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ABSTRACT

The effect of air pollution on human health has been studied extensively since the 1930's. Different study methods have produced results indicating that specific air pollutants, singly or in combination, impact on lung function.

This report reviews study results of two research methodologies involving human volunteers: environmental chamber studies and epidemiology studies. Chamber studies allow precise assessment of the change in lung function which may result from exposure to a known pollutant concentration for a specific time period. The exposure time in such studies is relatively short, making it difficult to adjust for the effects of adaptation and the clinical significance of lung function changes may not be apparent.

Epidemiology studies examine respiratory morbidity among free-living populations. Recent epidemiology studies utilizing improved measurement techniques and study designs have detected effects of selected air pollutants in study populations with respiratory illness. The results of these studies and their impact on future research are discussed.

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RESPIRATORY ILLNESS AND AIR POLLUTION

1 INTRODUCTION

One of the many problems facing governments in the world today is the promulgation of laws to limit the levels of pollutants which are to be allowed within their environments. It is, first of all, not easy to ascertain what the concentrations of these various materials are in air, water, food, and soil. Having surmounted that technical hurdle, the far larger barrier then looms of determining which substances should be controlled, based on adverse human health effects, and complicated by economic considerations. Determining what constitutes an "adverse human health effect", which at first glance may seem to be simple, is extremely difficult. We are dealing with a multitude of substances which may, singly or in combination, cause effects so subtle as to be lost in the general array of human complaints or so delayed in action as to render cause and effect relationships virtually impossible to deduce, much less prove. This paper reviews research efforts to determine the association between adverse health effects in the human respiratory system and selected air pollutants.

2 RESEARCH METHODS

There have been numerous attempts to investigate the possible relationships between levels of air pollutants and adverse human health effects. These fall into three categories, based on approach:

1) Laboratory animal studies, in which small and shorter-lived species are exposed to unusually high levels of a single substance or a mixture of several substances in an attempt to predict human responses based on those in animals.

2) Environmental chamber studies, in which groups of human volunteers are subjected to controlled and measured levels of one or several substances over a period of time rarely exceeding eight hours. Selected physiological parameters are measured before and after exposure to determine whether any acute adverse effects result.

3) Epidemiological studies, in which researchers seek to determine health effects through examination of general or selected populations exposed to pollutants in ambient air. There is no interference with subjects' usual living pattern. These studies may focus on mortality or morbidity and fall into three main design categories:

   a) the cross-sectional design in which a sample of people to be measured is randomly drawn from one or more locations; the number of cases of a disease is counted and histories are taken to determine what exposures people have had to the risk factors being studied. This means that both the cause and the effect measurements are made at the same point in time.

   b) the case-control (or case-comparison) design involves selecting people with an illness (case) and people without an illness (control or comparison). The exposure that both groups had to air pollutants is estimated from personal histories and statistical analysis determines whether the cases had significantly greater exposure to pollutants.

c) the cohort study is one in which a group of subjects (the cohort) is followed for a selected period of time (often months or years) and changes in levels of air pollution are compared to changes in health.

Each approach to studying the effects of air pollutants on human health has advantages and disadvantages. The animal laboratory studies provide the opportunity to control all the factors that might influence response but it is uncertain how applicable results in non-human animal species are to human populations. Failure to reproduce in another animal a cause-effect association that is suspected in man may be a reflection of man's unique characteristics in regard to that particular association.

Environmental chamber studies resulted from speculation about effects of air pollution in human volunteers. Studies in the 1960's tested responses of healthy subjects to one or a combination of air pollutants. More recently chambers have been adapted to expose subjects to ambient air that is monitored for concentratons of selected components. Early studies indicated that selected pollutants could cause reduced lung function in healthy subjects. It was then hypothesized that there would be a more pronounced reduction in persons with hyper-reactive airways or with actual disorders. Therefore, volunteers with hyper-reactive airways disease, such as asthma, were selected for chamber studies along with healthy subjects. Chamber studies have the advantage of controlling the environment and the period of subject exposure. It is, however, difficult to relate chamber study results to air pollutant exposure effects in free-living populations because the exposures are for short time periods and, until recently, only exposed volunteers to selected pollutants, not to ambient air mixtures. There are also ethical considerations about chamber studies because volunteers are exposed to selected pollutant concentrations greater than those in ambient air and the studies are designed to potentially induce an adverse respiratory response.

