificates may also be filed in the place where the person lived at the time of his death rather than the place he lived most of his life, thus making comparisons between mortality and local pollution levels misleading.

In using mortality data to assess effects of pollution levels exact exposure levels are impossible to obtain. Investigators have often used measurements of pollutants, typically sulfur dioxide and smoke, over one year to determine the relative exposure levels of several groups under study. Since areas which are high in air pollution usually remain high due to the stability of pollution sources, this method appears to be an adequate means of

determining gradients of exposure among population groups. However, caution must be used in interpreting these studies as air pollution measurements are not likely to be representative of the true lifetime exposure. Furthermore, dose relationships derived from them may not be tenable. Therefore, in evaluating studies in this particular area, it seems best to look at general trends that have been verified by repeated studies. Hechter has addressed a number of the problems encountered in the use of mortality data for studying air pollution effects (Hechter, 1961). He found that various environmental factors exhibited distinct seasonal patterns plus irregular oscillations in his study of daily cardiac and respiratory deaths in Los Angeles County from 1956 to 1958. The seasonal component was removed by a technique known as harmonic analysis. No influence of daily air pollution levels as measured by oxidant levels and carbon monoxide on day to day mortality could be found when correlation analyses were performed.

For the years 1950-1952, Pemberton and Goldberg found significant correlations between sulfur dioxide, as measured by sulfation rates and deaths from bronchitis in men age 45 and over in the county boroughs of England and Wales (Pemberton and Goldberg, 1957). A similar association was noted in women in two of the six sets of data. Using pollution exposure based on domestic coal consumption over the same time period in England and Wales, Daly found that the same positive correlation existed between exposure to high pollution levels and death from bronchitis in men aged 45 to 64 years (Daly, 1959). After adjustment for differences in social class and overcrowding the correlation still existed but was lower than before. Daly found that deaths from pneumonia and bronchitis in women also correlated with pollution as measured by domestic coal consumption. When mortality rates for bronchitis were compared with total

coal consumption, the correlation was very weak (r = .24). No explanation was offered.

Bronchitis mortality has also been associated with deposit and smoke in the country boroughs of England and Wales even after adjustment for population density (Stocks, 1959). In an evaluation of a smaller area, Stocks found bronchitis mortality to be significantly correlated with dust deposit but not with smoke. The opposite was true for lung cancer.

The pH of winter precipitation has been found to be strongly inversely related to bronchitis mortality in England, Scotland, and Wales (Gorham, 1958, 1959). The winter sulfation rate was also significantly correlated with bronchitis mortality, but the correlation was smaller than that found with pH of winter precipitation.

A 15-fold excess of mortality from bronchitis was recorded in England and Wales when compared with that in Denmark. Both countries used the same classification system (ICD) for causes of death on certification. When cigarette smoking was considered, it accounted for approximately half of the difference. Apparently age distribution, social class, climate and pollution were not important factors. According to Christenson, there is a real difference in mortality that requires further study (Christenson, 1958).

In their study of postal workers in the United Kingdom, Fairbairn and Reid found that bronchitis mortality and morbidity were related to the frequency of fog as measured by percent of occasions on which an object at 1,000 yards was invisible (Fairburn and Reid, 1958). No relationship of lung cancer deaths to fog or to domestic crowding was found. A strong relationship between lung cancer and population density was noted, however.

Higher lung cancer rates found in migrants from the United Kingdom to New Zealand and to South Africa compared to the British population born in those countries, point to a possible effect of air pollution (Eastcott, 1956; Dean, 1959), but adequate comparative data on smoking were not available.

According to Goldsmith, many studies have found that lung cancer deaths are more frequent in cities than in rural areas (Goldsmith, 1969). A 20% excess mortality in urban areas has been observed even when only non-smokers are considered.

Haenszel found that the effects of residence and smoking were synergistic with respect to lung cancer (Haenszel, 1962). Smokers residing in urban areas had a greater rate of lung cancer than would be expected from simply adding the individual effects of residence and smoking.

Few studies relating lung cancer mortality to measured air pollution levels have been attempted. Buck and Brown compared standardized mortality ratios for the years 1955-59 with smoke and SO_2 measured in March 1962 for 219 areas of the United Kingdom (Buck and Brown, 1964). In general, they found no association of lung cancer mortality with smoke and SO_2 levels.

Lung cancer mortality has been correlated with various indices of air pollution such as smoke deposit, 1:12 benzperylene, 3:4 benzopyrenel domestic pollution based on fuel consumption and areas considered more polluted due to high levels of smoke and sulfur dioxide (Stocks, 1958, 1959, 1960; Daly, 1959; Pemberton, 1961; Burn and Pemberton, 1963). Several investigators have also found a positive association between lung cancer mortality and population density (Fairbairn and Reid, 1958; Stocks, 1958; Buck and Brown, 1964). In none of these was there control on tobacco use. In an earlier study conducted with nonsmokers, Doll found no such effect on lung cancer mortality (Doll, 1953). At this time there is not sufficient evidence

to link lung cancer mortality to air pollution. However, an urban factor still remains important in lung cancer mortality.

When assessing the effects of air pollution by means of variation in weekly mortality, it is particularly important to consider other factors, such as meteorological conditions and influenza epidemics that may be contributing to changes in mortality. Boyd took this into consideration in his study over a period of 7 winters in Great Britain. Boyd attempted to investigate the associations between mortality, meteorological conditions as measured by temperature and absolute humidity, and air pollution as measured by sulphur dioxide, smoke, and fog (Boyd, 1960). Low temperatures were found to be highly correlated with deaths which occurred two weeks later. Among the pollution factors studied, SO_2 was most highly correlated with mortality, particularly from respiratory causes. However, correlations with mortality were lower for pollution factors than for temperature and humidity. The mortality trends seemed to suggest that the effects of pollution were more serious when accompanied by low temperatures.

According to the report on Air Quality and Stationary Source Emission Control published in 1975, there has been an increase in the combined mortality from bronchitis, emphysema, and asthma in the United States from 6.9 to 12.1 per 100,000 during the period 1958 to 1967. However, there has been a decline in deaths due to asthma. While asthma once accounted for 60 percent of all chronic respiratory disease deaths, by 1967 it accounted for only 10 percent. Therefore, the increase in chronic respiratory disease deaths has been due to bronchitis and emphysema. Furthermore, it has been more noticeable among white males. During this period, death rates from influenza and pneumonia combined have remained fairly constant.

An interesting follow-up study of 4,092 survivors of the Donora, Penn. episode in 1948 was conduced by Ciocco in 1957, eight and one half years after the episode (Ciocco, 1961).

By means of mailed questionnaires and personal interviews over 99 percent of the 4,092 persons were traced to 1957. People who reported acute illness at the time of the smog episode had higher subsequent mortality and prevalence of illness than other people in the community.

A series of mortality and air pollution studies conducted by the Public Health Service has been reported by Rumford (Rumford, 1961). In one such study, health districts in Philadelphia were used to compare mortality and pollution for the years 1954-1956. Significant correlations were found between dustfall and tuberculosis, pneumonia, chronic rheumatic heart disease, other diseases of the heart and arteriosclerotic heart disease. Multiple correlation analysis suggested that only chronic rheumatic heart disease was more strongly correlated to dustfall than to indices of socio-economic conditions used (income, crowding, education, race).

In another study, mortality variations were comapred among white female residents who lived in manufacturing versus non-manufacturing areas of Chicago. The results suggested that residents of the manufacturing areas experienced higher mortality, particularly in deaths due to cancer of the respiratory tract and heart diseases. A second approach compared mortality between residents who lived less than one mile and one to two miles from a large integrated primary metals plant. When mortality by census tracts, with comparable socioeconomic levels were compared, the mortality among residents of tracts less than one mile from the plant was over 30 percent higher than mortality in tracts one to two miles from the plant. Unfortunately, no air pollution measurements were made.

Pneumonia deaths have also been linked to air pollution. From a comparison of death rates in 1932-35 in Pittsburgh over a period of decreasing air pollution, it was shown that deaths from pneumonia also decreased

Likewise, Mills found excess pneumonia mortality in the most polluted area of Chicago when compared to the cleanest area as determined by sootfall and SO_2 levels (Mills, 1952).

Winkelstein conducted a number of studies relating mortality from specific causes to air pollution. From death certificate data collected between 1959 and 1961 in Buffalo and Erie counties in New York, a positive association was found between chronic respiratory disease mortality and suspended particulates for white men aged 50-69 (Winkelstein, 1967). The standardized mortality ratios for chronic respiratory diseases were 76 at pollution level I (lowest, suspended particulates less than 80 micrograms/m^3, 98 at level II, 112 at level III, and 137 at level IV (highest, suspended particulates over 135 micrograms/m^3). No association was found between pollution and cancer of the bronchus, trachea, and lung. An inverse relationship was found between mortality and economic levels. Five different economic groupings were used in this study. There was a paucity of cases in the high economic-high pollution group and the low economic-low pollution group. Only economic level II (Level I-lowest level) had cases in each of the four air pollution levels. For this level, mortality from all causes in men aged 50-69 was 50 percent higher in the highest air pollution level compared to the lowest. For chronic respiratory disease mortality the rate was 64 percent higher in the highest pollution area compared to lowest in men aged 50-69. No data were available on past smoking habits of the cases or on occupation.

A second study by Winkelstein compared total mortality with oxides of sulfur (Winkelstein, 1968). A positive association was found between chronic respiratory disease mortality and sulfation in the two lowest economic levels in white men 50-69 years. The high and low sulfation areas together accounted for only 37 percent of the population of white men aged 50 years and over. Winkelstein emphasized that these associations were only indirect and no definite causal conclusions could be made. Other associations were

found between suspended particulates and mortality from prostate cancer, stomach cancer, and cirrhosis of the liver (Winkelstein, 1969b, 1969c, 1971). In the prostate cancer study Winkelstein alluded to the possible association of cadmium oxide dust in the air and prostate cancer. This association has been reviewed by other investigators in relation to occupational studies. In all of Winkelstein's studies presented here, air pollution was measured in 1961-63 and mortality data was collected for 1959-61.

An association of prostatic cancer and suspended particulates measured by soiling index was also found by Hagstrom in a study conducted as part of the Nashville Air Pollution Study (Hagstrom, 1967). This study also reviewed other malignant neoplasms. During the twelve years studied (1949-1960) 2,912 deaths from cancer occurred. The relationship between cancer and air pollution was compared in a population of middle socioeconomic status. The four pollution variables measured were soiling index, SO_2, dustfall and sulfation rate. A positive association was found between stomach cancer and dustfall and between esophageal cancer and soiling index. Mortality from cancer of the bladder was higher in higher air pollution areas for all four pollutants measured. Total mortality from cancer by age showed a direct relationship to the level of soiling for ages 34 and over and an inverse relationship for ages 25-34. No data were available on smoking habits or occupation. As part of the Nashville Air Pollution Study, Zeidberg reviewed respiratory disease mortality and its relationship to soiling index, SO_2, sulfation rate and dustfall (Zeidberg, 1967). Three socioeconomic strata were designated. Total respiratory disease death rates were found to be inversely related to socioeconomic class. To control for socioeconomic effects, the middle class was used in assessing the effects of pollution since all three levels of pollution were represented in this group. Sulfation rates and dustfall were based on 123 sampling areas where soiling index and SO_2 were measured at only 36

stations. Mortality rates for influenza, pneumonia, and tuberculosis in the highly polluted area, especially in relation to sulfation rate and soiling index, were significantly higher than in moderately polluted areas. This study has been criticized on the basis that the middle socioeconomic level used for controlling on this factor was very broadly defined and the removal of the socioeconomic effect may have been incomplete.

Zeidberg also looked at cardiovascular disease mortality including total cardiovascular disease, general arteriosclerosis, rheumatic heart disease, myocardial degeneration and hypertensive heart disease (Zeidberg, 1967). A significant relationship was found between soiling index and mortality from total cardiovascular disease, hypertensive heart disease, and other myocardial degeneration. Among females, mortality for all cardiovascular disease categories decreased with decreasing levels of pollution as measured by soiling index. The pattern for males was generally irregular with arteriosclerotic heart disease mortality inversely related to pollution levels. Mortality for total and specific cardiovascular diseases was higher at all pollution levels among non-whites.

Hodgson, in a statistical study on mortality and air pollution in New York City, November 1962-May 1965 utilizing multiple regression analysis, noted levels of respiratory and heart disease mortality to be significantly related to environmental variables, especially particulate matter and temperature. However, only one monitoring station was used to measure pollutant concentrations (Hodgson, 1970). An increase of one unit in the average daily concentration of suspended particulates during a month resulted in an increase of 13.25 in expected daily mortality from respiratory and heart disease during the same month. The definition of pollutant units was not clear. The author concluded by pointing out that seemingly harmless increases in concentrations of pollutants from day to day resulted in significant increases in mortality.

Glasser investigated daily deaths from 1960 through 1964 (particularly October through March) in New York City in relation to SO_2, smoke shade, temperature, windspeed, sky cover, and rainfall (Glasser, 1971). Daily mortality was valued in terms of deviation from normal and deviation from a moving average. SO_2 and smoke shade were measured from one sampling station and expressed as daily means.

Since the relationship between SO_2 and mortality was stronger than that of smoke shade and mortality, SO_2 was considered the main pollutant. Days with SO_2 levels of 0.22 ppm or less in comparison to days with SO_2 levels of 0.40 ppm showed a difference of 10-20 mean deaths per day. Regression coefficients were calculated between daily mortality and SO_2 and weather factors. This analysis showed that the relationship of SO_2 to mortality was stronger than for any weather variable.

Jacobs studied the relationship between cardiovascular disease mortality and suspended particulates in Charleston, S.C. (Jacobs, 1972). During the time period 1968-1972 air pollution decreased in this area due to the control of industrial emissions. Mortality rates were observed before and during the reduction of air pollution. The population from the industrial area of Charleston was found to have a significantly higher risk of heart disease mortality than the total county population in 1968 but not in 1970. This was felt to be due to the reduction of suspended particulates from a range of 74.4-227.6 microgms/m^3 in 1968 to 55.3-120.5 microgms/m^3 in 1970. Jacobs suggested that the decreased mortality might also be the result of fewer temperature inversions in 1970 which exposed the population dangerous concentration of pollutants less frequently. There appeared to be no controls on economic status or smoking habits in this study.

Schimmel estimated excess mortality due to air pollution by examining daily mortality rates and air pollution for

January, 1963 through December, 1968 in New York City (Schimmel, 1972). Air pollution measurements were made for SO_2 and smoke shade. Seven daily weather variables were also examined. The estimated average daily excess mortality ranged from 18.12-36.74, with an intermediate estimate of 28.63. This is equal to about 10,000 deaths a year. Eighty percent of the excess was calculated to be due to smoke shade and 20 percent due to SO_2. This excess represented approximately 12 percent of the deaths which occurred during the six years of study.

Buechley in a study of the metropolitan New York-New Jersey area, attempted to detect a relationship between air pollution (primarily SO_2) and mortality (Buechley, 1973). This was part of a larger analysis of daily mortality in 422 places in the U.S. during 1962-1966. In addition to SO_2, other factors considered were seasonal influences, extreme heat waves, influenza epidemics, warm and cold weather, holidays, and day of the week influences. Only one monitoring station was used to measure air pollution levels.

Results indicated that with SO_2 levels below 30 microgms/m^3, mortality was 1.5 percent less than expected and with SO_2 levels above 500 microgms/m^3, mortality was 2 percent greater than expected. Coefficient of haze was found to be as good as SO_2 in predicting mortality. The estimated mortality resulting from the study is much lower than than predicted from Schimmel's study which included only New York City. The discrepancy may be due to more intensive adjustment for temperature variables and the inclusion of the effects of influenza in Buechley's study. The higher estimates in Schimmel's study may have resulted from using pollution concentrations on days preceding the day of death.

A comparison study of the relationship between mortality from respiratory cancers and pollutants (smoke) during 1940-1969 was studied in both the U.S.A. and England and Wales (Higgins, 1974). For the U.S. males, age specific respiratory cancer mortality rates have increased from 1940-1969 and for females, the rates have increased since 1955.

In England and Wales, men aged 25-34 have experience declining death rates since 1943. In men aged 35-44, the rates have increased to 1954 then decreased to original level. For the 45-54 year age group there was an increase to 1950 then a leveling off 1955-65, with a decline 1965-69. The 55-64 year group experienced increased deaths with a leveling off at 1960. The 65-75 year group still experienced increasing death rates. In the U.S. 1955-1970 the number of men who never smoked increased for those under 45 but decreased in those over 45 years of age. For England and Wales 1955-70 there was a greater proportion of cigarette smokers than in the U.S. Even with differences in smoking controlled, respiratory cancer mortality rates have been leveling off for men in England and Wales. A slightly greater decline for lung cancer was found in the Greater London area. This was found to parallel a dramatic decrease that has occurred in Greater London in smoke pollution levels, a decrease far greater than in many U.S. cities or even other areas of England.

Henderson published a study on lung cancer mortality for 1968-1970 and lung cancer incidence in 1972 for southcentral Los Angeles County, California, where an excess of lung cancer had been previously reported (Henderson, 1975). Air pollution data were collected for suspended particulates and polynuclear aromatic hydrocarbons on alternate weeks, June 13 through August 1, 1973. The polynuclear aromatic hydrocarbons specifically of interest were benzo (e) pyrene (BEP), benzo (a) pyrene (BAP), benzo (ghi) perylene (GEE), and coronene (COR). The excess lung cancer mortality in males was 33 percent or 87 deaths per year. Fourty-six of these deaths occurred in the under 65 year age group. No excess of oral cavity, pancreatic, laryngeal or bladder cancer was found. From observing the wind patterns of the study area, it was found that air pollution could remain in the study area for long periods of time after it was generated. A correlation between the distribution of the lung cancer cases and the location of the industries responsible for the pollution was found. In relating air pollution and cancer mortality data from the same time period, questions about the validity of the results arise

because of the long latency periods associated with many cancers. The author in this case, however, points out that the industrial plants have been located in the same place within the study area for the last 30 years and that the carcinogenic factors in the air were probably at even higher concentrations 30 years ago. Therefore, the author concluded that the excess of lung cancer in southcentral Los Angeles was probably due to an excess of carcinogenic particles in the air.

Carnow reviewed a number of studies on airborne benzo (a) pyrene and pulmonary cancer which compared urban and rural populations, migrant populations and different demographic units (Carnow, 1973). From urban-rural studies, he associated a 100 percent increase in mortality with a 6.2 unit rise in benzo (a) pyrenel (concentration of benzo (a) pyrene of 6.6 microgms/1000m^3 for urban areas and 0.4 microgms/1000m^3 rural areas). From the migration studies, Carnow found that death rates for pulmonary cancer followed closely the levels for air pollution with benzo (a) pyrene. Carnow reviewed a study by Hitosagi in 1968 carried out in Japan involving family interviews of 259 pulmonary cancer cases and a random sampling of an adult population 35-74 years old. Data on smoking, occupation, residence, and previous medical histories were collected. Pollutants collected included benzo (a) pyrene, SO_2, dust, and particulate matter. Increases in mortality rate were found to be associated with higher pollution levels for the most part. Carnow summarized his paper by theorizing that from the epidemiologic studies conducted, a 5 percent increase in pulmonary cancer mortality per unit increase in benzo (a) pyrene can be estimated.

A study of two communities in Pennsylvania, one with higher pollution than the other was published by Morris (Morris, 1976). Because of a coal powered electric plant, the more highly polluted area of Seward had 9 times the SO_2, 6.2 times the sulfation rate, 3.2 times the dust fall, and 1.4 times the suspended particulates of New Florence.

Mortality data were collected from 1960-1972 for sample populations in the two communities. Age and sex adjusted mortality rates for Seward exceeded those for New Florence for 10 of the 11 years of the study ($P < 0.05$). The excess was not in heart and respiratory disease categories as expected but in cancers.

The original sample population studied consisted of volunteers. Differences between nonrespondents and respondents were not explored. No occupational data were collected, but Seward was believed to have a higher percentage of coal miners and steel workers. Using standard mortality ratios, no difference in mortality was found between the male population, but females in Seward had higher mortality ratios than females in New Florence. When smoking and length of residency were adjusted for, a pattern of increased mortality was observed in each smoking and sex category for those with more than 20 years of exposure to Seward's air. Those who resided for 20 years in Seward were found to have a higher relative risk than those with shorter residencies. A pattern consistent with this was not found in New Florence. Among males smoking more than one pack of cigarettes per day, those in Seward exposed to 20 years of air pollution had a slightly higher mortality than those in New Florence. The data were found to be consistent with an hypothesis that the effects of air pollution and smoking are additive.

Mahoney tested the hypothesis that no differences existed between different levels of pollution and respiratory mortality rates in Los Angeles in 1961 (Mahoney, 1976). Ozone, SO_2, and suspended particulate levels were measured in 1961. Temperature data were also collected. There was an increase in mortality with increasing levels of ozone from 41.8/100,000 to 65.2/100,000 ($p < 0.025$). No increase in mortality was noted for SO_2, but the author found tha the ozone levels and SO_2 levels were inversely proportional so that an effect produced by SO_2 would have to be quite large in order to be detected. SO_2 was well controlled at this time also.

A trend of increasing mortality with increasing level of suspended particulates was statistically significant. A problem existed with this association in that the high concentrations of suspended particulates were concentrated downtown around the skid row area. This increase could, therefore, be due to the special subgroup exposed.

Stocks published a three part study on lung cancer and bronchitis mortality in Great Britain (Stocks, 1966). Part one involved mortality data collected from eight cities in England and Wales from 1955. Population surveys were also conducted to ascertain smoking habits, occupation, and residency histories. In four of the cities previously collected data from other studies were used. Air pollution measurements were made for total smoke, polycyclic hydrocarbons, and trace elements. These measurements were made at the time that mortality data were collected. Correlations were found between the average number of cigarettes smoked per day, the proportion of the population smoking 20 or more cigarettes daily, and lung cancer mortality. Correlations were also found between lung cancer mortality and total smoke, 3,4-benzopyrene, 1,12-benzopyrene, and trace elements.

In Part II, Stocks collected data on mortality from lung cancer and bronchitis in 19 different countries apparently from 1958-59. Data on fuel consumption 1951-52 and 1955-58 were also collected along with the annual consumption of cigarettes from 1921. Using fuel consumption rates 7 years prior to mortality data, the partial coefficients after correction for differences in cigarette consumption were 0.68 at age 35-44, 0.47 age 45-54, 0.45 at age 55-64, and 0.41 at age 65-74 for men. These were apparently significant relationships.

Stocks repeated this study with 20 countries during the years 1962-63 for lung cancer and 1960-61 for bronchitis mortality (Stock, 1967). He found a significant correlation of 0.446 between lung cancer mortality, males age 55-64, and solid fuel consumption measured 6 years before. Adjustments were made for cigarette consumption.

In Part three, Stock studied urban/rural differences for stomach cancer, lung cancer, and bronchitis mortality from 1921 in different regions of England. After adjustments were made for social factors and smoking, an urban excess of lung cancer was found. This excess was attributed to air pollution from coal smoke. Stocks concluded his study with the hypothesis that smoking and air pollution could act on lung cancer mortality by accelerating the latent stages of an already initiated disease process.

Lung cancer and bronchitis mortality were studied by Ashley in 84 county boroughs in England and Wales 1958-63 (Ashley, 1967). Air pollution measurements for smoke and SO_2 were measured at the same time that cancer mortality data were collected.

Twenty four counties specializing in coal and textile industries were found to have high ratios of bronchitis to cancer of the lung. Fifty three of the 84 counties had air pollution data available. Of these, 24 had smoke concentrations greater than 130 microgms/m^3 with 11 of these being from the coal and textile industrial areas. In comparing the towns with high pollution without textile or coal industries to areas having coal and textile industries, the latter still showed a decreased lung cancer mortality rate. Ashley hypothesized that the inhalation of dust provides the lung protection against carcinogenic substances. This would be indicated by the high bronchitis lung cancer mortality ratio. The protection theory may involve a mechanism in which the lung, laden with dust, is in a better immunological state to attack abnormal cells when they are produced. Ashley also found support for an hypothesis that air pollution is not correlated with lung cancer but is correlated with bronchitis.

In 1971, Watanabe conducted a study in Osaka, Japan (Watanabe, 1971). An excess of deaths found in the city over the suburban areas was thought to be the result of increased air pollution with cold temperature.

Lebowitz utilized a stimulus-response method to determine the relationship between environmental stimuli (suspended particulates and SO_2) and mortality (Lebowitz, 1973a). Using mortality data

from Tokyo, a multiple stepwise regression analysis was applied first to delineate the importance of specific variables and to designate the direction of the relationship. The correlation coefficients between excess mortality (response) and the environmental variables (stimuli) were found to be high in winter, lower in the summer, and, overall, high for the entire period. The theory that air pollutants contribute to increased mortality independent of temperature was supported in this study.

Lebowitz conducted similar studies in New York, Philadelphia, and Los Angeles (Lebowitz, 1973b). Mortality was found to be related in time to pollution and weather variables. The stimuli-response method showed a significant relationship between the magnitude of the abnormal environmental event (stimulus) and the mortality response.

In Dublin, Ireland Kevany analyzed data on mortality and morbidity from cardiovascular disease and respiratory diseases. Ischaemic heart disease, the main component of the cardiovascular disease category, was found to be significantly correlated with SO_2 with a lag time equal to zero. Different lag times ranging from 0-3 days were applied to the data to allow for effects that did not derive as immediate responses. At lag of one day, the correlation became insignificant, except for valvular heart disease and this was not sustained for a lag of two days. Three and seven day averages were also used. Smoke at levels of 100 micrograms/m^3 showed a significant correlation with a seven day moving average for ischaemic heart disease ($r=0.74$ $p=0.004$) and valvular heart disease. It was concluded that smoke may have a more gradual effect on increasing mortality over a longer period, with SO_2 having a more immediate effect. The mortality for respiratory disease showed a less consistent association with air pollution. For SO_2 levels up to 75 micrograms/m^3, no significant response in mortality was seen. At 100 micrograms/m^3 SO_2 and over there was a strong correlation with death from acute respiratory disease. With levels of SO_2 at 150 micrograms/m^3, a strong correlation with mortality from chronic bronchitis, emphysema, and asthma was seen with both three and seven day moving averages. No significant correlation existed for smoke.

Occupational and socioeconomic levels were not considered and no mention was made of the ages of the population studied, the proportion of males and females, and the total number of people. A reference was made to smoking in that it was thought to remain constant in the total population over the short periods which were studied.

Many of these mortality studies were faced with problems in the collection of pollution data. The pollution data often were collected at the time of the study and were related to mortality from a preceding time. Also some diseases under study, such as cancer, have a long latent period and comparisons between these mortality rates and present pollution measurements may not at all be appropriate.

One of the problems relating to any study of air pollution involves controlling for other factors which may be related to the variables studied. These include meteorologic factors, the presence of epidemics such as influenza at the time of the study, and seasonal influences. Some of the studies presented have taken these into account, others have not.

All of the studies reviewed above have found some relation between an air pollutant and increased mortality. No conclusion can be made as to which specific pollutant, if any, is responsible for the increase in mortality. Furthermore, it is difficult, based on available studies, to determine the specific causes of death attributable to air pollution.

A summary of these mortality studies is presented in Table 9.

EPIDEMIOLOGIC STUDIES ON THE EFFECTS OF SO_2 AND PARTICULATES ON MORTALITY

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
UNITED STATES							
Mills 1952	30-75 yr and over M & F 2 communities in Chicago	Mortality	"cleaner vs. dirtiest" community				1) death rates for pneumonia higher in polluted area 2) respiratory tract cancer death rates among males rise a full decade earlier in polluted areas
			Not stated	Not stated	dirty .40 ppm	160 tons/ mi^2/mo	
					clean .1 ppm	20 tons/ mi^2/mo	
Ciocco 1961	follow-up of 4,092 residents surveyed in 1948 Donora, Penn.	1) personal interview 2) mailed questionnaire 3) mortality 8 1/2 yr following episode	exposed to pollution episode in 1948				1) person who reported acute illness at time of smog episod have had subsequent higher mortality and prevalence of illness than other people in the community 2) persons with severe complaints in 1948 demonstrated higher mortality and morbidity than thos with mild complaint
Winkel-stein 1967	Males and Females Age 50 and over	Death certificate data 1959-1961 Buffalo and Erie County, N.Y.	4 levels I < 80 II 80 - 100 III 100 - 135 IV > 135 $\mu g/m^3$ per 24 hours	Not stated	Not stated	——	Positive association between pollution level & total mortality in white men and women age 50 - 69. Positive association found wi chronic respiratory disease mortality white men aged 50-6 years. No association found between pollution and cancer the bronchus, trachea or lung

urce	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
nkel-ein 68	Males and Females	Death Certificate Data 1959 - 1961 Buffalo - Erie County			Oxides of Sulfur 3 levels I <0.30 mg/ sq cm II<0.30 - .45 mg/sq cm III>0.45 mg/ sq.cm per 30 days	——	No association found between sulfation & total mortality or mortality from cancer of the bronchus, trachea & lung in white men 50 years and over. Positive association found between chronic respiratory disease mortality & sulfation in the two lowest economic levels in white men 50 - 69 years. No synergistic effect was found between sulfation rate and suspended particulates
nkel-ein 69	198 White male prostatic cancer cases Age 50 and over	Death Certificate Data 1959 - 1961 Buffalo - Erie County New York	4 Levels I < 80 II 80-100 III 100-135 IV 135+ $\mu g/m^3$ per 24 hours	Not stated	Not stated	——	Suspended particulates positively associated with prostatic cancer in age 50 and over group. In age 50 - 69 years mortality rate in the highest pollution area 2.7 times the rate in the lowest area. For the 70 and over group 1.7 times.
nkel-ein 69	95 White male and 36 White female Stomach cancer cases age 50-69	Death Certificate Data 1959 - 1961 Buffalo - Erie County New York	4 Levels I < 80 II 80-100 III 100-135 IV 135+ $\mu g/m^3$ per 24 hours	Not stated	Not stated	——	Found positive association between suspended particulates and stomach cancer mortality men and women aged 50-69 years Mortality rates two times higher in high pollution areas than low pollution area. No association for ages 70+ over with suspended particulates and stomach cancer mortality

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Winkel-stein 1971	224 White men and 78 white females age 50 and over cirrhosis of the liver cases	Death certificate Data 1959 - 1961 Buffalo-Erie County, New York	4 Levels I <80 II 80-100 III 100-135 IV 135+ $\mu g/m^3$ per 24 hours	Not stated	Not stated	——	Found positive association between suspended particulates & cirrhosis mortality in males aged 50 & older in a lower economic level. Has gradient increase in mortality rate from 28/100,000 in lowest pollution area to 173/100,000 highest pollution area. The females 11/100,000 in lowest population to 47/100,000 highest.
Zeid-berg 1967 Nash-ville Air Pollu-tion Study)	32,067 males and females white and non-white mortality all causes respiratory-mortality used specifi-cally in the study	Death certificate Data 1949 - 1960	Not stated	Soiling Index COHS per 1,000 linear ft. High $\geq$ 1.1 MOD 0.351-1.099 Low $\leq$ 0.350	High $\geq$0.013 ppm MOD 0.006-0.012 ppm Low $\leq$0.005 ppm per 24 hours	Dustfall tons/ mi^2/mo High $\geq$ 12 MOD 5.01-11.99 Low $\leq$ 5 Sulfation (SO_3) mg/ 100 cm^2/ day High $\geq$.400 MOD .151-.399 Low $\leq$.150	Respiratory disease mortality in high pollution area was significantly higher than moderate pollution area, except for bronchies cancer. SO_3 and soiling index had the most direct relationship to mortality. The direct relationship between total respiratory disease mortality and SO_3 levels was found at age 25-75 years.

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Zeidberg 1967 (Nashville air pollution study)	32,067 males and females white and nonwhite mortality all cases Cardiovascular mortality specifically used in study	Death certificate data 1949-1960	Not stated	Soiling index COHS per 1,000 linear ft. High ≥ 1.1 MOD 0.351 1.099 Low ≤ 0.350	High ≥ 0.013 ppm MOD 0.006-0.012 ppm Low ≤ 0.005 ppm per 24 hours	Dustfall tons/sq. mi/mo high ≥ 12 MOD 5.01-11.99 Low ≤ 5 Sulfation (SO_3) mg/100 sq cm/day high ≥ .400 MOD .151-.399 Low ≤ .150	Statistically significant inverse association found between socio-economic class & total cardiovascular disease mortality, hypertensive heart disease & other myocardial degeneration mortality. Significant relationship found between soiling index & mortality from total cardiovascular disease, hypertensive heart disease & other myocardial degeneration. For females a regular pattern of association between pollution and mortality for all cardiovascular diseases was found.
Hagstrom 1967 (Nashville air pollution study)	All deaths due to malignant neoplasms	Death certificate data 1949-1960	Not stated	Soiling index COHS per 1,000 linear ft. High ≥ 1.1 MOD 0.351-1.099 Low ≤ 0.350	High ≥ 0.013 ppm MOD 0.006-0.012 ppm Low ≤ 0.005 ppm per 24 hours	Dustfall tons/sq. mi/mo high ≥ 12 MOD 5.01-11.99 Low ≤ 5 Sulfation (SO_3) mg/100 sq cm/day high ≥ .400 MOD .151-.399 Low ≤ .150	Mortality for all cancers higher (p 0.05) in high pollution area than moderate pollution area for suspended particulates measured by soiling index. Stomach cancer mortality had significant differences by dustfall level. Found direct relationship between soiling index level & mortality for cancer of esophagus, prostate & bladder no consistent relationship found between mortality from all cancers & sulfation or SO_2.

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Hodgson 1970	Males and Females	Mortality Data November 1962-May 1965 New York City	No specific values given	Not measured	No specific values given	Not measured	Significant relationship found for ages 65 and over and 64 and under between respiratory & heart disease mortality and environmental variables especially particulate matter & temperature. Deaths from other causes were not significantly related to pollutants.
Glasser 1971	Males and females	Daily mortality 1960-1964 (April-Sept. omitted) New York City	Not measured	Range <1.0 - 6.0 COHS daily means	Range ≤ 0.10-$\geq .60$ ppm daily means	Not measured	Mortality increased with increased level of SO_2. A difference of 10-20 deaths per day found between the mean number of daily deaths on days with mean SO_2 levels of ≤ 0.20 ppm compared to days with ≥ 0.40 ppm SO_2 levels
Jacobs 1972	In 1968; 1,958 deaths males and females. In 1970; 1,718 deaths males and females. (All causes.) Study specifically deals with cardiovascular deaths	1968-1970 Death certificates Charleston, South Carolina	1968 74.4-227.6 $\mu g/m^3$ 1969 57.9-170.7 $\mu g/m^3$ 1970 55.3-120.5 $\mu g/m^3$	Not measured	Not measured	Not measured	Population from industrial area was at significantly higher risk of heart disease death than total county in 1968 but not 1970. Believe due to a reduction in air pollution 1968-1970 1968: $p = 0.001$ 1970: $p = 0.23$

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Schimmel 1972	Male and female deaths for ten mortality variates	Death certificate data for 1963-1968 New York City 2,192 days of study	Not measured	Daily data Jan.1, 1963-December 31, 1968 mean 21.63 COH units x10	Daily data Jan.1, 1963-Dec. 31, 1968 mean 17.25 ppm. 100	Not measured	Estimated ave. daily excess mortality in range of 18.12-36.74, Intermediate estimate 28 63. This equals about 10,000 deaths a year. 80% of excess mortality believ ed due to smoke shade & 20% to SO_2.
Buechley 1973	Male and female deaths all causes	Daily mortality data collected for New York-New Jersey area 1962-1966	Not measured	Not measured	Mean values yearly range 228.91-297.09 $\mu g/m^3$ Seasonal range 157.1-363.2 $\mu g/m^3$ Day of the week range 217.6 - 305.1 $\mu g/m^3$	Not measured	Found days with SO_2 levels below 30 $\mu g/m^3$ had mortality 1.5% less than expected and days with SO_2 levels above 500 $\mu g/m^3$ had mortality 2% greater than expected.
Higgins 1974	Males and females. Study deals specifically with cancer of the respiratory system	U.S., England & Wales mortality compared. 1940-1969	Not measured	Decreased 1959 ≥ 300 $\mu g/m^3$ to 1967 65 $\mu g/m^3$	Not measured	Not measured	Found respiratory cancer mortality rates have leveled off in United Kingdom whereas in U.S. rates have continued to rise. This found even though cigarette smoking highe in United Kingdom. Greater London area found to have slightly greater decrease in lung cancer possibly attribute to the dramatic decrease in smoke pollution which had occurred in this area.

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Henderson 1975	5841 male and 1881 female lung cancer mortality cases and incident cases from 1972 combined	Lung cancer mortality data 1968-1970 & incident cases 1972 Los Angeles	Mean value 98.7 $\mu g/m^3$ Range all stations 83.7 - 116.4 $\mu g/m^3$	Not measured	Not measured	Polynuclear aromatic hydrocarbons in suspended particular matter components: BEP 0.44 ng/m^3 BAP 0.24 ng/m^3 GEE 1.7 ng/m^3 COR 0.98 ng/m^3 all mean station values	Excess risk of lung cancer in south central Los Angeles males believed due to an excess of carcinogenic air pollution

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Morris 1976	116 male and female deaths Seward. 137 male and female deaths New Florence.	Mortality data sample population two communities Seward (s) and New Florence (N.F.) Pennsylvania 1960-72	(N.F.)109 $\mu g/m^3$ (S) 151 mg/m^3 values are averages	Not measured	Not measured	Dustfall (N.F.) 26 tons mi^2/mo (S) 83 tons/ mi^2/mo Sulfation (N.F.) 0.6 $mg/SO^3/100cm^2$ per day (S) 3.7 $mg/SO^3/100cm^2$ per day values given are average	Males with 20+ years of residency in Seward had about one-tenth the excess mortality of those smoking more than one pack of cigarettes per day in New Florence and one-fifth the excess mortality of moderate smokers in New Florence. Data consistent with an additive effect of smoking and pollution.
Mahoney 1976 [111]	1,046 respiratory deaths white males and females	Death certificates 1961 Los Angeles	Deficient in data for some areas 90 - 120 Km units x 10	Not measured	Range 4 - 25 pphm	Ozone 17.5 - 27.5 pphm	Increase in mortality with increase in level of ozone No association found between SO_3 and mortality. Found increase in mortality parallel to increasing levels of suspended particulates, statistically significant ($p < 0.01$).

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
FOREIGN STUDIES							
Pemberton and Goldberg 1954	45-64 yr 65+ yr M & F county boroughs of England and Wales	number of deaths from Registrar General; Annual Review 1950-1952	Not stated	Not stated	approx. 5-40 mg SO_3/1,000 cm^2 lead peroxide candle	total solids	1) significant correlation between sulphur dioxide and death from bronchitis in men age 45 and over; similar association noted in women in 2 of the 6 sets of data 2) no significant association between average sulphur dioxide and number of person/room and income classification 3) association between bronchitis and solid matter not as consistent as with SO_2

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Daly 1954	45-64 yr M & F 83 county boroughs of England and Wales	average annual mortality from bronchitis 1950-52	based on domestic coal consumed annually by each town (18% of all coal consumed)				1) domestic coal consumption significantly correlated with death from bronchit in men ages 45-64 (r = .59) allowing for difference in social class and overcrowding (r =.5 2) domestic coal consumption correlated with deaths from pneumon and bronchitis in women ages 45-64 (r = .54)
Hewitt 1956	all ages 0-4 yr 5-14 yr 15-24 yr to 85+ yr Administra-ive county of London	number of deaths from statistical Review of the Registrar General 1930-32, 1942-54 and from the county medical officer of Health for county of London, 1952	Not stated	Not stated	measured	Not stated	1) mortality rates correlated closely with indices of social status and crowding 2) observed variation may be due to some other factors - possibly air pollution 3) air pollution exert effects on mortalit from bronchitis 7 times as great as o non-respiratory di

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Fairbairn and Reid 1958	45-64 yr M & F 37 areas United Kingdom	1) death rates from bronchitis, pneumonia, pulmonary, tuberculosis, lung cancer and influenza (1948-54) 2) total sickness rates for postal workers (1948-54)	Not stated	Not stated	Not stated	fog index	1) bronchitis deaths related to fog frequency 2) total sickness positively associate with fog and population density 3) fog showed no direct relationship to pulmonary tuberculosis mortality which does show relationship in each sex to domestic overcrowding 4) death in both sexes from pulmonary TB, and cancer of the lung show high association with population density 5) lung cancer mortalit rates did not show any relationship to fog or domestic crowding 6) significant relation ship of influenza with domestic overcrowding in males
	15-59 yr males and single females	1) sickness record for all permanent civil servants born on the 18th of any month (1946-53)					

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Stocks 1958	all ages M & F 17 localities North Wales and Liverpool	S.M.R. for cancer of the lung and bronchus, intestine and rectum	Not stated	1.7-62.4 $mg/100m^3$	.3-3.49 $mgSO_3/100cm^2$ of lead peroxide	benzpyrene 20-106 ppm benzpery-lene 74-260 ppm pyrene 42-140 ppm fluoran-therne 56-280 ppm	1) high population density associated with lung cancer mortality (concentration of smoke may be related to this association) 2) 1:12 benzperylene significantly correlated with lung cancer mortality independent of population density; 3:4 benzpyrene shows same type of correlation though not significant 3) independent relationship of SO_2 to lung cancer mortality very small and of doubtful significance 4) no correlation between smoke concentrations and intestinal cancer mortality 5) no firm conclusions can be made due to small number of localities considered

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Stocks 1959	all ages M & F 1) county boroughs England and Wales 2) administrative areas of Lancashire and West Riding of Yorkshire 3) all urban areas of Lancashire	deaths from cancer of the lung (1950-54) and deaths from cancer of stomach, intestine with rectum and breast and from bronchitis (1950-53)	Not stated	8-44 mg/100 cm^2	Not stated	deposit 96-731 $g/100m^2$/mo	1) bronchitis and lung cancer mortality was positively correlate with deposit and smoke 2) breast cancer shows negative correlation with pollution 3) stomach cancer significantly related to smoke and deposit 1) bronchitis mortality significantly correlated with deposit but not smoke. Lung cancer correlated with smoke but not deposit 2) stomach-cancer mortality significantly related to smoke and deposit only in females 3) breast cancer shows no association with pollution

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Daly 1959	almost entirely males 45-64 yr (1948-54) 65-74 yr (1950-54) 83 county boroughs of England and Wales	death from a) bronchitis b) pneumonia c) respiratory tuberculosis d) lung cancer e) other respiratory diseases f) all non-respiratory diseases	based on fuel consumption a) industrial pollution b) domestic pollution c) power station				1) domestic pollution highly correlated with bronchitis correlated to lesser degrees to pneumonia, respiratory tuberculosis, lung cancer and all non-respiratory diseases in that order 2) correlation with bronchitis mortality still existed when allowance was made for social class differences 3) proximity to power station did not increase bronchitis death rate

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Stocks 1960	all ages M & F 53 county boroughs 74 administrative areas in Lancashire and West Riding of Yorkshire	mortality from cancers of the lung, stomach, intestine and the breast	Not stated	measured range 15-562 mg/1000m^2	Not stated	polycyclic hydrocarbon trace elements	1) lung cancer mortal and bronchitis correlated with smoke density 2) pneumonia in males strongly correlate with smoke density 3) cancers of the stomach and intestine are related significantly with smoke in the count boroughts in males 4) in females, cancer of the breast and other organs show no association wit smoke 5) for lung cancer an bronchitis 3:4 benzopyrene is the substance of prime importance but is apparently not imp tant in pneumonia

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Boyd 1960	<1yr ≥45 yr London, East Anglia (control)	1) weekly mortality from bronchitis, pneumonia and heart disease 2) daily meterological readings 1947-1954 winters	<.25 mg/m^3 .25-.40 mg/m^3 >.4 mg/m^3	Not stated	weekly average of mean daily concentration <.10 ppm .10-.15 ppm >.15 ppm	fog index	1) mortality increased with decreasing temperature and increasing humidity 2) among pollution factors, SO_2 showed highest correlations with mortality. SO_2 more closely associated with respiratory mortality than with heart disease mortality 3) trends suggest that increase in mortality associated with fog occur only when fog is accompanied by very low temperature (below 36°F)

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Pemberton 1961	1) population of Sheffield, England 30 stations in Sheffield, England 2) 90 men with chronic bronchitis 3) male working class	1) lung cancer mortality (ILN 162-163) Bronchitis mortality (ILN 500-502) 2) diary 3) number of men with new attacks of bronchitis from certificates of incapacity	not stated	mean winter range 9-88 $mg/100m^3$	measured in pphm no numbers given	not stated	1) bronchitis and lung cancer are more common in more polluted parts of the city 2) rise in number of men with bronchitis who became more ill with rise in pollution 3) number of new attac of bronchitis in working male popula tion increased with periods of high pollution

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Burn and Pemberton 1963	men 45-64 yr 5 wards in Salford defined by pollution	1) bronchitis morbidity determined by Ministry of National Insurance certificates for 2 years 2) mortality a) bronchitis (ICD: 500-502) b) lung cancer (ICD: 162-163) c) arterio-sclerotic heart disease (ICD: 420) d) cerebrovascular accidents (ICD: 330-334) e) all causes 1956-1959	Not stated	daily winter average 45-77 $mg/100m^3$	daily winter average 6-25 pphm	Not stated	1) bronchitis rates tended to be higher in more polluted area 2) excess number of deaths from "all causes", bronchitis and lung cancer als found in high pollution area

ource	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
tocks 966	Male and female lung cancer and bronchitis deaths	I. Mortality data collected and survey of air pollution and smoking made in four cities Data collected also from other studies England and Wales	Not measured	7 areas Range 51-312 mg/1000 m^3 2 different methods of measurement encompass this range Some measured by weight others by reflection.	Not measured	7 areas 3,4 Benzopyrene 3-48 µg/1000 m^3 1,12Benzperylene 5-45 µg/1000m^3 Arsenic Beryllium Molybdenum (Trace elements)	Correlation found betwee lung cancer mortality and total smoke, 3,4-benzopyrene, 1,12-benzperylene & elements (arsenic, beryllium, molybdenum) for males and females
122	Male lung cancer death rates	II. Death rates 19 countries 1958 - 1959	Not measured	Not measured	Not measured	Solid fuel consumption Range 239-4,212 (yrs. 1951 - 1952) 232-4,129 (yr. 1955) mean annual kg per head	Partial coefficents found for both solid fuel consumption and cigarette smoking with mortality independently.
	Male and female bronchitis, lung and stomach cancer deaths age 25-75+	III. 1921 - 1946 Death rates compared between urban areas and surrounding regions. England and Wales	Not measured	Not measured	Not measured	Not measured	After differences made in social class and other factors an urban excess of lung cancer existed and was attributed to air pollution.

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Stocks 1967	Lung cancer deaths males age 35-44 and 55-64 bronchitis deaths age 55-64	Death rates 1960 - 1961 20 countries (repeat of study noted in section II above)	Not measured	Not measured	Not measured	Solid fuel consumption Range 138-4129 kg/capita 1955 - 1958	Found significant correlation between mortality from lung cancer in males 55-6 years and solid fuel consumption 6 years before The coefficient when cigarette consumption held constant was +0.446. Lung cancer death rates in males aged 35-44 more closely related to cigarette consumption than solid fuel consumption.
Ashley 1967 [123]	Male and female deaths from lung cancer and bronchitis	Mortality data 1958 - 1963: 84 major urban areas of England and Wales	Not measured	Range 23-261 $\mu g/m^3$ Median 124 $\mu g/m^3$	Range 33-227 $\mu g/m^3$ Median 124 $\mu g/m^3$	Not measured	Significant correlation between smoke and SO_2 and bronchitis. A not significant negative correlation was found between smoke and SO_2 with lung cancer. An excess of bronchitis with a deficiency in lung cancer was found in mining and textile towns compared to other regions. This believed due to a protection inferred by inhalation of dust.

urce	Population	Method	Exposure: Particulates	Exposure: Smoke	Exposure: SO_2	Exposure: Other	Results
vany 75	Male and Female deaths cardiovascular and respiratory disease	Death certificates 1970-1973 Dublin, Ireland	Not measured	Not measured	1970 - 1973 Daily mean 150 $\mu g/m^3$ increase 1970 - 1973 in 50 - 100 $\mu g/m^3$ level	Not measured	Mortality for cardiovascular significantly correlated with SO_2 at increasing threshold levels with $r = 0.821$ at 150 $\mu g/m^3$. SO_2 appears to have an immediate rather than lag effect on cardiovascular mortality.
							Strong correlation of SO_2 at 100 $\mu g/m^3$ with acute respiratory mortality and at 150 $\mu g/m^3$ with chronic bronchitis, emphysema and asthma mortality.
tanabe 71	Not stated	Mortality data Nov. 1962 - Oct. 1967 Osaka, Japan	$<.49$ mg/m^3 $>.50$ mg/m^3	Not measured	$<.09$ ppm $>.10$ ppm	Not measured	Excess deaths found in city vs suburban area. These appear to result from increased pollution on cold days. Mortality found more affected by SO_2 than suspended particulates. SO_2 level of >0.1ppm deemed unhealthy.

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Lebowitz 1973	Winter average number daily deaths 123 ± 11.7 summer average number daily deaths 107.7 ± 6.5	Death certificate data April 1966 to March 1969 Tokyo, Japan stimulus-response study	Range 30 (± 11.6) - 41.1 (± 13.9) $\mu g/m^3$ Summer-winter range	Not measured	Range 4.4 (± 0.9) - 5.7 (± 1.3) pphm Summer-winter range	Not measured	Air pollutants have contributed to increase mortality independent o temperature. Correlatio coefficents between exc mortality (response) an abnormal environment events (stimuli) are hi in winter (r = 0.65) lower in summer (r = .48 and considered high for total period (r = .57)

2. Morbidity Studies

A summary of the morbidity studies reviewed in this section is presented in Table 10.

Morbidity studies are usually preferred over mortality studies since they are more representative of the effects of a factor acting on a population. However, presently there is no single method of measuring respiratory morbidity shown to be very effective. In fact, evidence of an association of relatively low pollution levels with respiratory tract infections, for example, is only slightly better than that provided by mortality data.

A number of different methods have been used to measure the effects of air pollution. These include questionnaires (such as the MRC), daily diary reporting, absence from work or school, hospitalization rates, clinic visits, and lung function tests. In addition, the populations studied have varied from well individuals to panels or groups of bronchitis and asthma patients.

Each type of study has problems that may possibly be obscuring the time associations between air pollution and morbidity. Even within each basic type of study, different definitions, methods or instruments preclude any easy comparison of results. As with air pollution confounding variables, such as meteorologic conditions, could have a greater effect on morbidity than on mortality. Such variables need careful consideration in these studies. However, this has not been done in the majority of studies. Even among those studies that do consider meteorologic conditions, often only temperature is used. Complete meteorologic data would greatly clarify the associations between air pollution and morbidity found by epidemiologic studies.

Morbidity studies in relation to air pollution have been concerned primarily with respiratory illnesses such as chronic bronchitis, emphysema, and asthma. However, many authors, rather than looking at specific disease entities, included

respiratory symptoms such as increased cough, sptum production or dyspnea. This can obviate problems of comparability of diagnoses and inclusiveness within such diagnoses.

Goldsmith pointed out that non-disease effects should also be considered in epidemiologic studies (Goldsmith, 1969). These effects included sensory irritation, odor and reactions to odor, central nervous system reactions, psychomotor test performance, temporal discrimination, biochemical changes, and hematocrit changes.

Prindle compared two neighboring communities in West central Pennsylvania with widely differing air pollution levels utilizing a questionnaire, lung function tests, and x-rays (Prindle, 1963). A greater proportion of males in the more polluted community (Seward) had pneumoconiosis as revealed by the x-rays. There were more males with emphysema in the less polluted community of New Florence. One possible interpretation is that selective migration had occurred between the towns (Anderson, 1964).

In a preliminary report on the prevalence of chronic respiratory disease in Berlin, New Hampshire in 1961, Ferris and Anderson demonstrated that cigarette smoking and aging were the major determinants of chronic respiratory disease (Ferris and Anderson, 1962). An approximate two-fold increase in the prevalence in each disease category in non-smoking men in the most polluted area did suggest an effect by air pollution, but the difference was not statistically significant. The possible influences of ethnic, economic, and social differences could not be determined.

A later paper by Anderson suggested that the occurrence of selective migration may explain these results (Anderson, 1964). This was based on a review of residence 10 years prior to the study of a subsample of the diseased persons, and on the prevalence of respiratory disease in females who had never smoked. The results indicated that disease persons did move but concurrent migration of well people was not considered.

Ferris and Anderson suggested that this failure to demonstrate any significant association between air pollution and respiratory disease may have been due to the low levels of air pollution exposure or to the similarity of exposure actually experienced in contrast to that measured (Ferris and Anderson, 1964). In order to determine the health effects of pollution, they chose to compare the health status of people in Berlin, New Hampshire to people living in Chilliwack, British Columbia, a community with practically no air pollution. Methods used to survey the residents of Chilliwack were comparable to those used in Berlin. More respiratory symptoms and lowered lung function were observed in Berlin. The decreased pulmonary function in Berlin could not be explained entirely by increased cigarette smoking. The findings seem to point to possible air pollution effects, but the authors suggested that ethnic differences or other variables might also explain this difference.

In a survey of 3,000 households in Nashville, Tennessee, morbidity was most consistently related to soiling index and 24 hour SO_2 levels for individuals 55 year or older in the middle socioeconomic class (Zeidberg, 1964). Morbidity rates tended to be higher in females. This might possibly have been due to the fact that the adult female was usually the respondent and she might have reported more illness for herself than for other members of the household. Observations showed that employed females experienced less morbidity than housekeeping females. Several speculations are offered to explain this difference, but further data are needed such as the specific occupational exposure. Problems which have been pointed out in a previous review include the absence of cigarette-smoking information, the lack of a relationship of air pollution to respiratory illness, and the broad definition of the middle class. It has also been emphasized that Nashville experienced relatively low levels of pollution during the study period.

Fairbairn and Reid collected sickness absence data on outdoor postmen and indoor clerical and executive staff (males and single females) during 1946-53 (Fairbairn and Reid, 1958). Absences due to bronchitis and pneumonia were associated with fog, but the association was barely significant. Total sickness rates for postmen, grouped according to their place of work from 1948-54, showed significant associations with both fog and population density.