Epidemiologic study techniques have also been employed to determine the relation between air pollutants and health effects. Acute episodes of increased concentrations of pollutants and subsequent increased mortality and morbidity were documented by cross-sectional studies as early as the 1930's (25, 26, 27, 28, 29). These studies identified the need for further research to examine the respiratory effects of a range of air pollutant concentrations. Such studies were economical because data on both exposure and response were gathered at the same time during a brief period. Because the increase in pollutant concentrations was large and occurred over a few days during the acute smog episodes, the association between cause and effect was easily distinguished. Usually, however, cross-sectional studies are limited to research of causes that are reasonably permanent characteristics of individuals (for example, blood type) so that there is a high probability that the status of the cause in people is the same at the time of the study as at the time the disease was induced. In the studies referenced above, the likely cause of increased morbidity and mortality was increased pollutant concentrations. Particular pollutants could not be identified as causing the responses and little or no allowance could be made for confounding factors such as age, sex or social status.

Case-control (or case-comparison) studies, a second type of epidemiological study, have not been used often to research the effects of air pollution in persons with acute respiratory illnesses. The study approach is to select some people with a disease and some without. Then the frequency with which each person was exposed to the possible causative agent must be determined through personal histories recalled by the subjects. This methodology eliminates the possibility of quantifying the subjects' exposure because air pollution concentrations have not necessarily been monitored near the

subjects. General impressions of "high" pollution periods and "low" periods can be identified but individual causative agents cannot be. Since the study occurs after the effect it is also not possible to identify what confounding variables, aside from the pollutants themselves, might have caused a response.

Cohort studies are designed so that exposure to air pollutants determined prior to or during the study and subjects are monitored to determine whether they develop respiratory symptoms. This means that air pollutant concentrations can be measured continuously for a selected time period. Subjects with respiratory diseases that have intermittent symptoms, such as asthma or bronchitis, are monitored at the same time the air pollutants are monitored. When the study is complete the air pollution variables and the health variables can be analysed for associations between the two types of variables. This methodology permits accurate quantification of exposure and response at the time they occur which is not possible with other types of studies. It is more expensive than cross-sectional studies and can be inconclusive if there are no high pollution episodes during the selected study period. Good measurement is critical to this method's success and quality control must be rigorous. This type of study, if well conducted, can potentially distinguish causative agents from the array of exposure variables being measured. This advantage makes it the method of choice for studies of acute respiratory health effects of air pollution.

3 ENVIRONMENTAL CHAMBER STUDIES

Certain air pollutants, singly and in combination with other pollutants, and their effects on respiratory function have been studied extensively. These pollutants, most of which are regulated by national governments, include sulphur dioxide (SO_2), oxides of nitrogen (NO_x), carbon monoxide (CO), ozone (O_3) and particulates (TSP). Results of studies on these pollutants are discussed in detail below.

3.1 Sulphur dioxide

In chamber studies of SO_2 using healthy and asthmatic volunteers Jaeger et al. (32) determined there was no effect on either volunteer group after exposure to 0.5 ppm (1425 $\mu g/m^3$) SO_2 for 3 hours. However, when Sheppard et al. (33) included light exercise with exposure at levels varying from 0.10 to 1 ppm (285-2850 $\mu g/m^3$) SO_2, they concluded that exercise increased SO_2-induced bronchoconstriction. Linn et al. (34) detected small but significant increases in airways resistance after SO_2 exposure with subjects breathing oronasally, as opposed to only oral breathing, the method used in several previous studies. This conclusion was supported in a study by Kirkpatrick et al. (38). Eight atopic asthmatics observed by Koenig et al. (35) also demonstrated exercise-induced bronchospasm. Tan et al. (37) detemined that selected treatment prior to SO_2 exposure could block the response in atopics but had varying responses in asthmatics. The majority of these chamber studies indicated that SO_2 had some adverse effect on lung function in both healthy and asthmatic subjects. The level at which a response was induced was fairly high but all exposures were for a few hours only and exposed subjects to SO_2 alone.