Marked and consistent differences in respiratory illness absences lasting more than seven days were noted among women employees of the Radio Corporation of America in eight different cities during 1955, 1957, and 1958 (Dohan, 1960, 1961). The incidence of respiratory disease was significantly correlated with mean suspended particulate sulfate concentrations ($r = 0.964$) within the city in which the women worked. An association between sulfate concentrations and bronchitis and influenza, but not pneumonia was noted when the data were evaluated by types of respiratory disease. Interestingly, in the year of a major influenza epidemic, the areas with the higher sulfate concentrations had greater increases in respiratory illness absence rates. The four areas experiencing the highest illness absence rates had mean annual suspended sulfate concentration of 13.2 - 19.8 micrograms/m^3. Sulfate data were only available for one other city (7.4 micrograms/m^3) which experienced lower illness absences. Although total suspended particulates were generally unrelated to respiratory illness, the cities with the two highest illness absence rates also had the highest concentrations of particulates (173 and 188 micrograms/m^3). The mean concentrations of nickel and vanadium (for 4 cities in which measurements were made) were found to be greater with higher rates of respiratory illness. Apparently age distribution, number of children in the household, local weather and climate, or occupational exposure do not account for the 5-fold intercity variation in incidence of respiratory disease. Mean annual sulfate concentrations, however, were based on but 21-25 determinations in 4 of the 5 cities for which data were

available which is a shortcoming of the study (Air Qual. Stat. Emm. Cont., 1975). However, the observed correlation of 0.964 was unusually high and strongly suggested an effect of suspended sulfat

A similar relationship was noted among employees at a Radio Corporation plant in Camden, New Jersey and a publishing company in Philadelphia, using visits to company dispensaries as an index of respiratory disease (Respiratory Disease Incidence Index), over a period of 15 months (Dohan, 1962). Weekly mean suspended particulate sulfate concentrations ranged from 12.7 - 36 microgms/m^3. The author suggested that several years of observation are needed to determine if there was a temporal relationship between fluctuation in incidence of respiratory disease and fluctuations in air pollutants.

Records of absences of 4 to 182 days attributed to bronchitis were used as an index of morbidity among nearby 60,000 London Transport employees during the years 1952-56. The occurrence of prolonged fogs was associated with an increase in sickness absence due to bronchitis. The lower morbidity in the county divisions tended to support the hypothesis of pollution as a factor in bronchitis. Some 20-25 percent of the overall sickness absence rate could be ascribed to air pollution according to a comparison of overall absences with those for a southern county division considered relatively pollution free due to prevailing winds. No measurements of pollution were made, however (Cornwall, 1961).

One hundred and fifty patients with chronic obstructive pulmonary disease were examined daily for 21 weeks (Spicer, 1962). Sputum analysis and lung function tests were included in the daily visit. Patients all became better or worse together, suggesting that some environmental factor was the cause. However, no consistent relationship between the patients' condition and atmospheric pollutants could be established.

In Cincinnati, a city with air pollution well controlled, Carey studied cardiorespiratory "cripples" by means of diary

sheets and various lung function tests (Carey, 1958). The preliminary results revealed a prolonged fall in carbon monoxide uptake about 5 days following a peak in air pollution. Six of the ten patients also showed an increase in symptoms 5 days after the first peak of smoke in their house. The number of patients studied was too small to draw any definite conclusions.

Becker reproted on an episode from November 23 to 25, 1966 on the eastern seaboard, with increased level of smoke and SO_2 (Becker, 1968). The subjects studied were workers at an insurance company in metropolitan New York City between the ages of 16 and 64. The subjects were divided into two groups: those without and those with prior respiratory disease, on the basis of employee physicals given to all employees at various intervals. A further subdivision was also made between smokers and nonsmokers.

During the episode period, a questionnaire was used to collect data on symptomatology. The response to symptoms such as cough, sputum production, eye irritation, and general discomfort increased with increases in pollution levels. Eye irritation was the single most common complaint. Persons with a previous history of respiratory diaase were significantly more affected by increased pollution than the normal participants.

No statistically significant differences in symptom response were observed between smokers and nonsmokers. Those smoking less than 10 or more than 20 cigarettes per day were found to have significantly greater symtom response compared to those smoking 10-20 cigarettes per day.

Heimann studied the November 1966 air stagnation period in the Boston metropolitan area and a period of less stagnation in October of the same year (Heimann, 1970). Data were collected on general population mortality, mortality and morbidity in nursing home residents, condition of neonates born to mothers pregnant during the episode, morbidity of a group of patients with chronic nonspecific respiratory disease, and data on the number of emergency room visits for heart disease and respiratory disease. Of the five different

measurements of health listed above, only one group showed adverse effects due to air pollution. This was in the group of patients having chronic nonspecific respiratory disease. In this group the number of visits to the clinic rose during the time interval after the air pollution episode and was especially increased in those living in the heaviest areas of pollution.

The levels of air pollution reached during the episode were not exceedingly high. The highest level for suspended particulates during the study was 222 microgms/m^3 and for SO_2, 12 - 40 ppm.

Cohen studied the presence of symptoms (eye irritation, throat irritation, cough, shortness of breath, chest pain or burning in the chest) during publicized and unpublicized air pollution episodes (Cohen, 1976). One hundred families from each of three communities with different pollution levels were interviewed by telephone. No significant difference was found in the incidence of symptoms between publicized and unpublicized episodes. Significant increases in eye and throat irritation, chest discomfort, and shortness of breath were noted in adults during the high pollution periods.

It was concluded that SO_2 levels above 0.11 ppm and suspended particulate levels above 145 mirogms/m^3 for a number of days could significantly increase irritative symptoms.

Holland reviewed pulmonary function, sputum production, and respiratory disease symptoms in male post office employees in Central London and three peripheral towns (Holland, 1965a). The over age 50 group in London had more respiratory symptoms, produced more sputum, and had significantly lower lung function test results. Corrections were made for smoking differences. Socioeconomic factors were presumed to be the same in the study areas. Occupational exposures were homogeneous. No quantitative air pollution measurements were presented, but it was concluded that the differences in respiratory morbidity

between the areas were related to differences in air pollution.

Holland also published a study on the prevalence of respiratory disease in post office workers in London compared with telephone company drivers in the U.S. (Holland, 1965b). A downward gradient was noticed in the prevalence of persistent cough and phlegm, and persistent cough and phlegm and chest illness from London to surrounding country areas to the U.S. The differences were most striking in the age group 50-59. In London, the results of the pulmonary function test ($FEV_{1.0}$) were lowest, with the higest value in the U.S.

The differences between the countries were attributed to the higher levels of pollution in England, although no quantitative measurements of air pollution were given. It was noted, however, that suspended particulates and smoke were at higher levels in London and the country towns than in the U.S. Examination of smoking habits revealed that this factor alone could not account for the differences.

Petrill reported the results of studies conducted in Genoa, Italy (Petrill, 1966). The frequency of respiratory disease symtoms were assessed by use of a modified British Medical Research Council questionnaire. Females age 65 and over who were nonsmokers and nonfactory workers were studied as well as an indigent population receiving free medical care.

Air pollution was monitored on a large scale in Genoa for 10 years. For these studies, air pollution data from 1954-1964 were used and indices of morbidity calculated for 1961 and 1962. The mean temperature was somewhat lower in the more polluted area.

A significant correlation was found between bronchitis and the mean annual SO_2 levels ($r = 0.98$). A nonsignificant correlation was found with suspended particulates ($r = 0.82$) and dustfall ($r = 0.66$).

In Rotterdam, Netherlands a study of male muncipal employees was conduced in 1966 (Biersteker, 1969). Information on

bronchitis symptoms was gathered through a questionnaire and peak expiratory flow rates were determined.

One hundred and eighty-one of 1,000 employees interviewed had chronic morning cough. The peak expiratory rates of males reporting symptoms were significantly different from the control group without symptoms. A significant difference was also found in the number of heavy smokers between those with bronchitis symptoms and the control group.

Exposure to air pollution was measured by the number of years of residency in Rotterdam, the number of years in a non-urban area, and the postal districts in which the subject resided. No differences were found between the bronchitis symptom group and the control group with respect to these variables. The authors concluded that the tool to measure the effect of air pollution may have been inadequate.

McCarroll published results of a study on the daily illness records of 1,090 well adults over the ages of 15 in New York City (McCarroll, 1965, 1967). The daily illness records were obtained by weekly interviews. The average length of participation for each person was 48 weeks. The population studied was from a restricted geographic area in New York City and was a mixture of white, black, and Puerto Ricans. Their housing ranged from middle income private homes to tenement slums.

Two main symptoms were assessed, cough and eye irritation. The population was analyzed in three groups, heavy smokers, moderate smokers, and nonsmokers. SO_2 and particulate density were used as indications of pollution. The data were analyzed by time-series analysis and the results were plotted in corregrams. SO_2 had an immediate effect in producing eye symptoms and a delayed effect in the production of cough. It was concluded that SO_2 was not the sole cause of cough and eye irritation, but was a contributing factor. Particulate density appeared to make no contribution to eye symptoms but did contribute to cough.

Two other studies have used data collected from the same New York population. Cassel attempted to clarify interrelationships between various environmental factors (Cassell, 1969). Seven meteorologic factors were considered along with particulate matter, hydrocarbons, CO, and SO_2. Using principle component analysis, five factors were derived. These factors showed the relationships among environmental variables and those between the environmental variables and reported symptoms. The difficulties in demonstrating a one to one relationship between an environmental factor and health were apparent.

Thompson using stepwise regression, attempted to relate the incidence and prevalence rates of the "common cold" to environmental variables such as SO_2, CO, particulate matter, temperature, humidity, wind velocity, barometric pressure, and solar radiation (Thompson, 1970). Results showed that meterologic variables appeared to be related more to common cold rates than did the pollutant variables.

Fletcher found a decrease in sputum production in a group of men followed between 1961-1966 (Fletcher, 1968). This decline was thought to be related to a decrease in particulate pollution in central London.

Using a random sample of white females in Buffalo, New York, Winkelstein studied the relationship between air pollution, respiratory symptomatology, and a history of bronchitis (Winkelstein, 1969). On repeat interviews to evaluate the reproducibility of anwers, it was found that questions relating to the persistence of cough and the history of bronchitis had low reproducibility. These characteristics were, therefore, excluded from the analysis. Air pollution data were collected from 21 sample stations. Isopleths were constructed showing four areas of differing concentrations of suspended particulates and three areas of varying SO_2 levels.

A nonsignificant positive association was found between cough with phelgm production and suspended particulates in nonsmokers age 45 and over. No association was found with oxides of sulfur.

When residential mobility of the population was considered, it was found that smokers with stable residential histories had a positive association between suspended particulates and cough with phlegm. Those having recently moved had an inverse relationship.

It is noted that the division of the area into four levels of graded ambient air quality was arbitrary and that a classification using the average values at each sampling site might have better delineated any real associations. Furthermore, the method of measuring SO_2 (lead peroxide candle) was rather crude and the range of values was narrow. The areas of high and low sulfation together accounted for only 39 percent of the total study population.

Using the British Medical Research Council questionnaire, a postal survey study of the prevalence of respiratory symptoms in England was conducted on a large sample of the population (Lambert, 1970). Although the sampling was not completely representative, the bias was considered to be minimal.

Only 30 percent of the sample lived in areas convered by the National Air Pollution Survey and even in these areas SO_2 measurements were not completely reported. All but 12 percent of the area had data on coal consumption. No reference was made to the monitoring devices used to measure the pollutants.

An increase in respiratory symptoms with aging and cigarette consumption was ound. Urban/rural gradients could not be explained by smoking differences alone. The results showed that increased cough and phlegm production in early adult life resulted from cigarette smoking. The cumulative effect of long time exposure to air pollution resulted in more serious bronchitic disease among the elderly.

It was found that air pollution exposure without prior cigarette smoking produced only a slight increase in chronic bronchitis in the over 55 age group. Occupational exposore to various pollutants was not considered.

In 1971, results were published of a follow-up study of data collected in 1961 in Berlin, New Hampshire (Ferris, 1971). The reason for follow-up was to ascertain whether changes in respiratory disease prevalence had occurred and if these were related to changes in air pollution levels.

A new random sample of the population was used in addition to the original sample. Data were collected through interviews and pulmonary function tests.

Due to the closing of some factories and stricter controls, pollution values were slightly less in 1966-67 than in 1961. The least change was noted for dustfall.

The results, after controlling for smoking, age, and sex, showed slightly lower levels of respiratory disease prevalence in 1967 than 1961. The forced vital capacity (FVC) in both men and women was significantly greater in 1967 than 1961. The forced expiratory volume in one second (FEV_1) had a less consistent pattern and the peak expiratory flow rate was slightly greater in 1967 than 1961. The failure of the FEV_1 test to show a consistent pattern similar to the FVC made the data from the FVC measurements less meaningful.

The small differences in disease prevalence noted from 1961 to 1967 were not felt to be due to observer differences between studies, the increased use of filter tip cigarettes or to normal random variations. It was concluded that the decrease in air pollution resulted in the changes.

In a later paper, Ferris noted that because of changes in smoking habits, the same kind of individuals were not being compared at both time periods (Ferris, 1973). An examination of those who had not changed their smoking habits over the study period, however, revealed again a slight decrease in respiratory symptoms.

A further follow-up study was published in 1976 dealing with the 1967 sample population. This group was felt to represent the healthier portion of the population (Ferris, 1976).

From 1967 to 1973 there was an increase in sulfation rate and a decrease in the concentration of particulates, these values being close to the Federal Primary Standard. In 1973-74 the mass respirable fraction made up 43 percent by weight of the total amount of suspended particulates. No data were available on particle size distribution in Berlin in the past.

No differences were found in respiratory disease prevalence or in the respiratory symptoms themselves when they were reviewed individually or in clusters between 1967 and 1973. It was concluded that the changes in levels of air pollution (1967-1973) had no associated beneficial effect on health and that present federal standards for SO_2 and particulates were adequate to protect public health.

Reichel conducted a survey of respiratory symptoms in three areas of West Germany, Duisburg, Bocholt, and Borken (Reichel, 1971). Dusisberg is a center for steel production and coal mining, Bocholt and Borken are rural areas.

No differences were found among the three areas in the prevalence of cough, sputum production or in lung function when the groups were standardized for age, sex, smoking, and social status. It appeared that possible occupational differences were not considered.

The SO_2 levels in the three areas ranged between 0.03 and 0.3 ppm with suspended particulates ranging from 0.01 to 0.39 ppm.

The prevalence of respiratory symptoms was ascertained by self administered questionnaires from 36,374 residents from seven areas with different pollution levels in Osaka, Japan (Tsunentoshi, 1971).

The prevalence of chronic bronchitis was found to be greater with the increasing levels of pollution. Based on these data, an increase of 2 percent would be expected in the prevalence of chronic bronchitis with an increase of the observed SO_2 of $1 mg/100 cm^2/day$. SO_2 levels under 1.0 mg/day were found to have no effect on prevalence rates.

A random sample of men and women selected from both a rural unpolluted and a polluted town was studied by questionnaire, lung function tests, intracutaneous allergy tests, sputum production, and chest x-ray (VanderLende, 1973).

No data were provided on the number of people involved in the study or on the levels of pollutants. In addition, meterologic factors were not considered.

The prevalence of persistent phlegm was higher in the polluted area than the rural area although no such disparity was evident for dyspnea. For those aged 15-39 an association between smoking and dyspnea was found in the polluted area. No significant relationship was found between smoking or pollution and FEV results.

The relationship of chronic respiratory symptoms and residence-associated air pollution were evaluated in a study of 4,377 male twins age 41-51 from the U.S.A. (Hruber, 1973). The advantages of twins in such a study include their similar characteristics, such as age and sex and, for many, their genetic equivalence.

Information on smoking, alcohol consumption, and socio-economic status was obtained by a mailed questionnaire. Air pollution exposure was measured by residence histories and by estimates based on emission and meterologic parameters. These estimates were obtained for SO_2, particulates and CO. No significant differences were found for respiratory symptoms between members of pairs when one twin lived in a more urban area than the other, or if one twin was exposed to higher measurements of air pollution. These comparisons were based on the twin pair having comparable smoking habits.

Neri conducted a study in two cities in Canada with different levels of air pollution. Sudbury, Ontario with a large nickel and copper smelter plant which emits considerably more SO_2 than the comparison city of Ottawa (Neri, 1975). Data on respiratory symptoms were collected by a questionnaire and measurements of forced vital capacity (FVC) and forced expiratory volume in one second ($FEV_{1.0}$) were made.

For both males and femals a significant difference was found between FEV_1/FVC ratios, with Sudbury having lower mean ratios than Ottawa. A higher prevalence of chronic bronchitis was found in Sudbury than Ottawa (97/1000 vs 77/1000) for both sexes combined. Males accounted for the greater share of the difference. No significant interaction was detected between air pollution and smoking.

A similar study impairing a polluted and unpolluted town was conducted in Hungary (Racaveanu, 1975).

A questionnaire was used to collect data on respiratory disease symptoms. Pulmonary function tests were also performed but the results of these were apparently not ready for publication. Subjects exposed to dusts, gases, or other irritating vapors were excluded from the study.

No values were given for levels of air pollution. The two cities were similar in climate, urbanization, and living conditions.

The prevalence of respiratory symptoms was found to be about two times higher in the polluted vs. the control town. Cough and sputum production was higher in both towns with higher proportions smoking. For these symptoms as well as wheezing and intercurrent chest diseases, smoking was a major risk faction; the risk for these symptoms being 3.5 - 6 times highers in smokers than non-smokers.

Grade III dsypnea was found to be almost three times more frequent in the polluted vs. control towns ($p < 0.001$) for both smokers and non-smokers and appeared to be more related to air pollution. It appeared that smoking and pollution had a synergistic effect.

In a study of the health effects of air pollution, Sterling used hospital data from the Blue Cross Association of Los Angeles (Sterling, 1966). All hospitals included in the study had at least 100 beds and were less than five miles from a pollution sampling station.

Four main disease categories were assembled to classify admissions: highly relevant diseases (allergic disorders, inflammatory diseases of the eye, acute upper respiratory infections, influenza, and bronchitis), relevant diseases (diseases of the heart, rheumatic fever, vascular diseases, and other diseases of the respiratory system), total relevant diseases (all of the above), and irrelevant diseases (all other diseases).

Suspended particulates, SO_2, CO_2, oxidant precursers, oxides of nitrogen, and ozone were measured.

A significant correlation was found between daily pollutant levels and admission rates for diseases grouped as highly relevant. Relevant diseases had fewer significant correlations with the most signficant correlation being with SO_2. When SO_2 was considered by itself, it was found that the number of admissions on days with high levels was greater than lower level days. For specific diseases the highest correlations were found for infectious diseases, acute upper respiratory infections, and bronchitis. Significant correlations were found between the length of hospitalization with highly relevant diseases, heart and central nervous system diseases and SO_2, NO_2, total oxides of nitrogen, and particulate matter. Since the day of the week was related to hospital admissions independent of other factors and since length of hospitalization was effected by the day of the week appropriate adjustments were made to the data. However, no consideration was given to seasonal fluctuations in hospitalization or pollution levels.

A study conducted by the British Ministry of Social Insurance used illness related absenteeism to assess the effects of pollution on health (Ministry of Pensions, 1965). Incapacity to work due to bronchitis was found significantly correlated with smoke and SO_2. The winter average concentrations ranged from between 100 and 200 microgms/m^3 to about 400 microgms/m^3. Also of interest in this study was that incapacity from arthritis and rheumatism was greater in the areas with heavy smoke pollution.

Verma collected illness-absence records from white collar workers of an insurance company in New York, 1965-1967 (Verma, 1969). The data were divided into respiratory illness-absences and non-respiratory illness-absences.

Multiple regression was used to related time, pollution, and climatic variables to the number of absences. All data were found to be influenced by a strong time dependence and yearly cyclical behavior. After removal of these factors, no strong positive relationship was found between respiratory illness absence and pollution as measured by smoke and SO_2.

Ipsen studied absenteeism in two industries in Philadelphia, for the period September 1960 to December 1963 (Ipsen, 1969). The data were collected weekly from the company dispensaries. Both air pollution and meteorologic factors were considered.

No significant independent association of any of the pollutants with morbidity, as measured by the incidence and prevalence of respiratory disease was found. The analysis demonstrated that weather had a major effect on respiratory morbidity. The place of residence of the worker was not taken into consideration, nor were actual monitoring data on pollutants presented.

In 1969 Ishikowa published the results of a study assessing the prevalence and severity of pulmonary emphysema in two cities (Ishikowa, 1969). Data were obtained from pathological studies on 300 lungs obtained at autopsy in the two cities. Lungs from cases who had occupational exposure were excluded.

More emphysema was found in St. Louis (industrial urban community) than Winnipeg (prairie-agricultural city). In neither city were severe cases of emphysema found in nonsmokers. In smokers severe emphysema was four times as high in St. Louis as in Winnipeg. It was concluded that the development of emphysema may be related to the synergistic effects of smoking and pollution. Other authors have felt that the data fit an additive better than a synergistic model.

Some studies used a population already affected with respiratory diseases to assess air pollution effects. Angel in London studied respiratory symptoms in 85 men, the majority with some evidence of chronic bronchitis (Angel, 1965). The 85 were selected from a group of 1,000 men aged 30-59 who were factory and office workers. These men were seen by a physician at least once every three weeks from October, 1962 to May, 1963. Air pollution, temperature and humidity data were collected. The smoke and SO_2 data were obtained from 12 sites. However, exact methods of monitoring these measurements were not presented in the paper.

Smoke appeared more strongly associated with the prevalence of respiratory illness than either SO_2 or temperature. Smoke and SO_2 were equally strongly associated with the attack rate of respiratory illness.

In another study in Chicago, 115 patients with the emphysema-bronchitis syndrome completed daily diary forms on the severity of cough, sputum production and dyspnea (Burrows, 1968). Marked seasonal fluctuations in the severity of symptoms were found. No significant correlation was found between air pollution measured by CO, SO_2, NO_2 nitrous oxide and hydrocarbons and the severity of symptoms. Even with these findings, the author does not deny that prolonged exposure to pollutants may aggravate or induce chronic bronchitis.

Carnow, using cardiopulmonary patients who recorded their daily health status, studied the dose-effect relationship between SO_2 and morbidity from respiratory disease in Chicago (Carnow, 1969). Each patient was classified into one of seven levels of exposure to SO_2. For those aged 55 years and older with Grade 3 or 4 bronchitis, the rate of acute illness with exposure to 0.25 ppm SO_2 was 50 percent greater than the rate at levels of 0.04 ppm or less. The differences in illness rates were even greater when illness occurring the day after exposure was considered. Those under age 55 did not have constantly greater illness rate with increasing SO_2.

Using patients as their own controls, significantly higher levels of SO_2 were found on the days preceding the illness than days preceding no illness. It was concluded that exposure to high levels of SO_2 was associated with the occurrence of acute respiratory illness in elder chronic bronchopulmonary disease patients.

In England, Gregory surveyed exacerbations of disease in 340 cases of chronic bronchitis in male employees at a Sheffield steel works (Gregory, 1970). Data were collected through sickness absence records. Smoke, SO_2, relative humidity, and temperature were measured.

Analysis of the data by monthly averages revealed a positive correlation between smoke and SO_2 with monthly illness rates. A negative correlation was found with temperature. The correlations with air pollution were assumed to be influenced by a dependence on temperatures which appeared to be the dominant factor.

A separate analysis was made of weekly averages of temperatures in the winter of 1957-1958. Temperature was found to correlated inversely with the prevalence rate of illness in the following week, and maximum and mean smoke pollution correlated with the incidence rate of the succeeding week. Both for monthly and weekly calculations temperature was associated with the prevalence rate. These low temperature correlations were considered to reflect the delay in returning to work of those already absent because of illnes. Smoke pollution was concluded to be a causative factor in exacerbations of bronchitis.

Lawther in London, observed daily changes in the conditon of bronchitis patients and pollution levels (Lawther, 1970). Data were collected through diaries completed by the patients. His paper presented results from a number of studies conducted in this manner. Studies carried out in 1955-1958 showed a correlation between pollution episodes and illness.

In 1959-1960 a study of over 1,000 cases showed a definite illness response for every episode of pollution greater than 1,000 microgms/m^3 (smoke and SO_2). The lowest concentration at which adverse effects occurred was about 600 microgms/m^3. A determination of which pollutant was more important was not possible.

In 1964-1965, further studies were carried out on 1,037 patients. Smoke concentration during this time had been significantly reduced with little change in SO_2. In evaluating peak pollution epidsodes from 1959-1960 and 1964-1965 with peak illness occurrence, definite relationships were observed.

The minimum pollution leading to a significant response was 500 microgms/m^3 of SO_2 together with 250 microgms/m^3 of smoke (24 hour average concentrations). The results also indicated that pollution rather than adverse weather was associated with illness exacerbations. It was not possible to assess the relative importance of either the SO_2 or the smoke in causing the illness responses.

Eighteen patients with varying degrees of chronic bronchitis were studied by Emerson (Emerson, 1973). Measurements were made of lung function at intervals of a week or more for 12 to 82 weeks. Temperature, humidity, barometric pressure, and wind were measured along with smoke and SO_2.

No significant correlations were found between FEV_1 and smoke levels and a significant correlation between FEV_1 and SO_2 occurred in only one patient. The most significant correlations were with temperature. The reason given for the lack of a correlation with pollution was that peak levels of smoke and SO_2 were not high enough or long lasting enough. The peak levels of SO_2 and smoke being 722 microgms/m^3 and 380 microgms/m^3 respectively.

Spicer conducted two similar studies of 14 bronchitis and asthma patients (Spicer, 1966). The patients as a group showed rises and falls in airway resistance suggesting some environmental influences but it was not possible to separate out an individual pollutant or meterological factor.

A further study in 1970 on healthy subjects revealed little correlation of respiratory function and air pollution (Spicer, 1970). Subjects with a history of asthma had significantly higher airway resistance levels even though asymptomatic at the time of the study.

Howard studied 178 patients (158 men and 20 women) with obstructive airway disease in Sheffield, England (Howard, 1974). Using questionnaire and pulmonary measurements for $FEV_{0.75}$ and FVC, a compariosn was made with similar patients from an earlier study. The present group had less productive cough, fewer winter illnesses, less severe dyspnea, and only one-third the rate of decrease in FEV. The findings were attributed to decreases in pollution levels which supposedly occurred between the study periods.

A study by Kalpazanov observed the effects of air pollution on the influenza epidemic 1974-1975 in Sofia, Bulgaria (Kalpazanov, 1976). SO_2 levels on the day of illness and the day before illness were found to be significantly correlated with the number of influenza cases. The range of SO_2 observed was .798 - .913 mg/m^3. Nitric oxides, oxidants, and formaldehyde were also shown to have an effect on the number of cases. The author made note of the fact that these data were valid only for the city of Sofia or other cities with similar climate, geographic and social conditions.

Another respiratory disease which has been the focus of air pollution studies is bronchial asthma. This is a disease characterized by attacks of marked hyperconstriction of the bronchioles resulting in a wheezing and gasping for breath. As with other respiratory disease, it is difficult to provide a clearcut definition of the disorder.

Many factors have been implicated as causes for bronchial asthma, particularly a wide variety of allergens. Meteorologic factors such as rapid decline in temperature have also been associated with promoting attacks. Among children emotional factors are thought to be of importance (Zeidburg, 1961).

With so many variables, it becomes difficult to establish adequate controls. Possibly due to this problem, investigators have often used "panels" of asthmatic patients for study, relying on the patients' reporting of asthmatic attacks. However, a great deal of error is introduced by this means. Each individual's defintion of an "asthmatic attack" varies to some degree according to the amount of wheezing or discomfort they are accustomed to. When using self reporting by patients, errors inherent in subjective evaluation cannot be avoided.

In a study of 49 adults and 35 children with bronchial asthma in Nashville, Tennessee, Zeidberg used a self-reporting technique to determine when asthmatic attacks were occurring (Zeidberg, 1961). He found that of all the meteorologic factors measured - temperature, humidity, barometric pressure, and wind velocity - only wind velocity showed any relationship with the attack rate. Wind velocity was inversely related to attack rates, as would be expected if air pollutant were related to asthmatic attacks. Sulfation levels were directly related to attack rates in adults but not in children. When attack rates on days with high and low SO_2 levels were compared, there were significant differences between them.

To determine whether asthmatic attacks were related to air pollution levels, a group of 157 patients with bronchial asthma was requested to mail reports of the onset of every attack experienced from September 3 to December 9, 1956, to their physician (Schoettlin, 1961). These reports were mailed weekly by 137 patients. Low positive correlations were found between oxidant levels and the number of persons having attacks. When oxidant levels were high enough to cause eye irritation (25 ppm), significantly greater number of persons had attacks. Temperature, relative humidity, and water vapor pressure also showed low correlations with the number of attacks occurring.

Severe outbreaks of asthma have occurred in New Orleans. From studies of the outbreaks occurring in 1955 and 1958, Lewis indicated that these outbreaks were associated with point sources of air pollution (Weill, 1966). The point source implicated was spontaneous underground buring in city dumps.

In a study on Tulane students and hospital patients in New Orleans, scratch tests were employed to determine the allergenic properties of plume extracts from the dump (Weill, 1964). The extracts appeared allergenic. This lent support to the importance of the emissions from the Agriculture Street dump as a factor in epidemic asthma in New Orleans.

A peculiar type of asthma known as "Yokohama asthma" has been reported in U.S. army hospitals in Yokohama, Japan since 1946. The disease was sufficiently dissimilar to any asthma found in the United States to warrant studies into its etiology. In looking at the meteorologic data, only wind velocity, precipitation, and temperature inversion appear to be statistically related to incidence of this disease. Incidence of this respiratory disease also appeared to be related to concentration of air contaminants and smog formation. Sulfur dioxide, ozone, nitrogen oxides, ether-soluble aerosols, and dust were investigated, but only ether-soluble aerosols and dust appeared to have a significant correlation with the incidence of this disease (Huber, 1954).

A study of approximately 2,000 Japanese employees in the Tokyo-Yokohama and Niigata area of Japan failed to find any cases of "Yokohama" asthma (Oshima, 1963). However, residents of the Tokyo-Yokohama area, the area of highest pollution, experienced increased incidence of sputum production, chronic cough and throat irritation. Persons working in the most heavily polluted area also had the lowest mean vital capacity. Overall, the results indicated that prolonged exposure to heavy pollution was associated with increased respiratory symptoms.

Greenburg using asthma visits to emergency clinics in New York, found that an increase in visits was not related to pollution levels of SO_2, smoke shade or CO (Greenburg, 1965). A correlation was found between increases in visits and a preceding drop in temperature. Also, a significantly greater proportion of visits was found among Negroes and Puerto Ricans than Whites.

Brown studied 314 persons with allergic rhiniti asthma or both in an effort to measure the severity of symptoms in relation to pollution (Brown, 1968). Mesurements were made of SO_2, particulates and smoke. Meteorologic measurements were also collected. The air pollutants were found to have no significant effect on the severity of symptoms. A trend, however, was noted for patients with non-ragweed allergic rhinitis to have increased symptoms with more particulate matter in the air.

Smoke measurements were obtained and an index of acute asthma was provided by visits to the emergency room of a Brisbane hospital (Derrick, 1970). Asthmatics in Brisbane showed a characteristic seasonal pattern of attacks. No significant association was found between smoke density and the number of weekly hospital visits. It was concluded that pollution measured by smoke did not contribute to seasonal or short term increases in asthma attacks. The levels of smoke observed in Brisbane were lower than those related to smog illness episodes.

Variation in frequency and severity of attack was observed in relation to air pollutants in a study of 84 cases of bronchial asthma (Landan, 1971). The subjects recorded daily the time and place of any attacks and any medications used. Meteorologic as well as pollution data were collected.

The most important variable of association was found to be "day from beginning of study", a variable obviously composed of a number of factors and of little predictive value without delineation of the contributory components. The next most important variable was the level of SO_2. No specific levels of SO_2 were reported in the study. The author concluded that the study suffered from a lack of pollen measurements. Another problem noted was that some asthmatics had no attacks at all during the study.

Cohen evaluated air pollution from a coal-fueled power plant and its relation to the frequency of asthma episodes in 20 patients (Cohen, 1972). Questionnaires were administered and daily reports on attacks were kept by the subjects. Suspended particulates, SO_2, and soiling index were measured.

Significant correlations were found between asthmatic attack rates and temperature ($r = 0.422$), SO_2 ($r = 0.32$), and soiling index ($r = 0.387$). Significant differences in attack rates were found between high and low pollution days and high and low temperature, humidity and windspeed days .

After the effects of temperature were removed, significant correlations remained between pollution levels and attack rates. A single pollutant could not be singled out as the prime cause of the asthma attacks. The levels of pollution involved were levels frequently found in large cities.

Sixty-eight colleges and universities reported on the number of cases of spontaneous pneumathorax found and the type of heating fuel used on the campus (Marienfeld, 1974). A significant association was found between oil and coal fueled power plants and the incidence of spontaneous pneumathor in college students.

The mechanism beyond the association may involve the absorption of acids on carbon particulates which are inhaled and result in chemical cauterization of the pulmonary epithelium. Since no measurements were taken of the amount of air pollution around the universities, the relationship was based solely on the type of fuel used. Also, the incidence of spontaneous pneumothorax was found to be more than twice as high in metropolitan colleges and universities than in such institutions in non-metropolitan areas.

A number of epidemiologic studies dealing with air pollution and health effects have been published under the acronym of CHESS (Community Health and Environmental Surveillance Systems). This is a national program of studies, the purpose of which is to evaluate existing pollution standards.

Studies were conducted in Los Angels, Salt Lake Basin, St Louis, New York/New Jersey, Chattanooga, and Birmingham/ Charlotte areas. The following studies are all part of this program. House, in a Salt Lake Basin study observed the effect of SO_2 and suspended sulfate on the prevalence of chronic respiratory disease symptoms. The four communities studied were near a large copper smelter, with the closest community 5 miles from the smelter and the farthest 38 miles. Data were collected by a self administered questionnaire on respiratory symptoms.

A significant increase in the prevalence of chronic bronchitis was found in smokers and non-smokers after an exposure of 4 to 7 years to elevated levels of SO_2 of 92-95 microgms/m^3 and suspended sulfates of 15 microgms/m^3, this being accompanied by low levels of suspended particulates (53 to 70 microgms/m^3). The effects of smoking and air pollution appeared to be additive. Occupational exposure to various pollutants was found to be a strong determinant of illness after age 40, having twice the effect of pollution and over half the effect of cigarettes. Hayes selected five communities in the Rocky Mountain Area, three with smelters and two without a smelter and no major air pollution sources. Data were collected by self-administered questionnaires. Those with occupational exposure to pollutants were excluded from the study.

Results showed that the smelter-exposed communities had a significantly greater prevalence of chronic bronchitis than non-exposed communities. Prevalence rates were 2.4 to 2.8 times greater in non-smokers in the smelter communities than non-smokers in the low exposure communities. Bronchitis was not found to be more severe in the high exposure areas. Smoking and pollution were again found to be additive. The effect of smoking on chronic bronchitis was found to be seven times stronger than that of air pollution.

The concentrations of pollutants leading to excess bronchitis were estimated at 177 to 374 microgms/m^3 for SO_2 and 7.2 to 19.9 microgms/m^3 for suspended sulfates.

A study of military recruits was conducted by Finklea as part of the Chicago-Northwest Indiana Studies. Self administered questionnaires were used to examine chronic respiratory symptoms. Chronic bronchitis rates were found to be higher in recruits from more polluted urban areas than recruits from rural areas. The excess in bronchitis rates was much smaller than found in other CHESS areas. Exposure for 12 years or more to levels of SO_2 of 96 to 217 microgms/m^3, suspended particulates of levels of 103 to 155 microgms/m^3 and suspended sulfates of 14 microgms/m^3 was found related to greater prevalence of respiratory symptoms.

Goldberg in New York again reviewed the prevalence of chronic respiratory disease symptoms. Three areas with different pollution levels were examined. Exposure up to 20 years to SO_2 levels of 144 to 404 microgms/m^3 and suspended sulfate levels of 9 to 24 microgms/m^3 were found related to greater prevalence of chronic bronchitis. This was found to be true for both sexes of ages 20 to 50 among smokers and non-smokers. In all the above studies, age, race, sex, socioeconomic status and occupational exposure were controlled. From the above data it was concluded that excess bronchitis appears associated with SO_2 levels of 92 to 95 microgms/m^3 and 15 microgms/m^3 suspended sulfates. These data are in support of the National Primary Ambient Air Quality Standards.

Another study by Goldberg, in New York, dealt with elderly subjects who were divided into four groups: the well, with heart disease, with lung disease, and with lung and heart disease. Diaries were used to collect daily data on symptoms present. Temperature and suspended particulates were measured.

In heart disease panelists' elevations in temperature were related to worsening of symptoms. Decreases in temperatures were related to induction or aggravation of symptoms in all other groups. Findings suggested that short term exposure to

SO_2, suspended particulates, and suspended sulfates may adversely effect health in the elderly even after current air quality goals are reached.

Suspended sulfates were found to have the most consistent and strongest association with aggravation of symptoms. The threshold level of suspended sulfates was estimated as 10 micrograms/m^3.

Stebbings using daily diaries studied panels of sick and well elderly in New York City (Stebbings, 1976). Increasing temperatures were found to aggravate symptoms in heart disease panels. No clear consistent relationship was found for the other panels. The well elderly panel had exacerbations of symptoms with elevations in the levels of suspended nitrates, suspended sulfates, SO_2, and suspended particulates. A weaker pattern was noted in the lung disease panel. Heart disease symptoms were found related only to suspended nitrate and total suspended particulates. No thresholds of effects for the pollutants were established. Finklea studied panelists of asthmatics in two different areas, Salt Lake City Basin and New York. In both studies patients recorded daily attacks of asthma in diaries.

The Salt Lake Basin study found total suspended particulate and suspended sulfates had significant effects on attack rates at minimum temperatures greater than 30°F. Suspended sulfate had the greatest effect. Temperatures alone were found to have a more constant correlation than any measured pollutant. The threshold level for suspended particulates was 107 micrograms/m^3 and 17.4 micrograms/m^3 for suspended sulfates at temperatures of 30° to 50°F.

In New York, asthma attacks were linked to suspended particulates and suspended sulfates. Also temperatures of a more moderate degree were related to attacks rather than colder temperatures such as was found for the Salt Lake region. The estimated threshold for suspended particulates was 56 micrograms/m^3 and 12 micrograms/m^3 for suspended sulfates.

TABLE 10

EPIDEMIOLOGIC STUDIES ON THE EFFECTS OF SO_2 AND PARTICULATES ON MORBIDITY

Source	Population	Method	Exposure				Result
			Particulate	Smoke	SO_2	Other	
UNITED STATES							
Carey 1958	10 cardio-respiratory cripples Cincinnati, Ohio	1) nurse visits 3 times/week 2) diary sheets 3) lung function testing a) TVC with 2 portable bellows spirometer b) MEP and MIP with modified aneroid gauge c) CO diffusion with box-bag 3 months	not stated	outdoor average 3.8 coh/1000 linear feet mean value for patients 2.1 coh/ 1000 linear feet	not stated	total gaseous acid outdoor average .047 ppm indoor average .024 ppm	preliminary findings: 1) TVC and pulmonary pressures do not clearly show changes in patients considered as a group 2) after a peak in air pollution the individual patient shows a decline in mean CO uptake 5 days later
Schoettlin 1961	137 patients with bronchial asthma M & F all ages Pasadena, Calif	weekly reports on asthma attacks completed by the patient for 98 days	measured but not given	not measured		CO measured Total oxidant measured	1) midnight to 6 am was the peak period for attacks of asthma 2) oxidant levels, temperature, relative humidity, and water vapor pressure showed low positive correlation with attack of asthma

Source	Method		Exposure				Result
			Particulates	Smoke	SO_2	Other	
Dohan 1961	female employees of the Radio Corporation of America 5 U.S. cities	illness-absence lasting more than 7 days. Followed for 3 years.	range 101-188 $\mu g/m^3$	not measured		sulfates 7.4-19.8 $\mu g/m^3$ copper .16-1.18 $\mu g/m^3$ nickel .013-.025 $\mu g/m^3$	1) incidence of respiratory disease significantly correlated with mean sulfate concentrates ($r = 0.96$) 2) no correlation found between respiratory disease rates and concentrations of zinc, copper, nitrates, benzene, soluble organic matter or suspended particulate matter 3) respiratory disease rates increased with increasing nickel and vanadium concentrations (4 cities)

ource	Population	Method	Exposure				Result
			Particulates	Smoke	SO_2	Other	
chan 1962	employees at 5 locations	Total number of individuals visiting the dispensaries where they worked weekly (RDII) (61 weeks)	not stated	not stated	not stated	sulfates weekly mean range 12.7-36 $\mu g/m^3$	1) weekly respiratory disease incidence index (RDII) for employees in adjacent cities show a high correlation which suggests that an environmental factor is playing a role 2) sulfate concentration possibly related to RDII
	Bell Telephone Company employees M & F Pittsburgh, Pennsylvania	absence for illness lasting more than seven days. July 1, 1935 to June 30, 1958	not stated	decline 1005-4100 hours of smoke	not stated	not stated	1) data suggest improvement in illness rates in Pittsburgh is a result of marked decrease in air pollution

Source	Population	Method	Exposure				Result
			Particulates	Smoke	SO_2	Other	
Zeidberg 1961	49 adults and 35 children with bronchial asthma; White and nonwhite; M & F Nashville, Tenn.	1) self recording of attacks mailed in weekly 2) pulmonary function tests on 34 adults, 22 children	Total 110.96 - 195.73 σ/m^3	.331 - 2.45 COHS/ 1,000 ft	0 - .042 ppm	Sulfation I. 0 - .149 II. .150 - .349 III. .350 and over $mg/100\ cm^2$/ day	1) in adults, the asthmatic attack rate varied directly with the level of sulfation in the residential environment. 2) wind velocity showed inverse relationship with attack rate. Temperature, humidit and barometric pressure apparently had no influence. 3) attack rates on days with highest SO_2 value were significantly higher than on days with lowest SO_2 values
Rokaw 1962	31 chronic respiratory patients Los Angeles hos ital	1) preliminary evaluation 2) pulmonary function a) VC, timed VC 3 sec, FRC measured with Collins 9-liter spirometer b) airflow velocity (FEV and cough) Silverman pneumotachograph	measured but not given	not stated	not stated	NO NO_2 CO O_2 measured	1) only 6 of the 31 showed correlation with pollution level 2) in 4 patients CO was possibly involved 3) analysis did not indicate a strong relationship between pulmonary performanc and the way the patient evaluated hi feelings about his respiratory disease at t f test

Source	Population	Method	Exposure				Result
			Particulates	Smoke	SO_2	Other	
Rokaw 1962		3) end-tiol and "rebreathings" CO_2 tension 4) airflow velocity Silverman pneumotachograph					4) 1 patient showed significant decay in pulmonary function prior to death
Spicer 1962	150 patients with obstructive airway disease 20-65 yr Baltimore	1) clinical exam daily a) Ra b) MEFR c) lung volumes body plethysmograph for 21 weeks	not stated	not stated	measured	NO_2 dirt measured	1) patients became better and worse at the same time suggesting that the change is due to environmental factors, possibly pollutants. 2) was not possible to find one pollutant that was responsible
			All measured 2 hr sampling but not presented in form that can be quoted				

Source	Population	Method	Exposure: Particulates	Smoke	SO_2	Other	Result
Prindle 1963	462 male and 486 female; ≥ 30 yr two communities in west central Pennsylvania	1) lung function tests 2) chest x-ray 3) questionnaire	NEW FLORENCE 109 µg/m^3	1.5 COHS/1,000 ft.	.01 ppm	sulfation 6 mg SO_3/100 cm^2/day dustfall 26 tons/mi^2/mo	1) average airway resistance and airway resistance X volume statistically different between the 2 communities after differences in height and guage were accounted for. May reflect difference in air pollution level
			SEWARD 151 µg/m^3	2.3 COHS? 1,000 ft.	.09 ppm	dustfall 83 tons mi^2/mo sulfation 37 mg SO_3/100 cm^2/day	2) more males with pneumoconiosis in Seward, more males with emphysema in New Florence
Ferris and Anderson 1964	558 adults 25-74 yr Chilliwack, British Columbia 1963 compared with Berlin, New Hampshire 1960	1) questionnaire interviewer (May-June '63) 2) pulmonary function a) FVC b) $FEV_{1.0}$ with Wright's peak flow meter	not stated	CHILLIWACK <.5 COHS/1,000 ft	average 1ppb	sulfation rate 50.3 SO_3 mg/100 cm^2/day dustfall 10.4 tons/mi^2/30 day	1) more respiratory symptoms and lowered lung function observed in Berlin (more polluted area)
			not stated	BERLIN .5 COHS/1,000 ft	not stated	sulfation 426 mg SO_3/100 cm^2/day dustfall 34.9 ton/mi^2/30 day	2) difference cannot be entirely explained by smoking difference but might be explained by ethnic differences

Source	Pop.	Method	Exposure				Result
			Particulates	Smoke	SO_2	Other	
Anderson 1964	1,261 25-74 yr 3 residential areas Berlin, New Hampshire	1) questionnaire similiar to one used by the British general practitioners survey 2) pulmonary function a) FVC b) $FEV_{1.0}$ Collins 61 recording vitameter c) PEFR Wright peak flow meter	Not stated	Not stated	range 5-17 ppb	dustfall ton/mi^2/ 30 days a) Total 20.5-46.7 b) insoluble 11.9-25.4 c) soluble 5.6-21.3 d) sulfate 2.3-10.6	1) prevalence of respiratory disease and pulmonary function abnormalities was not clearly or consistently related to pollution. 2) previous analysis of the data indicated that cigarette smoking was a more significant factor than air pollution.
Neill 1964	1) 118 students of Tulane University 2) hospital patients New Orleans	1) questionnaire 2) ventilatory test a) lung volume b) expiratory flow 3) scratch tests	No measurements made				1) plume extracts probably allergenic 2) higher reaction in those currently with symptomatic asthma

Source	Population	Method	Exposure				Result
			Particulates	Smoke	SO_2	Other	
				geometric mean			
Leidberg 1964	2,833 households white and nonwhite Nashville, Tennessee	1) interviewer administered questionnaire	24 hr a) ≤100 b) 101-199 c) ≥200 $\mu g/cm^3$	24 hr soiling index a) ≤.330 b) .331-.83 c) ≥.831 COHS/1,000 ft	24 hr a) ≤.005 b) .0051-.01 c) ≥.0101 ppm	dustfall a) ≤ 5 b) 5.01-15 c) ≥ 15 tons/mi^2/mo sulfation a) ≤ .15 b) .151-.35 c) ≥ .351 $mg/100cm^2$/day	1) morbidity consistently correlated with soiling index and SO_2 level in those ≤55 yr in the middle socioeconomic class 2) in those over 55 yr air pollution correlated with cardiovascular disease but not with respiratory disease 3) direct correlation between morbidity and white females who keep house and all nonwhite females

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
olland 965	Number of men available for survey: London 281, country area 455, USA 708	Post office van drivers in London and three English country towns compared to telephone company drivers in U.S. Completed questionnaire for respiratory symptoms. Given lung function test (FEV 1.0) and sputum sample collected	Both of these pollutants are at higher levels in London and English country towns than USA cities.				Found a British excess in the prevalence of respiratory disease, als a lower $FEV_{1.0}$ and increased sputum in Britain over USA. Attri buted possibly to the higher levels of pollution in England vs. USA.
terling 966 162	Males and females Los Angeles	Hospital admissions data obtained from Blue Cross Association Los Angeles 27 disease categories looked at. 223 days analyzed 3-17-61 to 10-26-61	Graphs only of distribution pattern by day of the week	Not stated	Graphs only of distribution pattern by day of the week	Graphs only CO_2, NO_2, oxidant precursors, oxides of nitrogen, ozone, nitrogen oxidants	Significant correlation between pollutants and admission rates for diseases grouped as highly relevant. Relevant diseases had fewer number of significant correlations, one consistent correlation was with SO_2. Concluded air pollutants exert a considerable effect on hospital admissions for certain diseases.
terling 967	Males and females Los Angeles	Length of hospitalization. Data obtained from the Blue Cross, Los Angeles 223 days analyzed 3-17-61 - 10-26-61	Same as above		Same as above	Same as above	Significant correlation found with diseases grouped as highly relevant, relevant and heart and central nervous system disease categorie for length hospital stay and SO_2, NO_2, total oxid of nitr[illegible] and particulate [illegible]

Source	Population	Method	Particulates	Smoke	SO_2	Other	Results
McCarroll 1967	1,090 normal adults over age 15 New York City	Daily illness records obtained by weekly interview	Graphs only of frequency distribution	Not stated	Graphs only of frequency distribution	Not stated	Correlograms showed SO_2 having an immediate effect on eye irritation symptoms and a delayed effect on cough production. Particulate density appeared to not contribute to symptoms of eye irritation but to contribute to production of cough.
Brown 1968	314 patients with asthma, rhinitis or both. 86 persons were under age 15. Philadelphia	Measurements of changes in severity of symptoms recorded daily in diaries August 1-November 1, 1963	No specific measurements given. Data presented in graph form.				Calculation of correlation coefficients showed no significant relation of the three pollutants to severity of symptoms. A trend was noted for non-ragweed allergic rhinitis cases to have increased symptoms with increasing levels of particulate matter.
Burrows 1968	115 patients Chicago, Illinois 1963-1964	Patients with emphysema -bronchitis syndrome recorded daily in a diary severity of symptoms (cough, sputum production & dyspnea)	No specific measurements given				Found no correlation between air pollution and severity of symptoms; ye author contends it canno be denied that long time exposure to air pollutan may lead to an aggravation or initiation of chronic bronchitis

ource	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
ecker #68	2,052 subjects male and female employees of insurance company age 16 - 64 New York City	Data collected from physical exams given to all employees at certain intervals depending on age. Questionnaire collected data on symptoms for five day period Nov. 23 - Nov. 27, 1966	not measured	Highest mean concentration observed 6.0 coh	Highest mean concentration observed 0.52 ppm	not measured	Response to symptoms such as cough, sputum production, eye irritation and general discomfort increased with increases in pollution levels. Persons with a previous history of respiratory disease were significantly more affected by increase pollution than normal participants. Breaking respiratory diseases into two groups chronic obstructive pulmonary disease and other respiratory disease, four those with chronic obstructive pulmonary disease had increased response to all symptoms except general discomfort when compared to other respiratory group. (Statistically significant at 5% level)

rce	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
rma 69	Males and females ages 16-64 New York City	Illness-absence data collected on workers in an insurance company 1965-1967	Not stated	2.7 COHS (7 year mean)	0.18 ppm (7 year mean)	Not stated	Found all data influenced by strong time dependent and yearly cyclical behavior. After removal of this trend no strong positive relationship found between respiratory illness absence and pollution variables. Statistical models suggest that even though no causal association inferred there is a relationship from one time period to another between respiratory illness absence, air pollution, and climate variables.
sen 69	Males and female Philadelphia	Illness-absence data collected on workers in two Philadelphia plants. 156 weeks analyzed. Weekly reports of symptoms of respiratory disease were reported from the company dispensaries	Not stated	Not stated	Not stated	Not stated	No significant independent association of any of the pollutants with morbidity found.
		Daily records of absenteeism collected from medical department of Bell Telephone Company, N.Y. Sept. 1961-Dec. 1963 850 daily consecutive measurements.	No specific values given.				Found high morbidity is preceded by a week of air pollution which exceeds the normal seasonal level.

ource	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
arnow 969	561 patients with chronic broncho-pulmonary disease Chicago	Patients reported on dates of duration of respiratory illnesses. October, 1966-January, 1968	———	———	———	———	In cases 55 years and older, with grade 3 & 4 chronic bronchitis, the rate of illness occurrin with exposure to 0.25 pp or more SO_2 was 50% greater than rate found with exposure to 0.04 pp or less. Differences in rate of illness between these levels was even greater when illness occurring day after exposu was used. Ages under 5 grade 3 & 4 did not have steady increase in illness rate with increasi SO_2 but rates at SO_2 levels of 0.30 ppm or more were higher than rates associated with levels of SO_2 0.04 ppm or less. Using patient as own control found SO_2 levels sign. higher for the day preceding the illness than day preceding no illness.

urce	Population	Method	Exposure: Particulates	Exposure: Smoke	Exposure: SO_2	Exposure: Other	Results
nkel- ein 59	842 white females age 25 and over Buffalo, N.Y.	1961-1963 Questionnaire and interview regarding respiratory symptomatology	4 levels I <80 II 80-100 III 100-135 IV >135 µg/cu m/24 hrs	Not stated	Not stated	Oxides of sulfur 3 levels I <0.30 II 0.30-0.45 III >0.45 mg/ sq cm/30days	Non-smokers 45-64 and a 65 and over had positiv association between pre valence of cough with phlegm and the level of suspended particulates ($0.25>p>0.10$) not found among smokers. For oxi of sulfur no such asso-ciation found. When resi dential mobility consid ered found smokers who had not recently moved had positive associatio with suspended particu-late pollution for coug with phlegm. An invers association found for smokers who had moved ($p<0.01$).
idau 71 shville : Pol- tion idy	84 cases of bron-chial asthma white and nonwhite children and adults apparently Nashville	July 14, 1958-July 12, 1959 weekly reports of time of onset, end of attacks, place of occurrence and medication recorded daily by subjects and mailed weekly	Not stated	Not stated	Not stated	Not stated	Most important indepen-dent variable associate with asthmatic attack was found to be "day fr beginning of study". The next important vari-able was found to be SO it being less significa in its contribution.