3.2 Nitrogen dioxide

Chamber studies of the effects of NO_2 in healthy subjects and volunteers with lung function disorder yielded variable results. Orehek et al. (39), after exposing 20 asthmatic volunteers to 0.1 ppm (205 $\mu g/m^3$) NO_2 for an hour prior to carbachol inhalation, had some subjects who responded adversely and some who did not respond. They concluded that very low levels of NO_2 can adversely effect some asthmatics. Asthmatic, bronchitic and normal volunteers were exposed to 0.50 ppm (1025 $\mu g/m^3$) NO_2 for two hours accompanied by light exercise by Kerr et al. (40). The results were varied but asthmatics reported more symptoms than bronchitics. When all subjects' results were analyzed together there was a significant decrease in selected lung function variables but

no decrease was detected when groups were analyzed separately. Kleinman et al (43) also detected a decrement in lung function after 31 asthmatics were exposed to NO_2 during light exercise. Although the decrements did not attain statistical significance there was a definite tendency toward lowered lung function after NO_2 exposure. As with the SO_2 chamber studies, the NO_2 studies had few statistically significant results indicating that NO_2 affected lung function adversely but in all the studies there was a definite tendency toward a decline in lung function after exposure.

3.3 Ozone

Effects of ozone exposure in humans has been studied extensively in environmental chambers. In a study of 8 healthy, non-smoking adults, Golden et al. (53) found that O_3 exposure had little effect on airway resistance but it increased bronchial reactivity for as long as a week in some subjects. Lategola et al (54, 55) in a series of studies designed to duplicate aircraft conditions, detected significant effects on symptoms and spirometry in two of three groups of study subjects. They concluded that the threshold for reversible airway effects from ozone exposure was 0.3 ppm (640 $\mu g/m^3$) after three hours. In 1982, Kulle et al. (56) chose 24 healthy, non-smoking volunteers and exposed them to 0.4 ppm (850 $\mu g/m^3$) O_3 for 3 hours per day for 3 weeks. Initially there was a significant decrease in some lung function variables but after a few days no further decrements were noted. Apparently the volunteers adapted to the exposure and then, during the second weeks' exposure, further decrements were noted. These studies almost all indicated an adverse response to ozone exposure and Kulle's work also indicates that adverse effects may not continuously increase during exposure but that some people may adapt to increased ozone levels for a while. Further exposure may then overcome the adaptive process and another decrement in lung function may occur if exposure is continued for two or more weeks.

3.4 Other pollutants

Other chamber study researchers have observed lung function decrements to other pollutants. Dahms et al. (50) detected a decrement in asthmatics but not in healthy subjects with exposure to cigarette smoke. Hyperventilation caused lung function decrements (49) in groups of asthmatic and healthy volunteers. Sulphate exposure produced a decrease in spirometry variables in asthmatics but not healthy volunteers in a study by Hackney et al. (51) but effects varied depending on temperature and humidity. Utell et al. (52) confirmed Hackney's study with adverse responses detected in asthmatics but not in healthy subjects.

3.5 Pollutant mixtures and ambient air pollution

A series of environmental chamber studies in which volunteers were exposed to combinations of O_3, NO_2, SO_2 and CO and also to ambient air detected responses to those pollutants singly and in combination. In one study (42) little effect was seen after exposure to NO_2, SO_2 and O_3. Another study (44) detected significant adverse effects after exposure to ozone alone. Additional exposures to NO_2 and CO produced no further significant decrement. Von Nieding et al. (45) measured similar decrements when subjects were exposed to NO_2 and SO_2 in combination and when exposed to NO_2, O_3 and SO_2 simultaneously. Kagawa (46) detected significant effects after O_3 exposure and no increased effects after NO_2 and SO_2 exposures, as did Hackney. When Avol et al. (48) and Linn et al. (47) exposed healthy and asthmatic subjects to ambient air the results varied. Linn et al. found no significant pulmonary decrement, a result that conflicted with a similar previous study they had conducted. They concluded that the differences in results were due to lower ambient pollutant concentrations during the second study. Avol et al. completed two studies in which healthy and asthmatic subjects were exposed to ambient air while exercising. The results contrasted markedly. In the first study the subjects showed statistically significant reductions in lung function when the