Source	Population	Method	Exposure: Particulate	Exposure: Smoke	Exposure: SO_2	Exposure: Other	Results
eimann 970	2,648 deaths all causes Boston, Massachusetts	Death certificate data Oct. 21 to Dec. 1, 1966	Range for whole study area Oct. 21 - Nov. 30, 1966 34 - 226 $\mu g/m^3$ Daily means	Range for whole study area Oct. 21 - Nov. 30,1966 0.26 - 2.20 COHS Daily means	Range for whole study area Oct. 21 - Nov. 30, 1966 2.3 - 12.4 pphm Daily means	not measured	No significant associati found between crude mortality rates and temp orally different air pol ution levels. Also no difference found betwee areas with different pol ution levels after adjus ing for age, sex and socioeconomic levels.
	9,697 nursing home residents in three pollution areas	Mortality data collected and hospitalization of patients for serious illness	"	"	"	"	Found no significant association between mortality or hospitalization and pollution levels.
	4,576 delivery records	Neonate mortality data at time of episodes compared to control periods	"	"	"	"	No significant associati between fetal deaths and air pollution
	309 subjects with chronic nonspecific respiratory disease	Collected data on number of clinic visits Oct. 17 to Dec. 19, 1966	"	"	"	"	Number of visits to the clinic rose during time interval after the air pollution episode and was especially increased in those living in heaviest pollu ted area.
		Data on number of emergency room visits for heart disease, respiratory disease and control group of acute surgical ailments collected for	"	"	"	"	No significant differenc noted for period before or after episode for any disease categories looked at in terms of emergency room visits

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Ferris 1971	Old and new sample combined 699 males 829 females age 25 to 74 and over Berlin N.H. 1967	Re-examined sample from 1961 study and also new random sample. Questionnaire with interview and FVC, $FEV_{1.0}$ and PEF measurements made.	1961 mean 180 $\mu g/m^3$ range 55-308 $\mu g/m^3$ 1966 mean 123.7 $\mu g/m^3$ range 26-288 $\mu g/m^3$ 1967 mean 139.2 $\mu g/m^3$ range 17-314 μ/m^3	Not stated	Not stated	Dustfall $g/m^2/30$ days mean values (1961) 18.4 (1966-67 same stations as 1961) 14.3 (1966-67 all stations) 9.7 - - - - - - - - - SO_3 mg/100 cm^2/day 1961 range 0.373-1.10 1966-67 same stations as 1961 range 0.084-0.980 1966-67 all stations range 0.010-.98	Results after controlling for smoking, age, and sex showed slightly lower levels of respiratory disease prevalence in 1967 than 1961. FVC in men and women were significantly greater in 1967 than in 1961. FEV_1 had a less consistent pattern. PEF slightly greater in 1967 than 1961.
Ferris 1976	521 men and 680 women re-interviewed Berlin N.H. 1973	Re-examined sample from 1967 study used health questionnaire. FVC, $FEV_{1.0}$, PEF measurements were made.	1973 80 ± 62 $\mu g/m^3$ Mass respirable particulates 1973 34 ± 22 $\mu g/m^3$	Not stated	1973 SO_2 equivalents 25 ± 8 ppb SO_2 10 ± 6.5 ppn	SO_3 µg/100 cm^2 per day 1973 901 ± 287	No differences were found for respiratory disease prevalence when symptoms reviewed individually or in clusters between 1967 and 1973. No pattern was found between air pollution and FVC, FEV_1, and PEF.

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
hen 72	Panel of 20 asthmatics, 80% adults. white. males & females. New Cumberland, West Virginia	Questionnaire administered and subjects completed daily reports on time of attack, place, duration and severity. New Cumberland, West Virginia	Demarcating point between high and low days 150 $\mu g/m^3$ high volume sampler	Not stated	Demarcating point between high and low days - .07 ppm couiometric method	Soiling index measured by AISI tape samples	All pollutants and temperature correlated significantly with asthma rate. [Temperature (r=.422) SO_2 (r=.32) and soiling index (r=.387).] Significant differences were found between high-low pollution days and high-low days of temperature, humidity and wind speed with attack rate. After the effects of temperature were removed significant correlations remained between pollution level and attack rate.
ubec 73	4377 male twin pairs U.S.	Questionnaire on respiratory symptoms, smoking and alcohol consumption	Not stated				As individuals a relationship found between respiratory symptoms and urban residency but not with more specific measurements of air pollution. Also in comparing twin pairs exposed to different levels of air pollution no significant differences were noted for respiratory symptoms.

Source	Population	Method	Exposure				Results
			Particulate	Smoke	SO_2	Other	
Cohen 1974	1121 male and female adults and children in three areas New York City	Telephone interviews about presence of symptoms in any family member during publicized and unpublicized air pollution episodes and control periods in three areas with different levels of pollution	Riverhead Publicized 26 $\mu g/m^3$ Unpublicized 44 $\mu g/m^3$ per 24 hours Queens Publicized 145 $\mu g/m^3$ Unpublicized 165 $\mu g/m^3$ Bronx Publicized 240 $\mu g/m^3$ Unpublicized 180 $\mu g/m^3$	not measured	Riverhead Publicized 0.03 ppm Unpublicized 0.01 ppm Queens Publicized 0.12 ppm Unpublicized 0.11 ppm Bronx Publicized 0.14 ppm Unpublicized 0.15 ppm	not measured	Significant increase fo eye and throat irritati chest discomfort and sho ness of breath noted in adults during high pollution episode Comparing publicized an unpublicized episodes n significant differences in symptoms found. Concluded SO_2 level abo 0.11 ppm and suspended particulate levels abov 145 $\mu g/m^3$ for a number days may significantly increase irritative symptoms

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Stebbings 1976	342 subjects age 60 or over New York	Each subject had interview with questions on symptoms, history of disease, occupation, smoking, and socioeconomic exposure, subjects divided into one of four panels. Weekly diaries containing information on daily symptoms were completed by panelists.	Mean daily values range over three areas 34.9-98.3 $\mu g/m^3$ Respirable suspended particulates range over three areas 26.3-44.4 $\mu g/m^3$	Not stated	Range over three areas 30.3-67.7 $\mu g/m^3$	Suspended sulfates 11.1-13.7 $\mu g/m^3$ Suspended nitrates 2.5-4.2 $\mu g/m^3$	Exacerbation of symptoms was found in the well panel with increase levels of suspended nitrates, suspended sulfates, SO_2 and respirable suspended particulates. Found similar but weaker association for lung panel. Suspended nitrate and total suspended particulate level appeared to be related to symptoms of heart disease.

Source	Population	Method	Exposure				Result
			Particulate	Smoke	SO_2	Other	
FOREIGN STUDIES							
Huber 1954	all ages with cases of "Yokohama" asthma Yokohama, Japan	incidence determined by visits to U.S. Army hospital	Not stated	smog formation days	.172 γ/liter	ether soluble aerosols .081 mg/m^3 dust index 3.8 ozone .17 γ/liter nitrogen oxides .52 γ/liter	1) of air contaminants studied only ether soluble aerosol and dust appear to be significantly correlated with incidence of "Yokohama" asthma 2) incidence of asthma also correlated with smog formation.
Cornwall 1961	approx. 60,000 transport employees male < 65 yr London	sickness absence due to bronchitis (4-182 days in length) 1952-1956	no measurements made				1) support observations that incidence of bronchitis is closely associated with occurrence of dense and prolonged fogs 2) differences between geographical areas support conclusion that pollution from domestic fires and industry are responsible for excess mortality invaliding rates and sickness absence due to bronchitis

Source	Population	Method	Exposure				Result
			Particulates	Smoke	SO_2	Other	
Cornwall 1961							3) English climate more conducive to bronchitis than most other countries
Work 1962	1) 40-64 yr males municipal transport system workers in Bergen, Norway 2) transport workers in post office service in London, England	1) interview 2) exam PRF blood pressure weight sitting height 3) sickness absence data 4) morning sputum specimens	no measure or comparison				1) higher prevalence of most respiratory symptoms found in London 2) PRF lower in London 3) differences could not be explained by socioeconomic factors or anthropometric measurements 4) smoking differences do not explain severe symptoms or lung capacity difference

Source	Population	Method	Exposure				Result
			Particulate	Smoke	SO_2	Other	
Oshima 1963	889 workers from a casting company in Tokyo Yokohama area and 1,463 from an oil company with branches in Kashiwasaki Niigata, Yokohama and Kawasaki 15-58 yr olds	1) questionnaire 2) physical exam 3) chest roentgenogram 4) pulmonary function tests a) FVC b) $VC_{1sec.}$	no measurements made		low - high pollution		1) residents of high air pollution area had a) increased incidence of sputum production, chronic cough, and throat irritation, b) lower mean VC. c) increased number of patients over 45 yr. with airway obstruction 2) cigarette smokers and persons with a history of allergies had most respiratory difficulty in highly polluted area

rce	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
lland 65	293 male mail-van drivers and maintenance men Central London 477 male mail-van drivers or engineering workers in and around three country towns in South England	Questionnaire Pulmonary function tests and collected sputum from participants from similar occupations but different areas	No measurements made at location of study but differences between levels in London and surrounding country noted				Over age 50 male post office workers in Londo had more and severer respiratory symptoms, produced more sputum and had significantly lower lung function test results. Concluded different levels of air pollution was most likely cause of difference in respiratory morbidity between areas studied.
igel 965	85 males volunteers most with prior history of chronic bronchitis London, England	Respiratory symptoms observed during winter months 1962-1963		Graph only no specific measurements given	Graph only		Prevalence of respiratory illness found to be related in time more closely to increased levels of smoke than to SO_2. Also relation in time found between incidence of respiratory disease and SO_2 and smoke No significant association found between disease and low temperature.
etrilli 966	Females age 65 and over non-smokers and non-factory workers	Measured respiratory morbidity by questionnaire 1961-1962	1954-64 Range residential to industrialized 19 sample sites 0.08-0.88 mg/m^3	Not stated	1954-64 Range residential to industrialized 19 sample sites .020-.152 ppm	Sulfation rates 1954-64 Range residential to industrialized 19 sample sites 0.18-2.16 mg SO_3/100 sq cm/day	Found significant correlation between bronchiti and mean annual SO_2 levels ($r=0.98$). A non-significant correlation was found with suspende matter ($r=0.82$) and dustfa ($r=0.66$).

urce	Population	Method	Particulates	Smoke	SO_2	Other	Results
etcher 68	1,000 men aged 30-59 London, England	Self-administered questionnaire, interviews about chest illness, $FEV_{1.0}$ measurements made and sputum collected		140 $\mu g/m^3$ declining to 60 $\mu g/m^3$ (source: air quality criteria for particular matter)	200 $\mu g/m^3$ declining to 160 $\mu g/m^3$ (source: air quality criteria for particular matter)		Decline in sputum production observed 1961-66. Possibly associated with decline in particulate pollution in central London.
ersteker 969	1,000 male municipal employees Rotterdam, Netherlands	Bronchitis questionnaire and PEF measurements taken October 1966	Not stated	60 $\mu g/m^3$ winter daily average	200 $\mu g/m^3$ winter daily average	Not stated	Found no difference between bronchitis group and a control group in respect to variables relating to chronic exposure to air pollution. A signigicant difference was noted for the percentage of heavy smokers between the two groups.
regory 970	340 cases of chronic bronchitis Sheffield, England	July, 1955 to June, 1961 collected sickness-absence records for all cases of chronic bronchitis in male employees of a steel works company	Not stated	Range July, 1955-June, 1961 6.9-81.3 mg $100m^3$ average per month	Range July, 1955 June, 1961 3.6-19.7 parts per 100 ml parts air average per month		Statistically significant inverse relationship between the incidence rate and prevalence rate of chronic bronchitis with temperature. A significant correlation found between incidence rate and both mean and maximum smoke pollution levels of previous week. No correlation found between rates and factors for the same week. Concluded smoke pollution was a causation factor i exacerbations of bronchitis.

:ce	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
:ick)	Males and females Brisbane, Australia	Index of acute asthma provided by visits to hospital at night (10 p.m. to 6 a.m.) 1960-62	Not stated	1960-1962 2 suburbs Chermside 0-1.7 mean 0.49 COH/1000 ft. Toowong 0-2.8 mean 0.73 COH/1000 ft.	Not stated	Not stated	No significant association between smoke pollution and hospital visits for asthma found
chel 1 177	8162 males and females from a random sample West Germany	1963-1968 survey of respiratory symptoms and lung function in 3 areas of West Germany, Duisburg, Bocholt and rural Borken.	Duisburg average 0.085 ppm range 0.01-0.39 ppm Bocholt average 0.047 ppm range 0.01-0.07 ppm Borken average 0.035 ppm range 0.02-0.06 ppm	Not stated	Not stated	Settleable Particulates Duisburg 2,780 Bocholt 390.4 g/100m^2/30 days Oxides of Sulfur Duisburg 220 average range 60-400 Bocholt average 67 range 29-159	Found no difference between the three areas with different pollution levels and the prevalence of cough and sputum production in males and females when the groups were standardized for age, sex, smoking habits and social status
ther 0	1071 patie :s with symptoms of chronic bronchitis, emphysema or asthma returned diaries London	October, 1959-March, 1960 Patients completed diaries on changes in their day to day condition	Not stated	1959-1960 range of means 264-435 $\mu g/m^3$	1959-1960 range of means 254-365 $\mu g/m^3$	Not stated	Found consistent response to pollution. Concentrations of smoke or SO_2 greater than 1000 $\mu g/m^3$ resulted in a sharp increase in the percentage of patients recording their condition Lowest co ntration leading t y effect was

Source	Population	Method	Particulates	Smoke	SO_2	Other	Results
Lawther 1970 (cont'd)	1037 patients returned diaries	October, 1964-March, 1965 again patients with bronchitis, etc. completed diaries		1964-65 range of means 109-158 $\mu g/m^3$	1964-65 range of means 228-292 $\mu g/m^3$		From looking at peak values for 1959-60 and 1964-65 concluded that patients are most sensitive to pollution change at the beginning of the winter. The least amoun of pollution leading to significant response estimated at 500 $\mu g/m^3$ with about 250 $\mu g/m^3$ of smoke.
Lambert 1970	9975 men and women age 35-69; England, Wales or Scotland	Postal questionnaire concerning respiratory symptoms and cardiovascular symptoms sent to a random sample of the population		⩽100 100- 150- 200+ μg/c.m.	⩽100 100- 150- 200+ μg/c.m.	Coal consumption very low low moderate high 1952 measurements	Results show that increased cough and phlegm production in early adul life is result of cigarette smoking and that the cumulative exposure to air pollution with older age increases the prevalence of more serious bronchitic disease. Air pollution exposure without prior cigarette smoking effects produced only a slight increase i chronic bronchitis in th over 55 year age group.
Tsunetoshi 1971	36,374 residents over 40 years of age - 17,798 male 18,576 female seven areas of Osaka, Japan	Self-given questionnaires about respiratory symptoms. 1962-1969. Vital or respiratory test also given	Not stated	Not stated	Range over seven areas 0.84-3.34 mg/100cm^2/day average value for three successive years	Dustfall range over seven areas 5.55-42.90 tons/km^2/month	Prevalence of chronic bronchitis in each area increased with increasin levels of air pollution especially SO_2 after standardizing for age ar smoking. Using mathematical formula found an expected increase of 2% in the prevalence of chronic bronchitis with an observed increase in SO_2 of 1 mg/100 cm^2/day. Also mathematically computed t minimum level of SO_2

Source	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
Emerson 1973	18 patients with varying degrees of chronic bronchitis and asthma 14 males, 4 females London	Lung function tests given at approximately weekly intervals. Period of study varied from 12-82 weeks	Not stated	Mean 45 mg/cu m air range over one year 5.5-380 mg/cu m air	Mean 193 mg/cu m air range over one year 38.5-722 mg/cu m air	Not stated	Found no significant correlations between FE and smoke levels and a significant correlation between $FEV_{1.0}$ and SO_2 occurred in only one patient. Most significant correlations were with temperature where six cases showed such correlations.
Howard 1974	178 patients with obstructive airways disease 158 men, 20 women mean age 59.6± 9.0 yr. Sheffield, England	Questionnaire on respiratory symptoms given and also $FEV_{0.75}$ and FVC measurements made at interval of one to three months. 1966-72	1966-1972: A fall occurred in levels of air pollutants.		Not stated	Not stated	Compared to a similar group of patients from a previous study found recent group had less productive cough, fewer winter illnesses, less severe breathlessness a about one-third the rat of decrease of FEV.
Neri 1975	Ottawa 3280 males and females, 1969-71 Sudbury 2208 males and females, 1972-73	Spirometric tests (FEV_1 and FVC) and questionnaire on respiratory symptoms compared between two cities in Canada	Ottawa 90.5 $\mu g/m^3$ Sudbury 52.1 $\mu g/m^3$ Geometric mean of annual geometmic means	Not stated	Ottawa 16.1 ppb Sudbury 32.5 ppb Arithmetic mean of annual arithmetic means	Not stated	Significant difference found between FEV_1/FVC ratios with Sudbury having lower mean ratios than Ottawa for both ma and female. Found highe prevalence of chronic bronchitis in Sudbury v Ottawa (97/1000vs.77/10 for both sexes combined Males rather than femal account for difference, the margin of differenc for males being 40/1000 ±18, and females 0/1000 ±19.

Source	Population	Method	Exposure: Particulates	Exposure: Smoke	Exposure: SO_2	Exposure: Other	Results
acoveanu 975	All males aged 40-60 who lived in one of the two towns studied for at least five years who were not previously exposed to dusts, gas, etc. for at least five years town A 544 males town B 753 males Bucharest	Examination of subjects by physicians and two assistants, obtaining height, and weight, pulmonary function tests and a questionnaire on respiratory symptoms. Results compared between a polluted town and a control town.	No values given				Prevalence of respirato symptoms found to be about two times higher polluted town vs. non-polluted town. Grade II dyspnea and over was found to be almost thre times more frequent in polluted vs. non-pollut town ($p<0.0001$) for both smokers and non-smokers.
alpazanov 976	Number of daily illness cases Sofia	Statistical correlation between number of daily illness from influenza epidemic 12-27-74 to 2-12-75 and meteorological and pollution factors	Not stated	Not stated	Range .798-.913 mg/m^3	Dust range .452-.473 mg/m^3 Nitric oxides range .020-.024 mg/m^3 Oxidants range .0172-.022 mg/m^3	Statistically significa relationship found between illness on one da and formaldehyde and nitric oxides levels tw days before. SO_2 levels on day of illness and day before illness significantly correlated with illness from influenza.

TABLE 11
SUMMARY OF CHESS STUDIES

Source	Population	Method	Exposure: Particulates	Exposure: Smoke	Exposure: SO_2	Exposure: Other	Results
ouse 974	7,635 parents of elementary junior and senior high school students from four communities with different exposures to air pollution. Utah	Self administered questionnaires on symptoms Fall 1970	Range 1940 - 1971 by community Low 78 - 108 $\mu g/m^3$ Intermediate I 81 - 151 $\mu g/m^3$ Intermediate II 45 $\mu g/m3$ High 53 - 70 $\mu g/m^3$	Not stated	Range 1940 - 1971 by community Low 8 $\mu g/m^3$ Intermediate I 15 - 28 $\mu g/m^3$ Intermediate II 22 - 50 $\mu g/m^3$ High 62 - 234 $\mu g/m^3$	Range 1940 - 1971 by community Suspended Sulfate Low 3.7 - 5.8 $\mu g/m^3$ Intermediate I 4.7 - 11 $\mu g/m^3$ Intermediate II 7.8 - 10 $\mu g/m^3$ High 12.4 - 28 $\mu g/m^3$	A significant increase in the prevalence of chronic bronchitis was found to occur in both smokers and nonsmokers of both sex after 4 - 7 years of residence in a area of elevated SO_2 (9 95 $\mu g/m^3$) and suspended sulfates (15 $\mu g/m^3$) The effects of air pollution and smoking appeared to be additive Occupational exposure t dust, gases, fumes or a osols was found to have twice the effect of pollution on chronic bronchitis prevalence for over age 40 groups.

ource	Population	Method	Exposure: Particulates	Exposure: Smoke	Exposure: SO_2	Exposure: Other	Results
nklea 974	211 total participants with asthma from four communities with different exposures to air pollution. Utah	A panel of asthmatics were interviewed and questionnaires completed. Participants kept daily diaries on asthmatic attacks These diaries were returned weekly March 7-Sept.4, 1971.	Range over four seasons by communities Low 58-70 $\mu g/m^3$ Intermediate I 58-86 $\mu g/m^3$ Intermediate II 36-44 $\mu g/m^3$ High 47-66 $\mu g/m^3$	Not stated	Range over four seasons by communities Low 4-10 $\mu g/m^3$ IntermediateI 7-14 $\mu g/m^3$ IntermediateII 4-19 $\mu g/m^3$ High 9-71 $\mu g/m^3$	Range over four seasons by communities Suspended sulfate Low 4-7 $\mu g/m^3$ Intermediate I&II 5-9 $\mu g/m^3$ High 7-13 $\mu g/m^3$	Increases in asthma attacks related to suspended particulate matter levels of 71 $\mu g/m^3$ with temperature $\geq 50^\circ$F and levels of 107 $\mu g/m^3$ with temperatures of 30-50° F. For SO_2 asthma attacks increased with levels of 23-54 $\mu g/m^3$ when temperature $\geq 40^\circ$ F. Suspended sulfate levels of 1.4 $\mu g/m^3$ with temperature $\geq 50^\circ$F and 17.4 $\mu g/m^3$ with temperature 30-50°F were related to increases in asthma attack rates.

urce	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
nklea 74	38,791 white males and 6,734 black males, all military recruits from three different areas Chicago area	Self-administered questionnaire given June 24, 1969-February 20, 1970. Contained questions about symptoms of chronic respiratory disease	Range 1950-1970 by area Urban 149-244 $\mu g/m^3$ Suburban 103-174 $\mu g/m^3$ Outstate 71-80 $\mu g/m^3$	Not stated	Range 1950-1970 by area Urban (from 1960) 96-282 $\mu g/m^3$ Suburban (from 1966) 100-217 $\mu g/m^3$ Outstate 19-70 $\mu g/m^3$	Range 1950-1970 by area Suspended sulfates Urban 14.1-20.6 $\mu g/m^3$ Suburban No values given Outstate 7.7-9.3 $\mu g/m^3$	Prevalence rates of chronic respiratory disease were significantly higher in higher polluted urban and suburban area of Chicago than in recruits from rural areas of outstate Illinois-Indiana area The effects of air pollution and smoking appeared additive Significant increases in the frequency of chronic respiratory disease symptoms found with residency for 12 years or more in area with elevated average levels of SO2 (96-217 $\mu g/m^3$), suspended particulates (103-155 $\mu g/m^3$) and suspended sulfates (14 $\mu g/m^3$)

urce	Population	Method	Exposure				Results
			Particulates	Smoke	SO2	Other	
nklea 74	148 subjects with asthma from three communities New York	All prospective panelists interviewed and questioned about their asthma. Panelists selected mailed in weekly diaries containing daily information on attack rates	Median daily levels range over all seasons by community Low 29-34 $\mu g/m^3$ Intermediate I 55-60 $\mu g/m^3$ Intermediate II 57-78 $\mu g/m^3$	Not stated	Median daily levels range over all seasons by community Low 8-18 $\mu g/m^3$ Intermediate I 29-56 $\mu g/m^3$ Intermediate II 19-64 $\mu g/m^3$	Median daily levels range over all seasons by community Suspended sulfates Low 6-11 $\mu g/m^3$ Intermediate I 9-14 $\mu g/m^3$ Intermediate II 10-14 $\mu g/m^3$	An excess of asthma attacks was found related to an estimated level of suspended particulates of 56 $\mu g/m^3$ (T_{min}=30 to 50°F) and levels of 12 $\mu g/m^3$ for suspended sulfates (T_{min}=30 to 50°F) Predicted that suspended sulfates at level of 35 $\mu g/m^3$ would be related to a 4% increase in attack rate on cool days and a 57% increase on warmer days A 22% increase in asthma attack rates could be expected with increases of suspended particulate to once a year allowable level of 260 $\mu g/m^3$

rce	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
es	5295 male & female total from five communities. Parents of elementary school children. Montana-Idaho area.	Questionnaires on chronic respiratory disease symptoms	Range 1940-1970 by community Low I 50 $\mu g/m^3$ Low II 45-60 $\mu g/m^3$ Low III 106-270 $\mu g/m^3$ High I 49-69 $\mu g/m^3$ High II 102-179 $\mu g/m^3$	Not stated	Range 1940-1970 by community Low I 10 $\mu g/m^3$ Low II 26 $\mu g/m^3$ Low III 34-67 $\mu g/m^3$ High I 153-203 $\mu g/m^3$ High II 217-374 $\mu g/m^3$	Suspended Sulfate Range 1940-1970 by community Low I 3.3 $\mu g/m^3$ Low II 4.9 $\mu g/m^3$ Low III 6.7-17.1 $\mu g/m^3$ High I 5.4-7.7 $\mu g/m^3$ High II 11.3-19.9 $\mu g/m^3$	Excess bronchitis morbidity found in nonsmokers, exsmokers, and current smokers males and females in the high exposure smelter communities. Morbidity for chronic bronchitis was related to SO_2 in a high exposure community lead to increases in excess bronchitis. Longer residence in a high exposure community led to increases in excess bronchitis. Specifically SO_2 in range of 177 to 374 $\mu g/m^3$ and suspended sulfates 7.2 to 19.9 $\mu g/m^3$ can lead to excess bronchitis in 2-3 year residents who are nonsmokers.

rce	Population	Method	Exposure				Results
			Particulates	Smoke	SO_2	Other	
dberg 4	4,764 parents of elementary school children in three communities. 50% between 31-40 year-old age group. New York	Self-administered questionnaire on chronic bronchitis 1970	Range 1949-1970 by community Citywide 101-203 $\mu g/m^3$ Queens 80-173 $\mu g/m^3$ Bronx 104-166 $\mu g/m^3$	Not stated	Range 1949-1970 by community Citywide 210-443 $\mu g/m^3$ Queens 144-404 $\mu g/m^3$ Bronx 210-395 $\mu g/m^3$	Range 1949-1970 by community Suspended sulfate Citywide 20-26 $\mu g/m^3$ Queens 9-24 $\mu g/m^3$ Bronx 16-22 $\mu g/m^3$	Increases in chronic bronchitis prevalence found among smokers, exsmokers and nonsmokers of both sexes with long term exposures (up to 20 years) to SO_2 levels of 144-404 $\mu g/m^3$ and suspended sulfate levels of 9-24 $\mu g/m^3$. Chronic respiratory disease frequency found significantly higher in communities with intermediate to high pollution exposures than in low exposure community. Could not be accounted for by age, occupation, smoking or race difference. Again air pollution and smoking effects appear to be additive.

Source	Population	Method	Exposure: Particulates	Exposure: Smoke	Exposure: SO_2	Exposure: Other	Results
Ldberg 74	797 elderly subjects divided into one of four panels 1) well 2)heart 3) lung 4)heart and lung on bases of physicians' diagnosis New York	Personal interview used to distribute cases between three disease categories and a category of healthy participants. Panelists given diaries to record daily any symptoms or changes in condition. Study carried on for 32 weeks	Median daily levels range over all seasons by community Low 29-34 $\mu g/m^3$ Intermediate I 55-60 $\mu g/m^3$ Intermediate II 57-78 $\mu g/m^3$	Not stated	Median daily levels range over all seasons by community Low 8-18 $\mu g/m^3$ Intermediate I 29-56 $\mu g/m^3$ Intermediate II 19-64 $\mu g/m^3$	Median daily levels range over all seasons by community Suspended sulfates Low 6-11 $\mu g/m^3$ Intermediate I 9-14 $\mu g/m^3$ Intermediate II 10-14 $\mu g/m^3$	Of three pollutants associated with exacerbations of symptoms suspended sulfates showed the most consistent association. A threshhold level was estimated for suspended sulfate at approximately 10 $\mu g/m^3$ levels of~10 are found in the major urban areas of the country Annual average suspended sulfate rates of 10 to 20 $\mu g/m^3$ would result, it was estimated, in a 6% morbidity excess on colder days and a 32% morbidity excess on warmer days

E. Health Effects of SO_2 and Particulates on Children

A problem inherent in all epidemiologic studies investigating the health effects of air pollution involves the ascertainment of the two groups similar in all factors (except for air pollution exposure) which might affect prevalence of disease. Among the factors which need to be considered are sex, age, socio-economic class, ethnic origin, occupational exposure, and smoking habits.