ozone level was 0.165 ppm (350 $\mu g/m^3$) and TSP was 227 $\mu g/m^3$. The second study showed smaller mean responses but the ozone level was 0.156 ppm (330 $\mu g/m^3$) and TSP was 166 $\mu g/m^3$.

3.6 Summary

Environmental chamber studies resulted in, if not clear-cut evidence, at least an indication that various pollutants effect human health adversely. Epidemiologists have attempted to confirm or refute chamber study results through population-based studies in which there was no interference with subjects' usual living patterns. Environmental factors and health responses were measured while subjects continued with their normal activities. A difficulty with epidemiologic studies is that measurement techniques are critical to success and they are still being improved. Also, each study location has a characteristic mixture of environmental pollutants, therefore results from one study area may not represent another. Because studies can span only a finite period there is always the risk that there has not been sufficient variation in air pollutants during the study period to permit conclusive statistical analysis.

4 EPIDEMIOLOGY STUDIES

4.1 Early studies

Epidemiology studies in the 1960's and 1970's mostly measured effects of outdoor air. Schoettlin and Landau (1) detected adverse health effects in asthmatics when the oxidant level was greater than 0.25 ppm. Zeidberg et al (2) found that asthmatic attacks increased as the degree of sulphation increased. An important aspect of Zeidberg's findings was that they determined the adverse effect of SO_3 was greater one day after exposure to the highest concentration than on the day of the high exposure. In a study of asthmatics by Cohen et al. (4) the asthmatic attack rate was significantly correlated with each of several pollutants (particulates, SO_2, sulphates

and nitrates) after the analysis was adjusted for change of temperature. Other studies (6, 12, 14) detected effects of pollutants, singly or in combination that were present in outdoor air. A study of bronchitics (3) concluded that increased bronchial reactivity was associated with increased pollutant concentrations but specific pollutants could not be identified.

Inconclusive epidemiology studies can provide useful information. Goldstein and Block (5) found a strong correlation with increased number of hospital emergency room visits by people complaining of asthma symptoms and increased SO_2 concentrations. However, the study of emergency room visits was conducted at two different locations. One area's data were strongly correlated, the second area's not. The authors concluded that SO_2 was not necessarily the causative agent but might implicate another confounding variable that was disseminated in a daily pattern similar to SO_2. Another study (7) in Houston, Texas, produced inconclusive results because many air monitoring values were missing due to insufficient air monitoring efforts. Keller et al. (8) concluded the reason for inconclusive results in their study was due to difficulty with health measurement. Subjects were unable to distinguish selected medical problems from others they experienced. In a study by Samet et al. (12) two analysis techniques were employed. One produced no significant results while the second detected a small but significant effect of total suspended particulates and SO_2 on increased respiratory symptoms. Samet's results indicate a need for careful, innovative statistical analyses. Some analytical techniques are not appropriate for application to particular sets of data and can produce inconclusive or spurious results.

In the 1970's increasing interest in the effects of indoor pollutants such as cigarette smoke and NO_2 from gas cookers and heaters was reflected in research. Studies by Weiss et al. (10), Hasselblad et al. (11), Comstock et al. (13), Lan and Shy (15) and Aderele (20) all detected increased respiratory

symptoms in both asthmatics and healthy people if there were smokers in the house. In two of these studies the smoking effect was associated most strongly with the person in the household who smoked and was in most frequent contact with the respondent, the mother. Aderele (20) came to the opposite conclusions; that the response was greater when smokers who were less frequently near the responsive subject smoked in the presence of the subject. In either case, the impact of cigarette smoke on respiratory function has been clearly identified and this factor should be accounted for in studies of effects of air pollutants on human health