In order to reduce the number of variables under consideration, many investigators have chosen to study children in whom smoking and occupational exposure would be minimized as they are less likely to be engaged in such activities than are adults. Children also experience fewer changes of residence. Due to this lesser mobility, it is felt that they have a more homogenous exposure to air pollution over relatively long periods of time.

Not only are children considered a more convenient group to study but they appear to be at greater risk of respiratory problems that might result from air pollution exposure. Presumably this is due to a greater degree of mouth-breathing, relatively greater total volume, and a higher frequency of respiratory tract infections than in adults.

Probably the most important reason children have been studied so extensively recently is the ever increasing concern about whether early childhood respiratory illness increases the likli-hood of respiratory disease.

A major study giving substance to this concern was conducted on respiratory disease in National Servicemen from the United Kingdom (Rosenbaum, 1961). It was found that the incidence of respiratory disease in these men was correlated with their home localities before call-up. Servicement from industrial areas appeared more susceptible to respiratory diseases than those from rural areas. Other studies suggest that environment in the early years of life can contribute to the development of chronic respiratory disease in later life (Eastcart, 1956; Dean, 1964; Holland, 1969)

Many authors have contended that a child with frequent respiratory disease episodes will outgrow this condition in time. Harnett and Mair in their study of "catarrhal" children reached no conclusions due to small sample sizes, but the trend did point to a positive correlation between the "catarrhal" child and the adult with bronchitis (Harnett and Mair, 1963). Although the association between the "catarrhal" child in the adult with chronic respiratory disease has not been established, the evidence thus far has greatly increased the interest in any factors increasing the incidence of respiratory illness in children.

Over one hundred publication on the effects of air pollutants on children have been reviewed by the American Academy of Pediatrics (1970). The subject has also been reviewed more recently (Wehile and Hammer, 1974). It is interesting to note that the major pollutant incriminated in the mining of copper was arsenic, although no clinical findings were associated with its presence. Clinical and laboratory findings associated with SO_2 and particulates included as increase in respiratory infections, headaches, nausea, impaired ventilatory function, anemia and related acute episodes of asthma.

1. Mortality Studies

Acute episodes of air pollution have long been associated with increased numbers of deaths within the affected population. In the past it was thought that these excess deaths occurred mostly in the older aged component of the population. However, in the four day London fag of 1952, Logan demonstrated that excess deaths do occur in children when exposed to high levels of pollution (Logan, 1953). He found that the mortality of new-born infants almost doubled, infant deaths more than doubled and deaths of children rose by one third during that four day fog.

More recently, Greenburg investigated an acure episode in New York City during January 29 - February 12, 1963 (Greenburg, 1967). He found no significant excess of deaths of new-born

infants (< 28 days old) when compared with the same period in the control years of 1961-1965)

Mortality has also been used as an indicator of air pollution effects between and within cities over periods of "normal" pollution levels.

Sprague and Hagstrom studied fetal and infant mortality in Nashville, Tennessee for five years (Sprague and Hagstrom, 1969). Dustfall alone or as an interaction variable was most frequently associated with white fetal and infant mortality. Sulfation was correlated positively (r=+0.704) and socio-economic class negatively (r=-0.5) with white but not with non-white infant mortality.

These findings were confirmed by Collins in his study of child mortality in England and Wales (Collins, 1971). Infant mortality (0-1 years) was associated with domestic and industrial pollution as measured by fuel consumption. Low socio-economic class, low education and high population density were also correlated with infant mortality. The ages, 1-4 years showed this same correlation but the association was much weaker. Children age 5-14 years showed no correlation between mortality and these variables.

In order to examine the relationship between sudden infant death syndrome (SIDS), a cause of dealth in children 1 week to 1 year of age and SO_2, Greenberg studied 942 deaths from SIDS over a four year period in Chicago (Greenberg, 1973). Autopsy reports, records describing the nature of death and data on the death certificates were reviewed to determine all sudden and unexpected deaths that occurred among infants 7 days to 1 year of age. The relationship between SO_2 concentration and SIDS was determined by comparing the estimated SO_2 levels in the community where the death occurred with SO_2 levels 7 days and 14 days, before and after the dealth, within the same community. Further comparisons were made in order to determine whether SO_2 levels were higher one or two days prior to the

occurence of the deaths. No relationship between SO_2 levels and SIDS was found. An inverse relationship between temperature and SIDS was found in three of the years of study. The author pointed out the possiblility that other pollutants, such as oxides of nitrogen, carbon monoxide, and suspended particulates, which were not measured, might be correlated with SIDS.

In 1974, Hunt and Cross studied 66 infants who died before they reached 1 year of age (Hunt and Cross, 1974). A live infant, born in the same hospital as the one who died was chosen as a control subject, matched for sex, race, and mother's age group. The two groups of infants were found to have experienced similar disadvantageous conditions of pregnancy and delivery which contribute to the increased risk of death for the newborn. Among the infants that died, more were born during three months of high pollution (53-80 tons/mi/mo-dustfall, 1.5-6.5 microgms/SO_2/m^2/day-sulfation rate) than the other nine months combined. The authors proposed that exposure of the pregnant mothers to high levels of pollutants was possibly related to fetal death. Important information was omitted such as occupational history of the mother, educational attainment, nutritional assessment, and, more importantly, the mother's smoking habits.

A summary is presented in Table 12.

2. Morbidity Studies

One of earliest community studies specifically considering children took place in an industrial center in the USSR (Yangsheva, 1957). High pollution levels were associated with an increased frequency of disease of the respiratory organs, the nervous system, skin, and lowered resistance to infectious disease. High pollution levels were associated with low hemoglobin levels in children. Kaplin confirmed this finding in Czechoslovakia (Kaplin, 1963).

Also in the USSR, Manzhenko associated high pollution levels (smoke-1.87-6.4 mg/m^3; SO_2=0.11-1.99 mg/m^3) with increased incidence of upper respiratory tract infections and a higher incidence of pulmonary conditions (Manzhenko, 1966).

TABLE 12

EPIDEMIOLOGIC STUDIES ON THE EFFECTS OF SO_2 AND PARTICULATES ON CHILDREN AS MEASURED BY MORTALITY

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
prague nd agstrom 969	<1 year olds	Nash-ville Tenn.	1) mortality (5 yr) 2) census tracts	Not stated	24 hr .0075 ppm Sulfation .224 mg SO_3/ 100 sq cm/day	Dustfall 7.305/ sq mi/mo Soiling .594 COHS/ 1,000 ft	1) white infant (1-11 mo) death positively correlated with SO_3 (r = 0.704) negatively with socioeconomic class (r = 0.52) 2) white neonatal (<28 days) death positively correlated with dustfall (r = 0.491) negatively with socioeconomic class (r = 0.455) 3) neonatal (<1 day) death is result of interaction of dustfall and socioeconomic class (r = 0.648) 4) no significant relationship of non-white mortality with variables measured
192							
ollins 971	0-14 year olds	83 county boroughs in England and Wales	1) mortality 1958-1964 2) social data 1951 census	1) domestic pollution 2) industrial pollution 3) power stations (supposedly correlated with SO_2 level)			0-1 year deaths correlated with 1) high domestic pollution (r = 0.583) 2) high industrial pollution (r = 0.448) 3) low social class (r = 0.510) 4) high population density (r = .404) 5) low education (r = 0.494) 1-4 year much weaker correlation 5-14 year no correlation
reenburg 973	1 wk - 1 yr 942 children	Cook County Illinois	1) mortality from SIDS (4 years) 2) meterological data	Not measured	Measured but no data given	Not stated	1) inverse relationship between SIDS and temp. 2) do not show that SO_2 levels affect SIDS
unt ross 974	66 matched pairs of children <1 year old	Dauphin County Penn.	1) monthly reports of mortality 1970 2) climatological and census data 3) clinical records	Suspended particulates 24 hours 33-140 $\mu g/m^2$	Range during July-Sept. sulfation 1.5 - 2.6 $\mu g/SO_2/m^2$/ day	Dustfall 18-28 tons/ m^2/mo 60-80% insoluble	1) more deaths occurred during July August, Sept. - high pollution months 2) geographic location associated with increased risk of death 3) exposure of pregnant mother to high pollutants [illegible]sibly related to fetal d[illegible]

The same year, a British study was published which has become one of the most cited studies in the literature on air pollution and respiratory disease in children (Douglas and Weller, 1966). In this study, a group of children were followed from birth in the first week of March, 1946 to their leaving school in 1961. Information on upper and lower respiratory illness was obtained by health visitors during interviews with mothers when the children were 2 and 4 years of age. School doctors obtained further information on illness during special examinations of the children at 5, 7, 11, and 15 years of age. Assessment of the air pollution levels (very low to high) was made on the basis of domestic coal consumption in 1952. These estimates were later compared with the levels measured during the year, 1962-1963. The concentration of pollutants showed the same increases from area to area as was predicted from coal comsuption data. Air polution estimation from coal consumption would appear to be adequate, at least for establishing a gradient of air pollution exposure. The results of the Douglas and Waller study showed that the frequency and severity of lower respiratory tract infections increased with increasing levels of pollution.

These results were later confirmed in another British study examining 5 year-old Sheffield school children in four areas of varying pollution (Lunn, 1967). However, Lunn also found a relationship between upper respiratory tract infection and increasing pollution, as did Mazhenko. This conflicting result may be due to the fact that in Lunn's study actual pollution data were gathered while Douglas and Waller estimated pollution levels from coal consumption.

A follow-up study of these Sheffield children was done four years later (Lunn, 1970). Data on 11 year-old children examined at the same time as the 5 year-olds in the original study were included here for comparison. At the time of the original study it was found that the 11 year-olds had a lower prevalence of respiratory illness than the 5 year-olds.

However, these same 5 year-olds seen four years later, when they were nine, had less respiratory illness than the 11 year-olds had in the original study. This appeared to correspond to the decreasing levels of air pollution over this period. Smoke decreased from 30 microgms to 169 microgms and SO_2 decreased from 275 microgms to 253 microgms in the heavily polluted area. However, the differences in respiratory illnesses may well be due to recall problems as 48.4% of the 5 year-olds in the original study with history of pneumonia or bronchitis disclaimed these diseases four years later.

A follow-up study of the same cohort of children involved in the Douglas and Waller study supported the hypothesis that exposure to air pollution and adverse social class conditions increase the risk of having lower respiratory tract infection in early childhood (Colley and Reid, 1973). However, at age 20 smoking was shown to be the dominant risk factor with air pollution exerting a non-significant influence when other factors were accounted for. Like the Douglas and Waller study, domestic coal consumption was used as an estimator of air pollution levels.

In a pilot study conducted in three town in British Columbia, Anderson used school absenteeism and lung function tests in order to measure possible health effects of emissions from a large kraft pulp mill (Anderson, 1966). There was a reduction in peak expiratory flow rate among the 1st-grade students in the more polluted areas. These children also experienced more frequent and longer lasting respiratory illnesses along with certain other illnesses such as inflamed eyes, headache, feverishness,and nausea. The association between these symptoms and air pollution could not be established as the control town fell between the two polluted towns in the incidence of these conditions. Ethnic differences, living conditions, and family size may explain the differences between towns.

Finklea conducted prospective surveys of respiratory disease in volunteer families with nursery school children age 2-5 years in Chicago. The families were called once every two weeks and asked about the presence of illness, fever, respiratory symptoms, restricted activity, and otitis media diagnosed by a physician, and other physician consultation visits. Standard questionnaires were used by trained interviewers to obtain the information. No information was given about those who did not volunteer. Individuals living for more than 3 years in areas of high pollution (SO_2=107 to 250 microgms/m^3; total suspended particulates=137 to 165 microgms/m^3) showed significantly higher rates of acute respiratory illness over those living in less polluted areas (SO_2=109 to 130 microgms/m^3; total suspended particulates- 121 to 123 microgms/m^3). Restricted activity and otitis media were also significantly higher among individuals in high pollution areas. Cigarette smoking among mothers seemed to be related to increased susceptibility in the youngest preschool children.

A similiar study was conducted in New York CHESS communities using volunteer families with at least one child twelve years or younger who resided withing 1 to 1.5 miles of an air monitoring station (Love, 1974). Acute lower respiratory tract illnesses were significantly increased among families exposed to elevated levels of air pollutants (SO_2=256 to 321 microgms/m^3; total suspended particulates=97 to 123 microgms/m^3; suspended sulfates=10 to 15 microgms/m^3) for two to three years. Residential mobility, socio-economic status, cigarette smoking in the home, and family history of chronic bronchitis all were found to be determinants of respiratory disease in children; but these did not account for the total differences in illness rates associated with differences in air pollution exposure.

Effects of nitrogen dioxide and elevated suspended particulate exposure on respiratory illness were examined among families with second grade children in a study conducted in Chattanooga (Shy, 1970). Respiratory illness rates were

consistantly higher in the exposed areas. Differences could not be explained by economic level, family composition, or prevalence of chronic conditions. Therefore, nitrogen dioxide exposure alone or exposure to elevated suspended particulates alone was proposed as being related to increased respiratory illness. Parental smoking habits did not appear to affect the illness rates in the second grade children.

Of particular interest are two studies conducted in four CHESS communities in the Salt Lake Basin and in five communities of the Rocky Mountain area (Nelson, 1974, Finklea, 1974).

In the Salt Lake Basin, the communities exhibited similar particulate and SO_2 exposures but varying SO_2 and suspended sulfate exposures. The primary source of SO_2 was a large smelter located five miles northwest of the high exposure community. Past pollution levels were estimated from monitoring and emmission data with consideration of meteorologic factors. Although these estimates are not precise they are useful for determining annual average exposures to pollution. Information on respiratory illness was obtained through questionnaires sent home with elementary school children and mailed to the parents of junior and senior high school children. The response to the questionnaires was 67%. Samples of nonrespondents seemed to indicate no difference between the two groups, but this may not have been sufficient to rule out bias. Frequency of single or repeated episodes of acute lower respiratory illness, bronchitis,and croup increased (40 to 50%) after exposure to elevated levels of SO_2 (91 microgms/m^3) and suspended sulfates (15 microgms/m^3) for over three years. These levels were found only in the high exposure community near the smelter. Parental smoking was found to increase in incidence of bronchitis and pneumonia among their children. The two most powerful determinants of illness were age and history of asthma which were controlled for in assessing the effects of air pollution.

In a very similar study, five communities in the Rocky Mountain area were selected and ranked as high or low on the basis of their estimated exposure to SO_2 during the study period 1967-1970 (Finklea, 1974). Anaconda, one high exposure community, has been the site of a large copper smelter since the end of the last century. Kellogg, the other high exposure community, has been the site of a lead smelter for over 76 years. Questionnaires were sent home with the school children with instructions for their mothers to give respiratory disease information on all children 12 years of age or younger. Information was requested for the previous 3 years. This study found significantly greater incidences of acute lower respiratory disease among asthmatic and non-asthmatic children who were exposed to estimated annual SO_2 levels of 177 microgms/m^3 and suspended sulfates 7.2 microgms/m^3, accompanied by low estimated annual average levels of particulates (65 microgms/m^3) for three or more years. The two high pollution communities studied were definitely less well educated, experienced more household crowding, and the parents were more likely to be cigarette smokers than those from the low-exposure communities. Socio-economic adjustment was made between communities, but no adjustment was made for smoking differences.

Despite the problems inherent in this second study, duplication of results tends to give validity to these studies. Other studies have confirmed the association between increased respiratory disease with increasing levels of air pollution (Paccagnell, 1969,,Zeidberg, 1964, Mountain 1968, Yoshida, 1974). Mountain found a positive association between the prevalence of respiratory symptoms and of particulate matter and CO among children under 8 years of age in the east side of New Your City. The prevalence rate of bronchial asthma has been positively correlated with concentrations of SO_2 in Japan (Yoshida, 1974).

Paccagnella performed daily examinations on school children, ages 7-12, in Ferrara, Italy and found that acute respiratory disease was related to smoke and SO_2 and to

temperature and humidity (Paccagnella, 1969). He felt that the influence of climatic factors was greater than that of air pollution factors.

Along slightly different lines, several studies have focused on the affect of air pollution on emergency room visits and hospital admissions for respiratory disease. These studies deal not so much with the incidence of respiratory disease as with the severity of the disease. In order for these cases to be detected, respiratory symptoms had to be sufficiently bothersome to require a hospital visit. Another important consideration is the affect of weather in precipitating an attack of asthma which often brings a child to the emergency room. It is known that sudden changes of temperature and barometric pressure cause more attacts than a slow drop over several days.

A three-fold greater incidence of asthma as measured by visits to a particular emergency room has been associated with high levels of air pollution (particulates, approximately 130-220 microgms/m^3 (Girsh 1967). In this same study a four-fold increase in incidence of bronchial asthma occurred during days of high barometric pressure. On days of high pollution and high barometric pressure a nine-fold increase in bronchial asthma attacks occurred.

Emergency room visits for all respiratory symptoms were compared with ambient SO_2 levels during a week includent three days of an acute pollution episode in New York, the week before and the week afterwards (Chiarmante, 1970). There was a significant rise in obstructive symptoms associated with a rise in SO_2 levels. This increase in respiratory symptoms was most marked 72 hr. after the peak SO_2 level (0.8 ppm). This may be due to a lag between SO_2 levels and respiratory symptoms or may just reflect a reluctance of the patients to seek medical attention over a holiday (the day of heaviest pollution fell on Thanksgiving). No data were given on weather or on other pollutants.

Smoke shade and sulfur dioxide levels were compared to patient visits for asthma to an emergency room in Brooklyn, New York (Rao, 1973). The number of patient visits did not vary with SO_2 levels and they actually decreased with increasing levels of smoke shade. The lack of association with SO_2 may well be due to the low levels of SO_2 (.099 ppm) recorded during this study period in contrast with Chiarmonte's study where SO_2 levels were rather high (0.8 ppm). Only changes in pollution levels and in number of visits were analyzed. Actual levels of pollution were apparently not considered. Another shortcoming with this study was the lack of temperature data.

In a comparison of two areas of contracting air quality, a strong correlation existed between the number of daily visits for asthma and daily levels of SO_2 in the area of supposed lower pollution levels but not in the area of higher pollution levels (Goldstein, 1974). No data on the actual levels of SO_2 and particulates were given, only ratios between the two areas. A strong relationship between asthma visitis and the first cold spells of fall were noted in both cities. Similiar results were obtained by Ribbon who found change in temperature to be related to changes in asthma visits to a New York Hospital (Ribbon, 1972). The authors felt that SO_2 itself was not the causative agent of increased asthma attacks but was associated with some other confounding variable. The conclusion was based on the fact that SO_2 was not consistantly associated with the increased attacks of asthma.

Greater hospitalizations for asthma, eczema, and croup syndrome have been associated with increased air pollution (Sultz, 1970; Emmerich, 1972). Sultz found no relationship between hospitalization for asthma and eczema and socio-economic class. There was a consistant relationship between higher hospitalization rates and higher levels of air pollution within each social class. Emmerich noted an

increase in croup cases, mainly in infants, when the SO_2 concentrations were 40-80 ppb, while levels over 80 ppb appeared to be promoting the onset of disease.

A number of studies have used lung function measurements to determine impaired health. In a well known study by Toyoma, 10-11 year-old school children in Kawasaki and Tokyo were found to have lower mean peak flow rates in areas of high pollution than in areas of low pollution (Toyomo, 1964).

Holland studied 10,971 children in four areas of Kent using a questionnaire on past respiratory illness and an examination which included measurement of the peak expiratory flow rate (Holland, 1969). Peak expiratory flow was affected by the level of pollution (as categorized by place of residence), the social class, the family size, and a past history of pneumonia, bronchitis or asthma. These four factors were found to act independently and additively. However, these factors only accounted for 10-15% of the total variation. This may mean that host factors play a greater role in air pollution effects.

No relationships between lung function values (mean Raw) and environmental factors were found in the 14 year-old school children from three districts of Budapest (Mandi, 1974). Based on the homogeneity of Raw values and questionnaire results for the three school classes, it was concluded that respiratory function values, respiratory complaints, and respiratory symptoms were not affected by the prevailing level of air pollution. It must be noted that the levels of air pollution were low (SO_2=0.1-0.9 microgms/m^3, dustfall 38 g/m^2/mo.) compared with other studies.

In a survey of 1,000 children from two areas of Rotterdam, one wealthy and unpolluted and the other poor and polluted, differences in the peak flow rates were primarily due to differences in height and weight between the two communities (Bierstaker, 1970).

School absences and lung function as measured by FVC and FEV_1 were used to study pollution effects on first and second grade children in seven schools in Berlin, New Hampshire (Ferris, 1970). School absences and respiratory illness were apparently not affected by air pollution. This may have been due to the fact that some of the children did not live close to their school and had been assumed. Pulmonary function tended to be lower in those children living in an area of high SO_2 (491 microgms $SO_3/100\ cm^2/day$) and particulate pollution (43.2 $ton/m^2/30$ days). The study suggests that the main contribution to this effect of the pollution is the amount of particulates in the air.

Mostardi compared 42 male high school students from an urban industrialized area with 50 male students from a rural area in Ohio on the basis of measurements of vital capacity (VC), one-second forced expiratory volume (FEV_1) maximal midexpiratory flow (MEF), and maximal indirect oxygen consumption (VO_2max) (Mostardi, 1974). These students had been studied three years previously on the basis of VC and $FEV_{0.75}$. Over the 3 years, air pollution levels decreased. During that time the FEV values improved, but VC did not. MEF rates showed no significant differences between the two areas. VC and VO_x max values were significantly lower in the more polluted area indicating that there could be some permanent impairment of cardiopulmonary function as a result of concentrations of SO_2 and particulates that were slightly above then current U.S. standards. This study is of interest because of the use of the measurement of VO_2 max which is not usually considered. It has been suggested that the differences in VO_2 max may have been influenced by the lack of routine exercise in the urban group although participation in orgainized sports seemed to be similar between the two groups in the study. Potential criticisms of the study included the relatively small numbers studied, the lack of analysis of data on cigarette smoking although such data were apparently collected, and the conceivable difference in urban-rural use

of non-tobacco cigarettes (Air Quality Statistics).

During emergency levels of particulates in Pittsburgh, Stebbings investigated the effects pollution had on lung function values ($FEV_{0.75}$ and FVC) among fourth to sixth graders (Stebbings, 1976). As pollution levels dropped, lung function values would be expected to improve in those areas that had experienced high pollution while remaining the same in the control areas. This did not occur. In fact, pulmonary function values declined slightly over the 7 day test period. Small permanent effects on lung function could not be detected in this manner; to do so would require measurements before the episode. There is also the possibility that a longer period of study is required in order to observe improvements in lung function. This study was also unable to detect effects that reversed in less than 48 hr.

As a part of the CHESS program, Shy conducted ventilatory function tests ($FEV_{0.75}$) on 2,364 New York school children four times during the 1970-71 school year (Shy, 1974). Age, height, socio-economic status, ethnic factors, migration history, temperature, exposure to indoor air pollutants and to pollutants not monitored, and concurrent respiratory disease were factors that were taken into consideration. Shy observed that children 9-13 years of age exposed to estimated annual average sulfur dioxide levels of 131 to 435 microgms/m^3, levels of suspended particulates estimated at 75 to 200 microgms/m^3, and suspended sufates estimated at 5 to 25 microgms/m^3 for a period of eight or more years showed significant decreases in $FEV_{.75}$. This was not observed in younger children age 5 to 8 years.

Ventilatory function as measured by $FEV_{0.75}$ was also determined for children attending 12 different schools in Cincinnati (Shy, 1974). Sulfue Dioxide levels were low in all areas studied with an arithmetic mean of 52 microgms.

The observed area differences were deemed as probably due to differences in suspended particulates suspended sufates or suspended nitrates. Since ventilatory performance varied strongly with variation in suspended sufates in all racial and socio-economic groups, the differences in $FEV_{0.75}$ were attributed to suspended sulfate concentrations.

Higgins and Ferris criticized both the New York and Cincinnati ventilatory function studies conducted by Shy as providing unconvincing evidence that differences in pulmonary function in school children were due to differences in exposure to air pollution (Higgins and Ferris, 1974). Various inconsistencies in these studies were pointed out and they concluded that "random scatter seems to be a much more likely explanation than air polution for these differences in lung function."

In another CHESS study conducted in Charlotte, North Carolina and Birmingham, Alabama, ventilatory lung function was used to compare the effects of air pollution on children (Chapman, 1974). $FEV_{0.75}$ was found to be lower among children from Birmingham which had higher levels of RSP (35% higher), TSP (34% higher), and suspended sulfates (25% higher). However, SO_2 levels were lower in Birmingham than in Charlotte. This finding led Chapman to attribute the lower lung function values to exposure to particulate pollution.

Of particular interest is a study conducted in a southern Arizona copper-smelting and mining town and Tucson, Arizona, which investigated the effect of air pollution and excercise on lung function (Lebowitz, 1974). Three groups were chosen: a group of 60 male and female white middle class fifth grad students half of whom were to excercise outdoors in Tucson; a group of 30 male six to twelve year-old white lower and middle class Mexican-Americans to excercise indoors in Tucson; and a group of 17 six to twelve year-old

white lower and middle class Mexican-Americans to exercise outdoors in the mining town. The outdoor exercise group in the mining town and the indoor group in Tucson were engaged in the same activities while the outdoor group in Tucson was divided into control (no excercise) and exercise (played as they usually did). In general, type or degree of exercise, eating lunch,and ethnic or social status was found to have no effect on lung function values. It was assumed that air conditions indoors reduced pollution to a level where it would have no effect on the children. The actual levels of pollution indoors were not measured.

Healthy children in the mining town experienced decreased lung function values on the 2 days of high pollution before exercise. These values decreased even more after exercise. Values of $FEV_{1.0}$ and FVC showed consistant decreases after the lunch-exercise period on high pollution day. No differences were found between subjects with or without a history of respiratory disease. No statistically different results were found between the light and heavy exercise groups. Unfortunately no monitoring data on air pollution level were given.

One concern mentioned in several studies has been the contribution of indoor air pollution to a person's overall pollution load. Love suggested that indoor air pollution caused by the domestic use of gas for cooking might be important in acute respiratory disease in children because of the association of cooking gas with nitrogen dioxide, a pollutant that supposedly alters susceptibility to respiratory disease (Love, 1974).

The importance of the indoor environment in air pollution exposure has been investigated (Binder, 1976). Portable personal air pollution samplers were used to measure the exposure of twenty male children to respirable particulates, sulfur dioxide, and nitrogen dioxide over a 24 hour period. Half had respiratory disease and half were normal controls. Of particular significance was the fact that all children

experienced exposures to particulates that were considerably higher than outdoor concentrations. This exposure exceeded the primary air quality standard in all but one child. Exposure to SO_2 and NO_2 was lower than outdoor values on the average. Among children who lived with one or more smokers, particulate exposures were significantly higher. Pollutant exposure was similar for control and diseased subjects, indicating no relationship between pollutant exposure and respiratory disease. It was apparent that outdoor pollution measurements did not accurately reflect the air pollution load experienced by individuals within the sampling area. The importance of indoor air pollution was emphasized by an analysis of reported daily activities that showed that children were indoors 60-80% on an average school day. Since adults tend to spend even more time indoors, the importance of indoor air pollutant concentrations are even more important for determining their pollution load. The implications of this study are intriguing, but the study should be replicated before any conclusions are drawn.

In summary, it appears that children, particulary infants, are a highly susceptible population to the effects of air pollution. Exposure to elevated levels of pollutants apparently increases the rate of acute respiratory disease, increases visits to hospitals for asthma, and decreases pulmonary function.

The morbidity studies on children are summarized in Tables 13 and 14.