Gas cookers and heaters have been shown to effect respiratory function or symptoms in studies by Speizer et al., Comstock et al. and Melia et al. Speizer et al. (9) determined that there was a significant association between presence of gas cookers and increased respiratory disease before age two. In Comstock's study men whose household had gas cooking were at greater risk of having each of several respiratory symptoms than those whose household had electric cooking. Melia et al (18) measured significantly different levels of NO_2 in different rooms in households. In a second study (19) they detected no statistically significant relation between the prevalence of having one or more respiratory conditions and the average weekly levels of NO_2 in either the bedroom or the living room. However, the prevalence of having one or more respiratory conditions tended to be highest in homes with high levels of NO_2 and lowest in homes with low levels. The three studies of effects of NO_2 on respiratory function detected some increased adverse health effects with increased NO_2 indicating a need to characterize NO_2 indoor sources in particular and indoor air pollutant sources in general when studying the effects of air pollutants on human health. The average person spends approximately 90% of his time indoors (30) and monitoring and data analysis should be designed to include the impact of indoor environments as well as outdoor pollutant levels on human health.

4.2 Recent cohort studes

Recently several epidemiology studies, based on results of previous studies and recommendations by other researchers, have expanded air and health monitoring techniques to include indoor and outdoor factors over extended periods of time (3 to 12 months). These studies, which are described in more detail below, were designed to adjust for the many confounding variables involved in human health responses to air pollutants by intensive measurement of many variables.

Frezieres et al. (17) measured health variables in 34 asthmatics in Los Angeles, California, for eight months while an air monitoring station located within 3 miles of each subject's home recorded changes in NO_x, O_3, CO, SO_2, total suspended particulates, pollens and meteorologic variables. The subjects completed daily diaries on respiratory symptoms and changes in respiratory medication. They also measured and recorded their peak expiratory flow twice daily. All subjects were rigorously screened by physician examination and pulmonary function tests to insure they were atopic asthmatics and all 34 who were accepted into the study completed it. Sulphate levels varied more and reached higher peaks than any of the other pollutants studies and the analysis focused on effects of changing sulphate levels in the asthmatics. There were 3 subjects who had strongly correlated adverse effects with increased sulphate levels, 4 appeared to improve with increased sulphate levels and 24 whose responses varied. The authors concluded the results suggest that as many as 9% of asthmatics may be sensitive to levels of sulphate in the ambient air and that reduction of sulphate levels to below 10 $\mu g/m^3$ would significantly reduce the frequency and severity of symptoms and needs for medication in these individuals. This was the first long-term study of its kind in which subjects were requested to monitor and record health variables twice daily and all the subjects completed the entire study. The

measurement of outdoor air pollutants as closely as possible to subjects' homes improved the characterization of the subjects' environments over previous studies that had monitored from distances further from usual environments. There was no monitoring of indoor air.

A study designed by Perry et al. (21) in Denver, Colorado, was similar to Frezieres' study and encountered similar and different problems. Forty-one asthmatics participated in the three-month study although the data from only 24 was included in the analysis because of criteria for inclusion of data that the researchers determined prior to the start of the study. Although all subjects recorded all the information requested of them during the study, the researchers had decided to eliminate observations for any 12-hour measurement period in which the subject reported an upper respiratory infection or was outside the Denver metropolitan area for more than 3 hours. There were two air monitoring stations in the Denver area and the researchers had no provisions for estimating pollutant concentrations outside the area. Because the study took place in the winter there was a fairly high incidence of upper respiratory infection. After applying these restrictions, any subject whose data was less than 60% complete was excluded from the analysis. Loss of health data and a very limited number of days during which high levels of suspended particulates were recorded combined to give inconclusive results although fine nitrates were associated with increased symptoms and increased aerosol bronchodilator usage. This study, as that of Frezieres, had long-term cooperation of subjects completing daily diaries and recording peak expiratory flow and medication usage. There was no indoor monitoring.

There are two more recent studies, one that has not yet completed collecting data and the other that is still analyzing the data, that have expanded air monitoring protocols to include monitoring of indoor and outdoor pollutants. Silverman et al. (16) are completing field data collection in Toronto and Hamilton, Canada, with an air

monitoring network designed to measure simultaneously indoor and outdoor levels in selected homes and places of daily occupation and to estimate the time spent by subjects in each (an activity profile). There are fixed air monitoring sites to characterize neighbourhood outdoor air. There are samplers placed inside and immediately outside subjects' homes to monitor the same pollutants in both places. There are also personal samplers that the subjects carry with them. Health effects are assessed by daily symptom, medication and activities diaries as well as simple pulmonary function tests. Subjects from Toronto are requested to complete diaries for one year and some have intensive air monitoring (indoor and personal) for 2 to 4 weeks twice in the year. There are 36 asthmatics and 18 healthy subjects in that study. In Hamilton, the subjects are school children and indoor and outdoor monitoring as completed at each of their homes once (3200 children). The preliminary results of air monitoring data indicate differences between fixed location, indoor, outdoor and personal monitoring. Further investigations will be necessary to confirm or refute the results of the final analysis as to whether fixed monitoring locations adequately quantify the level of pollutants to which each subject is exposed.

Holguin et al. (24) have completed data collection and the first analysis of the data from a study in Houston, Texas. Fifty-two carefully selected extrinsic asthmatics completed a six-month data collection period. Twice daily they recorded their activities, medication use and respiratory symptoms in diaries. Three times a day they measured and recorded their peak expiratory flow. The air monitoring system was organized in three tiers, similar to those described in Silverman's study. There were two outdoor monitoring stations, located within 2 1/2 miles of each subject's home, that monitored O_3, SO_2, NO_x, CO, particulates, pollens and meteorologic variables. There was a mobile van that monitored inside and outside homes simultaneously for a minimum of one week in each of 12 selected subject houses. The van monitored the same pollutants as the outdoor stations. There was personal

monitoring of more than half the subjects. The personal monitoring involved research staff measuring the particulates and ozone within 30 feet of a subject from 0700 to 1900. Rigorous quality assurance techniques were applied to the air monitoring and health data collection. Of the 52 subjects, data from 10 were excluded from the analysis. One subject's data were considered to be unreliable, one subject recorded asthmatic attacks daily and 8 subjects had fewer than 5 asthmatic attacks during the six months of data collection. The analysis, using the Korn-Whittemore (31) statistical model, detected a statistically significant increase of asthmatic attacks with an increase of O_3 concentration. The significance was enhanced when there was a simultaneous decrease in temperature. Neither NO_2 nor relative humidity influenced the model. Although pollens caused significant response in some individuals during Houston's high pollen concentration season (September and October), when all subjects' data were analyzed together, there was no significant effect. Fine inhalable particulates were not included in the first analysis. SO_2 and CO were also not included in the analysis because the concentrations were very low for SO_2 and CO produces different physiological responses. Although the analysis in the first study report included only 81% of the subjects' data when the 8 subjects with fewer than 5 asthmatic attacks during the study were included in the statistical model the results were unchanged.

4.3 Summary

The Houston study, as the Perry, Frezieres and Silverman studies, proves that subjects will participate in long-term, extensive data collection periods with appropriate encouragement by research personnel. Holguin's study was designed to deal with problems similar studies have encountered that affected their validity and reliability. The problems overcome by the Houston study design were 1) the inaccuracy of individual exposure estimates, 2) missing environmental or health effects data, 3) limitations of analysis, 4) lack of compliance by study subjects, 5)

confounding by concomitant respiratory diseases, 6) subjective symptom reporting, 7) lag time between exposure and event and 8) confounding by weather. This study design utilized recent improvements in air and health monitoring techniques and instruments. Other studies, following a similar design but carried out in locations with different characteristics of pollution or study population could provide further useful information on the effects of air pollutants in humans.