Table 13

EPIDEMIOLOGIC STUDIES ON THE EFFECTS OF SO_2 AND PARTICULATES ON CHILDREN AS MEASURED BY MORBIDITY

Source	Population	Area	Method	Exposure			Results
				Particulates	SO_2	Other	
UNITED STATES							
Firsh 1967	1,346 asthmatic children	St. Christopher's Hospital Philadelphia	1) total number of asthmatic patients coming to hospital outpatient dispensary July-May 1963-1965	Suspended dust heavy pollution area 130-220 mg/mc light pollution area 70-120 mg/mc	Measured but not stated	Nitrogen oxide, CO oxidants Settled dust Heavy pollution 50-75 tons/sq mi/mo	1) increased frequency of asthma associated with 1) high barometric pressure 2) increase air pollution 2) 9-fold increase in asthma with high barometric pressure and heavy air pollution
Chiarmonte 1970 203	8 mo-15 year olds 83 children same cohort 90 children	Long Island College Hospital New York	1) visits to the emergency room for respiratory problems (3 weeks) 2) allergy evaluations	Not stated	Nov. 23-29 episode .06-.8 ppm Nov. 16-22 .07-.26 ppm Nov. 30-Dec. 6 .07-.33 ppm		1) rise in obstructive symtoms associated with rise in SO_2 levels 2) rise more evident 72 hours following peak SO_2 level

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
Sultz 1970	Children <15 yr old	4 areas divided by air pollution, Erie County Buffalo	1) hospitalization with asthma or eczema	<80 - >135 $\mu g/m^3$	Not measured	Not stated	1) consistent increase in hospitalized asthma cases with increasing air pollution within social class 2) incidence in asthma and eczema in boys <5 yr show greater association with air pollution 3) no relationship between social class and hospitalization 4) 3 times more hospitalized cases <5 yrs than 5-16 yrs.
Ribon 1973	Asthmatic children	Metropolitan Hospital, New York	1) visits to the emergency room for bronchial asthma 2) hospital admissions for bronchial asthma	Not stated	<.07 - >.11 ppm	smoke shade <2.0->2.6 COHS/1,000 ft. Also CO and oxidant measured	1) the change in number of asthmatic visits appeared to be unrelated to change in level of smokeshade SO_2 or relative humidity. 2) a change in temperature tended to be associated with a change in number of visits for asthma
Rao 1973	1,742 children mostly black or Puerto Rican, low socio-economic class	Kings County Medical Center Brooklyn, New York	1) daily records of number of patients visiting emergency room diagnosed as acute asthma attack cases Oct. 1970-March 1971	Not stated	0 - .099 ppm	soiling 0-2.99 COHS/1,000 ft.	1) no change in patient visits to emergency room with varying SO_2 levels 2) number of patient visits decreased with increasing smoke level 3) correlation between smoke shade and SO_2 level (r = 0.46)
Goldstein 1974	children <13 years old and adults	Harlem and Brooklyn, New York	1) number of visits to emergency room for asthma Sept.-Dec. 1970	no consistent relationship between areas seen inferred SO_2 levels were higher in Harlem (only comparison between the two cities given).			1) increased asthma with cold weather 2) in Harlem no rise in asthma visits with SO_2 3) high correlation between daily SO_2 levels and daily visits to hospitals in Brooklyn (r = 0.5 4) more males than females with asthma (1.7x)

urce	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
untain 68	≤8 yr old and adults (1,820)	lower east side of New York	1) interviewer questionnaire (once a week) 46 weeks	≤1.50->2.01 COH units	<.10 ->2.01 ppm	CO ≤3.0->4.01 ppm Total hydrocarbons 4.0 - 5.01 ppm	1) prevalence of respiratory symptoms in children directly related to increasing levels of particulate matter and CO. In the summer not related to SO_2 and hydrocarbons 2) respiratory symptoms more prevalent in young children than in adults but headache and eye irritation more prevalent in older group
y 70	968 2nd grade children and their families (4043 individual)	4 areas in greater Chattanooga	1) biweekly postcards inquiring about illness followed up by telephone interview for 24 weeks	one area had elevated particulate levels	two other areas were controls no data given	one area elevated NO_2 levels	1) excessive acute respiratory illness among families of the high NO_2 area 2) illness rates peaked during A_2/Hong Kong influenza epidemic and influenza B epidemic. A consistent excess in respiratory illness was reported in the two exposed areas 3) parental smoking habits did not appear to influence respiratory illness rates of 2nd grade children
rris 70	716 1st and 2nd graders Jan-June 1966 692 1st and 2nd graders Sept.-June 1967 all white	7 schools in Berlin New Hampshire	1) absences from school follow-up with a questionnaire 2) lung function a) FVC Wright's peak flow meter b) FEV_1 Stead Wells spirometer	4.86-22.55 tons/mi^2/ 30 days/per 24 hours	206-619 µg/100 cm^2	dustfall 13.4-43.2 tons/mi^2/ 30 days	1) pulmonary function could be associated with pollution 2) particulate concentration might be as important as SO_2 concentration 3) school absences might not be a sufficiently sensitive index of the effects of air pollution

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
Mostardi 1974	jr. high school students 1970	Barberton and Revere Ohio	1) pulmonary function test a) VC b) $FEV_{0.75}$ 1970	TSP low - high 76.85 - 109.34 $\mu g/m^3$/24 hours	low - high .809 - 1.046 $\mu g/SO_2$ 100 sq cm/ day	dustfall low - high 5.4 - 30.9 tons/sq. mi/ mo.	1) VC and $FEV_{0.75}$ lower in high pollution area
	same cohort 92 16 yr. old males 1973		1) interview 2) pulmonary function Collins 9 liter spirometer a) VC b) $FEV_{1.0}$ c) MMF 1973	TSP low - high 70.9 - 77.3 $\mu g/m^3$/24 hours	method for measuring SO_2 changed for 1973 and could not be used comparatively	dustfall low - high 10.3 - 18.3 tons/sq. mi/ mo.	1) VC lower in high pollution area 2) $FEV_{1.0}$ can improve over a perio when air pollutants are reduced
	subsample of 30		VO_2 MAX 1973				1) VO_2 lower in high pollution area
Lebowitz 1974	60 5th graders M and F white middle class	Tucson outdoors	1) portable pneumotachygraph a) FVC b) $FEV_{1.0}$ 4 consecutive Thursdays in spring	85 - 107 $\mu g/m^3$	Not stated	Sulfate 2.9 - 3.9 $\mu g/m^3$	1) $FEV_{1.0}$ and FVC sign decreased after exercise on high pollution days 2) lung function decreased to a greater degree when temp. and pollution greater
	30 6-12 yr M white and Mex.-Amer. lower and middle class	Tucson indoors	1) Collins 13.5 1 spirometer a) FVC b) $FEV_{1.0}$ c) MMEF Monday and Friday for 5 weeks in summer	air-conditioned building pollutants considered to be much lower than outside valves			1) external air pollution and temp. did not affect lung function with exercise 2) ethnic group, social status, and respiratory history did not appear to affect lung function

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
Lebowitz (cont.)	17 6-12 yr. old white and Mex.-Amer. lower and middle class	Copper smelter mining town outdoors	1) Collins 13.5 l spirometer a) FVC b) $FEV_{1.0}$ c) MMEF 4 consecutive Tuesdays in summer 2) each study group divided into 2 or more groups that performed different levels of activity	relatively high ambient atmosphere concentrations compared to EPA standard or to non-CU mining town			1) high pollution days association with decreases in $FEV_{1.0}$, $FEV_{1.0}$ FVC, MMEF after exercise 2) no difference in lung function seen between a) those with and those without history of respiratory illness b) light and heavy exercise
Stebbings 1976	approx 270 4th-6th graders	6 schools around Pitts-burgh	1) pulmonary function test $FEV_{0.75}$ FVC 12 l - dry seal bellows type spirometer		range on higher pollution day .036-.130 ppm	soiling 1.95-7.37 COHS	1) no indication of consistent increases in pulmonary function with time
				no consistent decrease in pollution within areas			

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
UNITED KINGDOM							
Douglas and Waller 1966	3,866 children born March 1946	4 areas in Great Britain	1) interviews with mothers when child 2 and 4 yr 2) medical exam at 6, 7, 11, and 15 yrs of age	predicted from domestic coal consumption low - high estimated levels from measurements in 1962 91 - 142 $\mu g/m^3$	low - high 148 - 249 $\mu g/m^3$	Not stated	1) upper respiratory tract infection not related to air pollution 2) frequency and severity of lower respiratory tract infection increased with amount of air pollution
Lunn 1967	819 5 yr old children	4 areas of Sheffield	1) parental questionnaire 2) exam 3) $FEV_{.75}$ FVC with Poulton spirometer over a period of 3 summers	range mean daily levels 1964 97 - 301 $\mu g/m^3$	to 123-275 $\mu g/m^3$		1) upper and lower respiratory illness associated with area which reflected pollution level (increasing with increasing pollution) 2) social class, number of children in house and sharing rooms had little influence on disease 3) $FEV_{.75}$ FVC decreased in heavy pollution area only 4) past history of respiratory disease associated with reduced $FEV_{.75}$
Holland 1969	10,971 5-16 yr olds	4 areas of Kent	1) parental questionnaire 2) medical exam 3) PEFR with Wrights peak flow meter	winter months 1966-67 (daily average) high pollution area 28-96 $\mu g/mm^3$ low pollution area 12-50 $\mu g/mm^3$	similar to smoke levels		1) peak expiratory flow rate decreases with a) increasing family size b) lower social class c) past history of respiratory disease d) residence in areas of higher pollution these factors act independently and additively

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
olley nd Reid 970	10,887 6-10 yr olds	urban and rural areas of England and Wales	1) questionnaire 2) exam 3) PEFR, Wright peak flow meter	Not stated	winter mean 40 - 140 $\mu g/m^3$	Not stated	1) respiratory disease shows gradient (increasing) with 1) lower social class 2) increasing air pollution most evident in children of semi-skilled and unskilled workers 2) upper respiratory illness not associated with increasing levels of pollution 3) ventilatory function not affected by pollution
unn 970 212	500 9 yr olds same cohort studied in 1967 1,049 11 yr olds as studied 1967	4 areas of Sheffield	1) questionnaire 2) exam 3) $FEV_{.75}$ FVC with Poulton spirometer over a period of 3 summers	range mean daily level 1968 48 - 169 $\mu g/m^3$ to 94 - 253 $\mu g/m^3$			1) 11 yr olds had less frequent history of 3 or more colds, cough and colds going to the chest, lower respiratory tract illnesses, pneumonia and bronchitis than 5 yr olds in original study. 2) decrease in morbidity associated with decrease in pollution 3) $FEV_{0.75}$, FVC showed no association with air pollution 4) insignificant increase in $FEV_{0.75}$ with respiratory illness
olley 973	20 yr olds same cohort studied by Douglas and Waller 1966 (3,899)	Great Britain	1) questionnaire	estimates made 7 occasions from 1948 to 1957, very low, low, moderate, high			1) smoking is the dominant factor in developing respiratory disease 2) air pollution, social class, early respiratory disease showed insignificant effects on respiratory disease

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
JAPAN							
Toyama 1964	207 10-11 yr olds	2 areas in Kawasaki	1) exam 2) peak flow rate and TVC	Not stated	sulfation .48-1.7 SO_3 mg/d/ 100 cm^2/ PbO_2	dustfall 15.7-70 monthly ton/sq km/ mo	1) mean peak flow varied inversely with level of pollution 2) TVC not affected
	approx. 1200 10-11 yr olds	6 schools in Tokyo	1) exam 2) peak flow rate and TVC	Not stated	Not stated	Not stated	1) mean peak flow varied inversely with level of pollution
Kagawa 1974	20 M and F 11 yr olds	Tokyo	1) body plethysmograph a) raw b) Gaw/vtg. c) FRC d) FVC	pollutants measured but no numbers given suspended particulate	measured	ozone NO NOx NO_2	1) raw values increased with increasing temperature 2) during high temp. NO_x, NO_2, SO_2 SPM may affect upper and lower airways 3) low temp - NO_2, NO_x, SO_2 SPM may affect lower airway O_3 affect upper airway 4) 5 subjects showed significant correlation of their pulmonary tests with more than 3 environmental factors
Yoshida 1974	163 school children with bronchial asthma		1) questionnaire 2) interview of parents 3) pulmonary function $FEV_{1.0}$ 4) immunoglobulin assay	Not stated	average annual .07-.05 ppm	Not stated	1) prevalence rate of bronchial asthma higher in polluted areas 2) prevalence rate of bronchial asthma positively correlated with concentrations of SO_2 ($r = 0.705$) 3) many children with bronchial asthma have high E globulin levels

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
OTHER FOREIGN							
Yanysheva 1957	613 children of lower school age 8 years or older	2 areas in the USSR	1) morbidity data based on medical records (2 yr) 2) clinical exam	24.9 - 66.3 mg/m^3	13.3 - 33 mg/m^3	HS 6 - 1.6 mg/m^3	more polluted area associated with 1) low hemoglobin 2) increased frequency of disease of respiratory organs, nervous system, vision and skin 3) lowered resistance to infectious disease 4) induced susceptibility to rickets and anemia and brought early manifestations of diffuse pneumosclerosis
Manzhenko 1966	3,009 12 yr olds	2 districts in Irkutsk	1) school records 2) preliminary exam and living conditions and parent's income 3) x-ray	polluted area 1.87 - 6.4 mg/m^3	polluted area .11 - 1.99 mg/m^3	tarry substances .07 - 1.48 mg/m^3	more polluted area associated with 1) increased incidence of upper respiratory tract condition (1.9 times higher) 2) higher incidence of pulmonary conditions
Kapalin 1963	3,500 3-14 yr old males and females	several areas in Czechoslovakia	1) clinical exam 2) blood tests 3) investigation of home situation (nutrition and living conditions)	Not stated	low - high	high dust fallout	1) high SO_2 positively associated with relative hypochromic anemia microcytosis and polyglobulia 2) red cell values are dependent on quality of nutrition and physical activity

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
Anderson 1966	752 children in 1st grade	3 towns in British Columbia	1) enquiry of school absences with questionnaire 2) peak expiratory flow with Wright peak flow meter	"polluted vs. clean area"			1) tonsillectomy, inflamed eyes, headache, feverishness, nausea, more frequent in polluted areas 2) peak expiratory flow reduced in boys in more polluted areas 3) overall results nonconclusive
Paccagnella 1969	385 7-12 yr olds	3 districts in Ferrara, Italy	1) daily determination of child's health by medical assistants Nov.-April	carbonaceous particles .206-.399 mg/mc	range .065-.278 ppm	Not stated	1) association between temperature humidity, and air pollution 2) incidence of acute respiratory disease correlated negatively with temperature and positively with humidity 3) smoke and SO_2 levels significantly related to illness rate only in low socioeconomic area with low pollution
Bier-steker 1970	1,000 elementary school children	2 districts in Rotterdam, Netherlands	1) peak flow over 15 days Wyss-Hadorn pneumometer 2) questionnaire	low - high 50 - 75 $\mu g/cm^3$	low - high 200 - 300 $\mu g/cm^3$		differences in peak flow explained by age, height, and weight
Emmerich 1972	534 infants with croup	Germany	1) hospital admission	levels similar to SO_2 lower at high SO_2	0 - 20 ppb 20 - 40 ppb 40 - 60 ppb 60 - 80 ppb >80 ppb	Not stated	1) promotion of croup cases when SO_2 >80 ppb 2) increase in croup cases when SO_2 concentrations between 40 and 80 ppb 3) SO_2 just one factor involved

Source	Population	Area	Method	Exposure: Particulates	Exposure: SO_2	Exposure: Other	Results
Zapletal 1973	111 children 10-11 yr old who had lived in area for more than 5 yr	Most Czechoslovakia	1) FVC calculated from FEV with water spirometer	.15 - .52 mg/m^3	.15- .52 mg/m^3 .15 - .67 mg/m^3	Not stated Not stated	1) maximum expiratory flow volume appeared most valuable in studying effects of air pollutio 2) because no past history of respiratory disease was revealed the detected abnormality in lung function might be related to air pollution
	selected group of 19	Prague	1) special testing a) static lung volume b) FEV c) Raw d) MEF e) CL_{stat} f) CL_{dyn} g) Pst (1)				
Mandi 1974	86 14 yr olds	3 districts in Budapest, Hungary	1) questionnaire 2) monthly exams 7 months 3) vol. constant body plethysmograph a) ITGV b) Raw c) VC d) TC e) RV f) SGaw	38 $g/m^2/mo$	0.1 - 9 mg/m^3	Not stated	1) respiratory function neither affected permanently nor periodically by air pollution based on Raw 2) no connection between air pollution and a) respiratory complaints b) clinical conditions c) absences caused by respirator illness

TABLE 14

EPIDEMIOLOGIC STUDIES CONDUCTED BY CHESS INVESTIGATING THE EFFECTS OF SO_2 AND PARTICULATES ON CHILDREN

Source	Population	Area	Method	Particulate ($\mu g/m^3$)	SO_2 ($\mu g/m^3$)	Suspended Sulfate ($\mu g/m^3$)	Results
Shy 1974	5-13 year olds 2364 white children	3 areas of New York	Nat'l. Cylinder Gas pulmonary function indicator - $FEV_{0.75}$ (4 testing periods over 1 year)	75-200	131-145	5.25	No difference in 5-8 year olds who had been exposed less than 5 ye 9-13 year olds in more polluted areas had decreased ventilatory function - significant only in boys $FEV_{0.75}$ of children-in all grades - lowest in winter
Shy 1974 217	7-8 year olds 360 black and white children	6 schools Cincinnati	Stead Wells spirometer $FEV_{0.75}$ one weekly interview with questionnaire - 3 months November, February, March	76-131 nitrate 3.1 3.1	<52	9.5	Low $FEV_{0.75}$ values associated with: a) residence in polluted area b) blacks c) month of February Suspended sulfate exerted greatest effect on $FEV_{0.75}$ value Ventilatory performance not affected by pollutants on day of test $FEV_{0.75}$ of black and white children lowest in winter

Source	Population	Area	Method	Particulate ($\mu g/m^3$)	SO_2 ($\mu g/m^3$)	Suspended Sulfate ($\mu g/m^3$)	Results
Finklea 1974	2-5 year-olds and their families	3 areas of Chicago	Telephone interview once every two weeks, 11-69-11-70	During study TSP 111-151	51-106	Not stated	Individuals living more than 3 years in high pollution area had increased rates of: a) acute respiratory illness b) restricted activity c) otitis media Children in high exposure community had higher attack rates of respiratory disease in the first 3 years of life Cigarette smoking by the mother seemed to be related to increased susceptability among youngest preschool children
				high pollution area TSP 137-165	107-250	Not stated	
Love 1974	children $\leq$ 12 years and their families (white) (3000)	3 communities in New York	Telephone interview once every two weeks, 9-70-5-71	Range during study TSP 34-104 Nitrate 1.9-4.1	23-63	10.2-14.3	Illness frequency increased with: a) increasing socio-economic class b) recent family migration c) cigarette smoking in the home d) parental history of bronchitis Exposure to these levels of air pollution (estimated from the past 5 years) for 2-3 years was linked to excessive illness
				97-123		10-15	
				5 year estimated annual average 256-321			

ource	Population	Area	Method	Particulate (µg/m3)	SO_2 (µg/m3)	Suspended Sulfate (µg/m^3)	Results
inklea 974	1 - 12 yr olds (5,773)	5 communities in the Rocky Mountains	questionnaire filled out by a parent	99 - 115	67		acute respiratory morbidity in asthmatic children increased with exposure to these levels
				65	177	7.2	excess in acute lowe respiratory illness especially croup, among asthamtic and nonasthmatic expose to this level for more than 3 years
ammer 974[c] 21	1 - 12 yr olds	New York	questionnaire filled out by a parent	60 - 185	38 - 425	9 - 20	excess acute lower respiratory disease associated with these levels of pollution
							morbidity patterns similar for blacks and whites except pneumonia was more frequent and bronchitis was less frequent in blacks
							pneumonia and hospitalization were higher in low exposure white children

urce	Population	Area	Method	Particulate (µg/m3)	SO_2 (µg/m3)	Suspended Sulfate (µg/m^3)	Results
lson 74	9,000 1 - 12 yr olds white middle class	4 communities in the Salt Lake Basin	questionnaire filled out by a parent	highest estimated level 62 nitrate 2.0	91	15	significant increase in acute lower respiratory morbidity attributed to exposure to these levels of pollution for more than 2 yrs asthmatic history, age, socioeconomic status, and cigarett smoking in the home also had significant effect on frequency of illness morbidity excesses observed with 5 - 9 yr exposure to annua average levels of 9 µg/m^3 sulfate in the absence of elevated levels of other pollutants hospitalization & pneumonia not related to air pollution levels

Source	Population	Area	Method	Particulate ($\mu g/m^3$)	SO_2 ($\mu g/m^3$)	Suspended Sulfate ($\mu g/m^3$)	Results
Chapman 1974	5-13 yr olds 3,705 white and black children	Charlotte	1) NCG spirometer $FEV_{0.75}$ 2) self questionnaire	RSP 32 - 40.9 TSP 67.9 - 85.9	16	8.6 - 11.1	1) $FEV_{0.75}$ lower in polluted city strongly indicates that exposure to particulate pollution decreases pulmonary function
		Birmingham	1) CPI 12 1 spirometer 2) self questionnaire	RSP 39.9 - 49.4 TSP 104.5 - 119.8	11	1.8 - 13.7	2) intercity differences in $FEV_{0.75}$ were smallest in Fall and greatest in Spring. Particulate pollution differences paralleled these findings

F. Occupationally Exposed Groups

1. Sulfur Dioxide

Elevated levels of sulfur dioxide have been suspected in causing urticaria (Pirila, 1954, 1963), asthma (Romanoff, 1939), and even death (Galea, 1964) among groups occupationally exposed.

Upon exposure to sulfur dioxide, the usual reaction consisted of fits of coughing, sneezing, and a running nose. No measure of SO_2 exposure was given in these particular case reports. The association of SO_2 exposure with the subsequent reactions was made on the basis of exposure to unusually large concentration of SO_2 fumes several days before the onset of the symptoms.

In order to acquire accurate information on the health effects of occupational exposure to SO_2, Kehoe studied 200 refrigeration workers in Dayton, Ohio (Kehoe, 1932). One hundred men who were exposed to high levels of SO_2 (forty seven of whom had been exposed for 4-12 years) were compared to 100 men who were not exposed to detectable levels of SO_2 within the same plant. The two groups were comparable in age, height, weight, number of years they had worked in the plant, systolic and pulse pressures, erythocyte and leukocyte count, and hemoglobin level. A significantly higher incidence of nasopharyngitis, of alteration in the sense of smell and sense of taste and of increased sensitivity to other irritants was found in the group of workers exposed to SO_2. Abnormal urinary acidity, tendency to increased fatigue, shortness of breath on exertion, and abnormal reflexes were also all significantly increased in the exposed group. Of the exposed group, 80 percent became acclimatized to the SO_2 exposure within approximately 3 ± 2 months. Acclimatization was defined as the ability to withstand the basic exposure to SO_2 without experiencing a notable intensity of 1) hemoptysis, 2) chest constriction, 3) epistaxis, 4) cough and 5) irritation of the respiratory tract. In other words, those who were considered

acclimatized still experienced these symptoms, but to a lesser degree than when first exposed to SO_2. In spite of these findings, the author concluded "that there is no appreciable danger to health" in a more or less continuous exposure to endurable concentrations of SO_2 and that exposure to unendurable concentrations is negligible under conditions which allow for escape. A positive relationship existed between frequency of heavy exposure and increased fatigability and shortness of breath on exertion. No relationship was found between frequency of heavy exposure and the frequency of severity of initial symptoms. Colds lasted 2-3 times longer in the exposed group although incidence was not increased.

A possibly long-term effect of SO_2 exposure was also investigated by Anderson among oil refinery workers from the Anglo-Iranian Oil Co. in South Persia (Anderson, 1950). Two areas were chosen for study: the refining plant and the special products plant. Within each area, two groups of workers were chosen, those who were exposed to SO_2 and those who had no record of exposure to SO_2. Clinical exams were performed on each man including an estimation of vital capacity and a radiograph of the chest. The group exposed to SO_2 in the refining plant showed a significantly better mean vital capacity than the control group. The x-rays did not show any uneven distribution of abnormalities among the four groups. There was no evidence of an adverse effect on health with sulfur dioxide exposure.

In Norway, a group of 54 pulp mill workers exposed to 2-36 ppm SO_2 were compared to 56 paper industry workers not exposed to any "objectionable" gases (Skalpe, 1967). The two groups were comparable as to age and smoking habits and were assumed to be of similar social class due to the similarity of the two jobs. A higher frequency of cough, expectoration and dyspnea on exertion was evident in the exposed group. The maximum expiratory flow rate was lower in those under 50 in the exposed group. No differences were found between the men over 50 in the two groups. The author porposed that this

is due to respiratory disease being rare in younger age groups so that a small change is easier to detect than in older age groups where respiratory disease is more common.

Pulp mill workers were also compared with paper mill workers in Berlin, N.H. (Ferris, 1967). The pulp mill workers were exposed to approximately 1.71-2.06 ppm SO_2 and .001 ppm Cl_2 at the time of the survey. No difference in respiratory disease or lung function was found between the two groups. Men exposed to Cl_2 did experience poorer lung function and more shortness of breath than those exposed to SO_2 but the difference was not statistically significant. The fact that these two groups exhibited a lower prevalence of respiratory disease than the general population suggests that they were not representative of the population. Upon further examination of the data, self-selection was noticed among the paper mill workers. Those who found SO_2 exposure disagreeable tended to work for the paper mill, where SO_2 levels were undetectable. In this way, those who were more sensitive to SO_2 exposure were more likely to work in the paper mill, thereby reducing the differences in respiratory illness between the two occupational groups.

In a study designed to investigate the relationship of respiratory cancer mortality with occupational exposure to arsenic, sulfur dioxide, silica, lead fumes,and ferromanganese, 8,047 white male smelter workers were compared with the white male population of the same states during 1938-1963 (Lee and Fraumeni, 1969). Smelter workers experienced an excess total mortality, mainly due to malignant neoplasms of the respiratory system, diseases of the heart,and cirrhosis of the liver. A three-fold increase in mortality from respiratory cancer was observed among smelter workers with a gradient related to exposure to arsenic, SO_2 and length of employment. The highest rate of cancer was found among men with heavy arsenic exposure and medium to heavy SO_2 exposure. Smoking histories were not available on these men but according to the authors it seemed unlikely that smoking alone could account for these

great differences. Greater excess mortality was noted for foreign-born than native-born residents of the U.S. This difference might be explained, in part, by the fact that they generally had longer periods of employment than native-born workers. An inverse relationship existed between excess respiratory cancer and silica exposure. This may just reflect the fact that work areas with high arsenic or high SO_2 exposure provide a light silica exposure.

Of those men who were exposed to iron in the form of ferromanganese dust, a significant number died of lung cancer (5 out of 317 exposed). Two of these deaths occurred among persons with high SO_2 exposure and 1 death occurred in a person with high silica exposure.

This study was unable to distinguish between the influences of arsenic and SO_2, but was consistent in its association of heavy arsenic exposure, possibly in interaction with SO_2, with excess numbers of death from respiratory cancer among smelter workers. Since SO_2 has never been implicated as a carcinogen in man, the author proposed that SO_2 possibly enhances the carcinogenic effect of arsenic.