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APPENDIX A

RESPIRATORY ILLNESS AND AIR POLLUTION

EPIDEMIOLOGIC STUDIES

RESPIRATORY ILLNESS AND AIR POLLUTION
A. EPIDEMIOLOGIC STUDIES

AUTHOR	YEAR PUB.	SAMPLE SIZE	DIAGNOSTIC CRITERIA	VARIABLES	RESULTS
1 Schoettlin & Landau, E.	1961	137 asthmatics	Not stated.	Health: Self-reported asthmatic attack- symptoms. Pollutants: Oxidants, particulates, (High Volume Sampler) carbon monoxide. Other: Temperature, humidity. No information on methods, location or timing of pollution monitoring.	Correlation coefficients not significant for particulates and CO. Multiple correlation relating attacks to oxidant, temperature, and humidity was low. When oxidant exceeded .25 ppm, the mean number of subjects with attacks was significantly greater than when it did not, indicating that high levels may be hazardous.
2 Zeidberg, L.D., Prindle, R.A. & Landau, E.	1961 Part I	49 adults & 35 children, all with chronic bronchial asthma	For asthma: medical records, physical examination, pulmonary function tests and skin tests for sensitivity to grasses & trees. For response: Statistically significant increase in asthmatic attacks during periods of higher pollutant concentrations.	Health: Daily reporting by diary of asthmatic attacks, length of attacks & medication usage. Weekly reporting to a study office with pulmonary function tested during many visits. Pollutants: Sulfur trioxide (SO_3) annual mean expressed as mg SO_3/100 cm^2/day; SO_2 24-hour samples. Other: Wind direction, wind velocity, temperature, humidity, barometric pressure & precipitation.	For the whole group of subjects the asthmatic attack rate showed direct correlation with the degree of sulphation. The correlation was not seen for the children. For adults the rate was three times as high for those living in the high pollution areas, compared with those in the low. Attack rates were more significant when shifted over one day from the days with the highest levels, taking into account possible delayed effects. Tem-

					perature, humidity & barometric pressure showed no effect on attack rate, but wind velocity showed an inverse relationship. Pulmonary function tests indicated that subjects with a one-second timed vital capacity of less than 50% of the vital capacity had significantly higher attack rates than patients with more than 75% function.
3 Lawther, P.J., Waller, R.E., & Henderson, M.	1970	3 studies: 1. 1954-55 had 529 patients who attended chest & emphysema clinics. 2. 1959-60 had 1071 patients from London clinics whose "symptoms of of chronic bronchitis, emphysema or asthma were likely to be made worse by air pollution". 3. 1964-65 had 1037 patients from chest clinics.	Bronchitis: Criteria not stated for any study. For response: Subjects completed daily diaries stating whether they felt better, worse or the same as the previous day. Significant response was defined as a significant increase in numbers of people feeling worse on days when air pollution levels increased.	Pulmonary distress: Subjective reporting in daily diaries of general health. Pollutants: SO_2, smoke mg/m^3. Other: During the series of studies the daily diaries were altered in an effort to increase reporting information & accuracy.	Authors conclude (from results of all 3 studies) that pollution rather than adverse weather is associated with exacerbations of bronchitis. They could not determine which pollutant or combination of pollutants is responsible but that the concentrations of smoke & SO_2 can only be regarded as indices of the active agents. The second purpose of the studies was to improve the diary method of collecting information. The authors conclude that the diary technique is only applicable in studies of patients with diseases in which frequent changes of condition occur. The subjects favored pocket diaries &