Archer cited several studies that were designed primarily to give data on cancer among copper smelter workers (Archer, 1977). One of these, by Milby and Hine, indicated that 10 percent of deaths were due to non-malignant respiratory disease in a smelter having relatively high levels of SO_2 vs. 5.1 percent for one with lower levels of SO_2. Apparently no age adjustment was made so these differences may not be meaningful. Rencher and Carter are quoted by Archer as having found a rate of 77.3/10,000 deaths from circulatory disease among smelter workers compared to 71.9/10,000 among open pit workers. By using a relative mortality method, they also examined non-malignant respiratory deaths, finding 12.3 percent of such deaths among smelter workers as compared to 11.9 percent among mine workers. Of these deaths, 3.4 percent were due to emphysema and 7 percent to pneumonia among smelter workers as compared to 2.2 percent and 6.8 respectively among

mine workers. Although these differences were not statistically significant, they suggest that excess deaths due to chronic respiratory disease do occur among those occupationally exposed to SO_2.

Lee and Fraumeni reported an SMR (standardized mortality ratio) of 141 for tuberculosis, 329 for malignant neoplasms of the respiratory system, 118 for diseases of the heart, and 79 for influenza and pneumonia among workers exposed to high levels of SO_2. Pinto and Bennett reported 150 deaths from cardiovascular disease as compared to 134 deaths expected among smelter workers exposed to high levels of SO_2.

In a recent study by Archer, a copper smelter and the open pit mine which supplied it with ore were chosen to study the chronic effects of low level occupational exposure to SO_2 (Archer, 1977). Questionnaire interviews provided information on occupational history, respiratory symptoms, tobacco, smoking habits, past illnesses, and social factors. Pulmonary function tests were performed with a spirometer computer. FVC and $FEV_{1.0}$ were inversely related to smoking and to time spent in the smelter. Among those who smoked cigarettes and were exposed to SO_2, there was a clear trend for SO_2 exposure to be associated with a decrease in FVC and FEV_1, than was heavy cigarette smoking. The effects of these two agents were found to be additive.

Problems which arose in the conduct of this study included representative sampling, use of the data backup system (more frequently used among controls), selective withdrawal of persons with respiratory disease from the study population, possible differences due to prior work exposures, physical fitness, influences of weather, differences in the time of day of examinations, altitude differences, contaminating dust or gases (other than SO_2), and ethnic and socioeconomic differences in pulmonary function. None of these factors appeared to negate the results, but in fact probably artificially decreased the actual differences between the two groups.

Chronic exposure to SO_2 in the 8-hour time-weighted average (TWA) range of 1-5 mg/m^3 (.4-2 ppm) accompanied by small amounts of sulfur oxides and other particulates was found to be associated with significant reductions of FVC and FEV_1, increase in some symptoms of respiratory disease and days off for illness.

This study indicated a need for reconsideration of the present TWA standard for SO_2 which is 5 ppm. It also warned those exposed to significant levels of SO_2 of the extra risk of cigarette smoking.

Smith has assessed the exposure of workers at a smelter located in Garfield, Utah from 1940-1974 (Smith, 1977a). The reverberatory furnace area was found to have the highest levels of sulfur dioxide. In 1974 the time-weighted average was approximately 30 mg/m^3 with brief "puffs" approaching 520 mg/m^3 (Smith, 1976). Sulfate compounds averaged 0.11 mg/m^3 and sulfites averaged 0.046 mg/m^3. Similar, but slightly higher levels were found in the converter area. Various protective measures that have been installed in the smelter were discussed with respect to subsequent changes that have occurred in sulfur dioxide concentrations. Total particulate levels were described as highly variable (0.41 mg/m^3 to 2.03 mg/m^3 throughout the plant. Sulfate compounds in all areas of the plant were found to be largely in the respirable fraction (approximately 80 percent). Sulfite compounds consisted of various particle sizes with a fairly uniform spread.

Personal monitoring devices were implemented in 1973 to measure actual exposure of certain workers (Smith, 1977a). A comparison of smelter area and personal samples indicated that area measurements in high exposure jobs overpredicted worker exposure. For example, an average of 3.5 mg/m^3 SO_2 TWA was determined for reverberatory furnace feeders, while samples from that area averaged 16.77 mg/m^3 during an eight hour shift. The reason for this discrepancy can be attributed

to the fact that workers spent approximately only 2 hours per shift on the fee dock with an average of 0.95 hours of mask use while on the dock.

Pulmonary function as measured by forced vital capacity and forced expiratory volume in one second were recorded for 113 of these workers during 1973 and 1974 (Smith, 1977b). The workers exposure was determined by personal air monitoring devices previously mentioned. Respiratory symptoms, smoking history, and occupational history were also recorded. After controlling for smoking, an excessive loss of forced expiratory volume in one second (70 ml per year as compared with 25-30 ml normally lost), and an increase in respiratory symptoms was found with exposure to 1.0-2.5 ppm SO_2. The study also suggested that a differential sensitivity to SO_2 exists. Thirty percent of the total workers examined were determined to have acute responses to SO_2. This group experienced even greater losses of pulmonary function. No significant interaction between SO_2 and respirable particulates seemed to occur in relation to an effect on pulmonary function.

It is interesting that in the 7 epidemiologic studies investigating occupational exposures to SO_2 and its possible health effects, only the three most recent studies have concluded that SO_2 is a potential hazard to the exposed worker. The SO_2 levels in one of these later studies (Smith) was below the recommended TWA (.4-2 ppm) but were still associated with increased respiratory symptoms. Two of the early studies did show significant differences in respiratory symptoms among exposed workers--but the authors did not feel it was of importance.

SO_2 has been associated with increased respiratory illness among workers exposed to elevated levels over the eight-hour work-day. Exactly what levels constitute a threshold value below which no health effects are demonstrable still needs to be evaluated further with consideration of concurrent community exposure. The exposure to SO_2 itself must also be considered

in view of other sulfur oxides and particulates that might accompany it within the occupational setting and within the neighboring communities.

The U.S. Department of Labor, Occupational Safety and Health Administration (OSHA) recently held hearings to determine if the occupational exposure levels should be changed from the current 5 ppm TWA to a lower level as has been suggested by recent epidemiologic findings (Archer, 1977; Smith, 1977).

A summary of these studies is presented in Table 15.

Table 15

EPIDEMIOLOGIC STUDIES ON THE EFFECTS OF SO_2 ON OCCUPATIONALLY EXPOSED GROUPS

Source	Exposed Group				Control Group			Methods	Results
	Population	Number	Exposure	Duration	Population	Number	Exposure		
ehoe 932	Refrigeration workers Mainly from 1) SO_2 storage and distribution dept. 2) refrigerating unit charging department 3) repair dept.	100	average 30 ppm previous to 1927 80-100 ppm	mean 2-4.9 yrs. 47 men exposed 4-12 yrs.	Refrigeration workers Mainly from 1) assembling department 2) tool room 3) punch press room 4) carpentry shop 5) shipping department Matched on age groups	100	None	1) interview a) length and nature of SO_2 exposure b) past and present illness 2) physical exam a) blood and urine lab tests b) chest X-ray	1) higher incidence exposed workers o a) nasopharyngiti b) alteration in sense of smell and taste c) increased sensi tivity to othe irritants d) abnormal urina acidity e) tendency to increased fatig f) shortness of breath on exertion g) abnormal reflex 2) no association between frequency heavy exposure and frequency or severity of initia symptoms 3) positive associati between frequency heavy exposure to presence of fatigu and shortness of breath 4) duration of colds extended in expose group incidence is not significantly different 5) concludes SO_2 expo sure is not signif cantly dangerous t health

rce	Exposed Group				Control Group			Methods	Results
	Population	Number	Exposure	Duration	Population	Number	Exposure		
ierson 50	Oil refinery workers			1-19 yr.	Oil refinery workers			1) Clinical exam a) VC b) XR	1) Exposed group in refining plant showed better MVC than control 2) no evidence of adverse effects of SO_2 on healt
	1) refining plant 2) special products plant	97 36	0-25 ppm Occasionally 100 ppm	mean 8.15 yr. mean 2.91 yr.	1) refining plant 2) special products plant	100 35	no recorded exposure no recorded exposure		
ilpe 54	Pulp mill workers a) acid towers b) digester plants	54	2-36 ppm measurements all made on single day		paper industry workers	56	no objectionable gases	1) Exam a) symptoms b) VC with 'kifa' apparatus c) MEFR with Wright's peak flow meter	1) higher frequency of cough, expectoration, and dyspnea on exertion in exposed group, greater in those <50 yr 2) MEFR lower in those <50 yr. within exposed group 3) no difference in VC between two groups
rris 57	Pulp mill Workers	147	SO_2 - 1.71-2.06 ppm before 1958 13.2 ppm Cl_2 = <.001 ppm		paper mill workers	124	not stated	1) Interviewer questionnaire a) occup. history b) smoking history c) respiratory symptoms 2) Pulmonary function a) FVC b) FEV_1, with Wright's peak flow meter	1) No difference in disease or lung function between two groups 2) Working population of both mills had lower prevalence of respiratory disease than general population 3) Men exposed to Cl_2 had poorer respiratory function and shortness of breath than those exposed to SO_2

Source	Exposed Group				Control Group			Methods	Results
	Population	Number	Exposure	Duration	Population	Number	Exposure		
e and raumeni 69	White male smelter workers	8,047	a) arsenic - light - - medium - heavy b) SO_2 - light - medium - heavy c) silica d) lead fumes e) ferro-manganese	≥15 yr. before 1938 ≥15 yr. 10-14 yr. 5-9 yr. 1-4 yr.	White male population of the same state		not stated	1) mortality by death certificate	1) Excess death in expose group. O = 1,877 E = 1,634 2) respiratory cancer significantly in exces with gradient associate with length of employ-ment 3) respiratory cancer positvely related to a) arsenic exposure b) SO_2 exposure 4) highest risk associate with heavy arsenic, med to heavy SO_2 exposure 5) excess death in those exposed to ferroman-ganese E - 1.24 O - 5
cher 77	Copper smelter workers	953	0.4-2 ppm (TWA)	.1-9.9 yr. 10-19.9 >20 yr.	mine shop workers	252	not stated	1) Questionnaire interview a) occup. history b) respiratory symptoms c) past ill-ness d) smoking history 2) Pulmonary function a) FVC b) FEV_1 spirometer computer	1) Chronic exposure to SO_2 associated with a) reduction in FEV_1 an FVC b) increase in respira-tory symptoms and days off from work 2) The effects of SO_2 and smoking both increased with increasing length of exposure

urce	Exposed Group				Control Group			Methods	Results
	Population	Number	Exposure	Duration	Population	Number	Exposure		
ith 77	Copper smelter workers	113	varied according to work area - respirable dust, total sulfur, copper	not stated	None	-	-	1) Interview a) respiratory symptoms b) smoking history c) occup. history d) history of disease 2) Pulmonary function	1) 1.0-2.5 ppm SO_2 associated with excessive loss of FEV_1 and an increase in respiratory symptoms even after controlling for smoking 2) Those with an acute response to SO_2 experienced even greater loss of lung function.

2. Sulfuric Acid

Massive exposure to sulfuric acid has been associated with pulmonary fibrosis, bronchiectosis, and emphysema (Goldman and Hill, 1953). According to Williams, sulfuric acid has possibly been involved in death from edema or spasm of the larynx (Williams, 1970).

Apparently few studies on long term exposure to sulfuric acid have been made, except in men occupationally exposed. Malcolm and Paul studied the effects of sulfuric acid on the teeth of exposed and nonexposed workers in the storage battery industry and found that considerable erosion of incisor teeth occurred only in men exposed to acid mist in the forming department. The amount of acid in the air varied from 3 mg to 16.6 mg/m^3 on one day (Malcolm and Paul, 1961). According to Williams, dental erosion in forming workers was also found by Ten Bruggen Cate (Williams, 1968).

Williams investigated the certified sickness absenteeism and ventilatory capacity of men exposed to sulphuric acid in the forming department studied by Malcolm and Paul in 1961 and of men in other departments of the same factory who were not exposed. A slight excess of absences due to respiratory disease, particularly bronchitis, was found among men exposed to sulphuric acid mist as compared with controls. The excess of respiratory disease was attributed to the increased number of episodes in men attacked rather than to an increase in number of men attacked. No marked excess was seen in lower respiratory tract disease. Williams suggested that this latter might be due to the large particle size of the sulfuric acid mist. In another forming department, Williams has stated that the mass median diameter has been shown to be 14 microgms with only 4% being less than 4 microgms in diameter. Tests of ventilatory capacity showed no significant differences between groups.

El-Sadik compared 33 workers involved in battery manufacture in two factories with 20 men never exposed to any chemicals, who worked in the same factories (El-Sadik, 1972). The concentrations of sulfuric acid ranged from 26.12 to 35.02 mg/m^3 in one plant and

12.55 to 13.51 mg/m^3 in the other. No significant difference in chronic bronchitis or chronic asthmatic bronchitis was found between the exposed and control group. There was a decrease in $FEV_{1.0}$ in the exposed group that perhaps might be due to inhalation of sulfuric acid fumes. Dental infections apparently increased with duration of work.

According to Utidjian, it has not been possible to identify a threshold value of sulfuric acid mist concentration below which no detectable dental erosion occurs (Utidjian, 1975). At present the recommended occupational exposure limit of 1.0 mg/m^3 of air as a time-weighted average seems to be sufficient to prevent excess in respiratory disease but no conclusions can be reached on prevention of tooth erosion.

A summary of these studies is presented in Table 16.

EPIDEMIOLOGIC STUDIES INVESTIGATING THE EFFECT OF ATMORPHERIC SULFURIC ACID ON OCCUPATIONALLY EXPOSED GROUPS

	Exposed Group				Control Group				
	Population	Number	Exposure	Duration	Population	Number	Exposure	Method	Results
Malcolm & Paul 1961	workers in a storage battery industry a) forming dept. b) charging dept.	160	3.0-16.6 mg/m^3 .8-2.5 mg/m^3	varied	workers in a storage battery industry a) inspection dept. b) packers	117	free from acid mist or any other dental hazard	1) dental examination	1) only men exposed to acid mist displayed erosion of incisor teeth. 2) factors influencing the degree of erosion seemed to be the length of exposure, lip level, & concentration of the acid in the air.
Williams 1970	workers & exworkers in an electric accumulator factory a) forming dept. (Same as studied by Malcolm (1961))	--	not measured	few days to more than 40 years	workers & exworkers in an electric accumulator factory a) assembly dept. b) pasting dept. (workers only) c) plate cutting dept. (used for ventilatory companions)	--	no exposure	1) certified sickness absense 2) ventilatory capacity a) FEV_1 sec. b) FVC measured before & after shift on Monday & Friday	1) slight excess of episodes of respiratory disease particulary bronchitis among exposed group. 2) increased number of spells in attacked men rather than an increased number of men having spells. 3) no significant difference in ventilatory capacity

	Exposed Group				Control Group				
	Population	Number	Exposure	Duration	Population	Number	Exposure	Method	Results
El-Sadik 1972	workers in manufacturing dept. of two storage battery factories	33	1) 26.12-35.02 mg/m^3 2) 12.55-13.51 mg/m^3	varied	workers never exposed to any chemicals in same two factories.	20	None	1) exam a) occupational history	1) exposure to sulfuric acid does not cause (a) chronic bronchitis or chronic asthmatic bronchitis, (b) reduction in vital capacity. 2) FEV_1 decreased 82 ml. in exposed group. 3) saliva pH averaged 7 before work & 6.95 after work in controls, 6.9 before work & 6.7 after work was found in exposed. 4) dental infections increased with work duration.

3. Particulates

Determining the occupational effects of particulates is difficult because of the wide range of airborne material included under the classification of particulates. In most air pollution studies of ambient air the composition of the measured particulate is not determined. Most occupational studies on the other hand deal with high exposure to one particular kind of dust or irritant such as coal, silica, aluminum or barium in miners or even flour dust exposure in bakers. The literature is voluminous in regard to the health effects of these many different materials and a complete review of all the literature would not be possible. A few relevant studies relating occupational exposure to dust and summary articles, specifically on coal dust exposure, have been reviewed and are presented here.

Lowe studied the employees of two steel works in South Wales (Lowe, 1970). Data on respiratory symptoms and measurements of lung function were collected from 10,449 men who worked in one of 114 working areas of different pollution levels. SO_2 and respirable dust were measured although the actual levels in different areas were not given. Analysis demonstrated the importance of smoking in the etiology of bronchitis with its prevalence increasing with the amount smoked. For air pollution it was concluded that if a relationship exists with respiratory symptoms it was very slight and not detectable by the methods used in this study. Lowe noted that the failure of a relationship with airborne dust was not surprising because the mean level never exceeded $2mg/m^3$. The lack of an association with SO_2 was more surprising because the levels measured were five times the winter mean in London.

Lowe noted that attempts by other authors (Paul 1961; Brinkman 1962; Skalpe 1964; Ferris 1967) to demonstrate relationships between exposure to dust and SO_2 and respiratory symptoms in particular occupational groups have been either negative or unconvincing.

Paul studied 3,536 African copper miners and 1,815 non-miners (Paul, 1961). A very low incidence of chronic bronchitis was found to exist in the populations studied. No evidence was found that silica dust predisposes to the development of this disease. It was hypothesized that the low levels of chronic bronchitis were due to the moderate smoking habits of the population.

Brinkman studied 1,317 men in Detroit aged 40 to 65 (Brinkman, 1961). They were divided into four groups on the bases of exposure to silica dust. Cigarette smoking was found to be the most important factor in the cause of chronic bronchitis.

Doll reviewed mortality of selected groups of gasworkers in England for eight years (Doll, 1965). The men studied were between 40 and 65 years of age and had been employed in the industry for more than 5 years. Three broad occupational classes were defined; those with heavy exposure to products of coal carbonization, those with intermittent exposure, and those with no exposure. Results showed that the annual death rate was highest in the high exposure group and lowest in the low exposure groups. Two diseases, lung cancer and bronchitis, accounted for the largest amount of the difference, along with cancer of the bladder, cancer of the scrotum, and pneumoconiosis. Differences in mortality were not attributable to differences in smoking. No specific measurements on air pollution levels were made, the results being based on the four classes of postulated exposure.

Higgins published two studies on chronic respiratory disease in miners, foundryworkers, and other occupations in Derbyshire, England (Higgins, 1959, 1968). In the first study, 776 men, ages 25 to 34 and 55 to 64, were divided into four groups, nondusty workers, miners and ex-miners, foundry and ex-foundry and other dusty job groups. A questionnaire was used to collect data on symptomatology and ventilatory capacity (indirect maximum breathing capacity, MBC) was measured.

Wives of workers were also examined. Findings suggested that wives whose husbands worked in dusty occupations had a higher prevalence rate for cough and sputum and chest illness over a three year period compared to wives of those in dust free areas.

A follow-up study on this group was conducted after nine years. Results indicated that the nine-year mortality of miners and ex-miners was insignificantly higher than mortality for non-dusty occupations.

The average annual decline in forced expiratory volume was slightly greater in older men but the decline did not appear to be closely related to occupation. The decline was greater in smokers than non-smokers, suggesting that smoking was a more important factor in the development of respiratory problems than occupation.

Rogan studied the role of respirable dust particles in the development of chronic bronchitis in coal miners in Great Britain (Rogan, 1973). The study involved 3,581 coalface employees who worked in the most dusty part of the mine. The cumulative exposures to dust were calculated from sampling during a 10-year period and from data on earlier exposures. Low exposure levels were 0 - 99 gram-hours per cubic meter with high exposure levels being greater than 200 gram-hours/m^3.

A statistically significant reduction in $FEV_{1.0}$ was found with increasing cumulative exposure to dust. Miners and ex-miners were found to have a higher prevalence of respiratory symptoms and lower mean M.B.C. than men working in dust-free occupations. In the older age group these differences were not significant, in the younger group the differences in M.B.C. were significant.

The importance of coal dust was assessed by measuring the number of years on the coal-getting shift. Elderly miners without pneumoconioses had a significant increase in the prevalence of

of breathlessness with increasing years spent on the coal-getting shift.

A loss of $FEV_{1.0}$ greater than expected from the combined effects of dust exposure, smoking, and age was associated with increasing severity of bronchitis symptoms. It is possible that factors contributing to the development of the disease were not involved in the progression of the disease or the further deterioration of ventilatory capacity.

Smidt studied chronic nonspecific lung disease in 13,000 workers with and without occupational dust exposure in Germany (Smidt, 1976). Occupations included ceramic, asbestos, foundry, coal mining, machine factory workers, and cement workers. Dust-exposed non-smokers age 20 - 35 had a prevalence of bronchitis similar to the moderate smoker. For a middle age group the effect of dust exposure was less than that of smoking. The conclusion reached was that the effects of smoking and dust exposure were additive. The authors stated that because the data on smoking habits were more nearly exact than the data on dust exposure, the chances of proof of an effect of smoking were better than for dust exposure. Therefore, they would not conclude that smoking is a greater hazard in chronic bronchitis than occupational dust exposure.

Morgan, in a review article, stated that most studies have shown a greater prevalence of cough and sputum and a slightly lower ventilatory capacity among the local miners than among control groups (Morgan, 1976). It was pointed out that in 1965 the Medical Research Council of Great Britain reported that the intensity of dust exposure did not play a significant role in the determination of the prevalence of chronic bronchitis and airway obstruction in those with occupational exposure to dust. More recent studies have demonstrated that bronchitis becomes more prevalent as exposure to coal dust increases.

Morgan concluded that, based on recent evidence, the inhalation of most minerals and vegetable dusts can lead to an increased prevalence of cough and sputum. Also, prolonged

exposure to these materials can result in a slight decrease in lung function among some exposed workers.

V. DOSE-RESPONSE - SETTING THE STANDARDS

In reviewing dose-response relationships between air pollutants and respiratory disease, CHESS summarized their most current information. Table 16 shows the levels of pollutant associated with excess chronic bronchitis with current exposure and past exposure in the four study areas. From the data it appears that when a community is exposed to sulfur oxides alone, SO_2 levels of 92 to 95 $\mu g/m^3$ and suspended sulfates of 15 $\mu g/m^3$ are associated with excess bronchitis. When higher levels of particulate matter are present such as 120 $\mu g/m^3$, SO_2 at levels of 100 $\mu g/m^3$ and suspended sulfates at 14 $\mu g/m^3$ are associated with excess bronchitis. In none of the CHESS areas was elevated exposure to total suspended particulates found without concomitant increases in sulfur oxide levels. Finlea concluded that these data support existing primary ambient air quality standards of 80 annual mean (arithmetic) $\mu g/m^3$ for SO_2 and 75 $\mu g/m^3$ annual mean (geometric) for total suspended particulates (Finklea, 1974).

Tables 18 and 19 from the CHESS studies summarize the threshold levels for long and short term pollution exposures for the several health effects. Adverse effects which have been noted with particulates and SO_2 at levels below the national primary air quality standard have been attributed to suspended sulfate concentrates rather than SO_2 and particulates. Significant aggravation of cardiopulmonary symptoms was attributed to 24 hour suspended sulfate levels as low as 8 to 10 $\mu g/m^3$. No national standards have been set for suspended sulfates.

Higgins summarized the dose-response relationships found in a number of studies (Higgins, 1973). Levels between 80 and 100 $\mu g/m^3$ for particulates and SO_2 were found to be reasonable standards. It was concluded that maximum daily averages should not exceed 250 $\mu g/m^3$ for smoke and 500 $\mu g/m^3$ for SO_2. Higgins pointed out that the nature of particulate differs from place to place and other pollutants not even being measured may be more important. In fact, uniform standards for particulates for the entire country may not be justifiable. It was concluded that more research is needed in the area of air pollutants and health especially in the area of sulfuric acid and sulfates.

Table 20 presents a summary of the study results which led to the original air quality standards (Rall, 1974). Rall agrees that the current ambient air standards for sulfur oxides are reasonable and in a proper range.

TABLE 17

RANGE OF POLLUTANT EXPOSURES ASSOCIATED WITH EXCESS CHRONIC BRONCHITIS[1]

CHESS area	Current exposures (annual average), $\mu g/m^3$			Exposures within past 10 years (annual average)[a], $\mu g/m^3$		
	SO_2 (80)[b]	TSP (75)[b]	SS (no standard)	SO_2 (80)[b]	TSP (25)[b]	SS (no standard)
Salt Lake	62	66	12.4	92-95	53-70	15.0-15.3
Rocky Mountain	177-374	65-102	7.2-11.3	177-374	62-179	6.9-19.9
Chicago	96-217	103-155	14.5	100-282	118-177	14.1-17.3
New York	51-62.9	63.1-104.0	13.2-14.3	144-404	80-173	9-19

[a]Estimated from emissions data and pollutant trends

[b]National Primary Air Quality Standard. The particulate standard is a geometric mean; the equivalent arithmetic mean would be about 85 $\mu g/m^3$.

[1]Source: Finklea, 1974

TABLE 18

BEST JUDGMENT ESTIMATES OF POLLUTANT THRESHOLDS FOR ADVERSE EFFECTS OF LONG-TERM EXPOSURES[1]

Effect	Threshold (annual average), $\mu g/m^3$		
	Sulfur dioxide (80)[a]	Total suspended particulates (75)[a]	Suspended sulfates (no standard)[a]
Increased prevalence of chronic bronchitis in adults	95	100	15
Increased acute lower respiratory disease in children	95	102	15
Increased frequency of acute respiratory disease in families	106	151	15
Decreased lung function of children	200	100	13

[a]National Primary Air Quality Standard. The particulate standard is a geometric mean; the equivalent arithmetic mean would be about 85 $\mu g/m^3$.

[1]Source: Chess

TABLE 19

BEST JUDGMENT ESTIMATES OF POLLUTANT THRESHOLDS FOR ADVERSE EFFECTS OF SHORT-TERM EXPOSURES[1]

Effect	Threshold, $\mu g/m^3$		
	Sulfur dioxide (365)[a]	Total suspended particulate (260)[2]	Suspended sulfates (no standard)[a]
Aggravation of cardiopulmonary symptoms in elderly	>365	80-100	8-10
Aggravation of asthma	180-250	70	8-10

[a]National Primary Air Quality Standard.

[1]Source: Chess

TABLE 20

SUMMARY OF DOSE-RESPONSE RELATIONSHIPS FOR EFFECTS OF PARTICLES AND SO_2 ON HEALTH[1]

Averaging time for Pollution Measurements	Place	Approximate Levels of Pollution Particles $\mu g/m^3$	SO_2 $\mu g/m^3$	Effect
24 hr.	London	2000	1144	Mortality
24 hr.	London	750	700	Mortality
24 hr.	London	300	600	Deterioration of patients
Weekly mean	London	200	400	Prevalence or incidence of respiratory illness
24 hr.	New York	6[b]	1500	Mortality
Winter mean	Britain	100-200	100-200	Incapacity for work from bronchitis
nual	Britain	70	90	Lower respiratory infections in children
	Britain	100	100	Upper and lower respiratory infections in children
	Britain	100	100	Bronchitis prevalence
	Britain	100	100	Prevalence of symptoms
	Buffalo	100	300[c]	Respiratory mortality
	Berlin, N.H.	180	731[c]	Increased respiratory symptoms--decreased pulmonary function

[a]"Old" results, leading to original standards

[b]In coefficient of haze units (COHS)

[c]As $\mu g\ SO_3/100\ cm^2/day$

Source: Rall, D.P., Environ. Health Persp., 8, 97-121, 1974

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