					authors suggest that health changes be compared to previous days to avoid "wandering baseline". Long-term studies (over more than one season) chance loss of subject interest.
4 Cohen, A.A., Bromberg, S., Buechley, R.W., Heiderscheit, L.T., & Shy, C.M.	1972	20 asthmatics	For asthma: Initially identified during telephone interview as having respiratory symptoms. Screened by a staff physician for intermittent periods of respiratory distress. For response: Statistically significant increase in asthmatic attacks during time periods where pollutant levels increased.	Health: Self-reported asthmatic attacks, sometimes confirmed by a physician. Pollutants: Particulates (HV, COH), SO_2, sulphates, nitrates as measured at 3 monitors. Distance of subject from monitors unspecified. Other: Temperature, barometric pressure, wind speed, humidity.	Multiple linear regression defined no correlation of wind speed, humidity and barometric pressure with asthmatic attack rate. After adjustment for temperature, each pollutant was positively associated with attack rate. After adjustment for temperature & any one pollutant, none of the others explained a significant amount of attack rate variation.
5 Goldstein, I.F.& Block, G.	1974	4798 persons who went to the emergency rooms at 2 Brooklyn, New York, hospitals between Sept. & Dec. 1970; of those persons, the number of people going with complaints of asthma. Also, 1916 persons going to	For asthma: Attending physicians' diagnoses as asthma; the diagnoses were often separated further, e.g. bronchial asthma and allergic asthma, but no differentiation was made for the study because distinctions were not clear cut & physicians did not always agree on categorization. For response: Significant differences in numbers of persons reporting with asthma complaints on days of high vs. days of low pollution.	Health: Number of persons reporting with asthma complaints to emergency rooms of 3 hospitals. Pollutants: SO_2 & smoke shade. SO_2 categorized by high & low periods. High pollution was defined as $\geq$ 0.073 ppm based on $\geq$ 18 hourly readings per day. Low was defined as < 0.073 ppm based on $\geq$ 18 hourly readings per day.	In Harlem no significant correlation between daily visits to the emergency room for asthma complaints and daily levels of either smokeshade or SO_2. In Brooklyn there was a strong correlation (.61 & .42 for persons under 13 yrs. and .56 & .32 for persons 13 yrs. and older) between daily visits for asthma and daily levels of SO_2, but not smokeshade. Authors conclude that although other research has indicated asthmatics might be sensitive

		the emergency room of a Harlem hospital; of that number, those reporting asthma symptoms. Numbers of persons with asthma symptoms not reported for either hospital.			to SO_2, in their study SO_2 is not necessarily the causative agent, but might implicate another confounding variable that is disseminated in a daily pattern similar to SO_2.
6 Levy, D. Gent, M. & Newhouse, M.T.	1977	1780 patients who were admitted to any one of four hospitals for respiratory illness (acute exacerbations) in Hamilton, Canada.	For illness: Physician's diagnosis of acute respiratory disease related to bronchitis, bronchiolitis, emphysema, pneumonia & asthma that required hospital admission. For response: Significant increase in the total weekly number of hospital admissions for respiratory illness when the air pollution levels increased.	Health: Hospital admissions for respiratory illness. Pollutant: COH and SO_2 combined to calculate an air pollution index (API). Other: Temperature, wind direction & velocity, relative humidity & pollen concentrations.	Highly significant correlation coefficient was obtained when total weekly respiratory admissions for all hospitals were related to the API. Most significant associations were in February & October, during major climatic changes. Highest correlation at the hospital in the industrial area. Pollen concentrations were not related to hospital admissions. There was a moderate correlation between increased admissions and days of colder temperatures but no correlation with relative humidity.
7 Houston Chamber of Congress	1977	275 subjects with asthma, bronchitis and/or emphysema.	For health: Medical respiratory history reviewed by physicians for indications of one or a combination of the illnesses.	Health: Self-reported daily symptomatology, weekly spirometry tests on a subset of study subjects, self-reported medication use.	Results were inconclusive as many data on air pollutants were lost. Recently the Chamber of Commerce contracted the Stanford

			For response: Significant increase in respiratory symptoms on days of increased pollutant concentrations.	Pollutants: O_3, NO_x, PAN, particulates (HV), & CO monitored at 9 different sites within 2 miles of each subject's residence. Other: Pollens, temperature, humidity, wind speed, wind direction, barometric pressure.	Research Institute to reanalyse the study's data. The results of the reanalysis are not yet available.
8 Keller, M.D., Lanese, R.R., Mitchell, R.I.& Cote, R.W.	1979	441 families divided into 2 groups; those utilizing gas for cooking & those utilizing electricity for cooking.	Families completed diaries & were contacted every two weeks for 12 months and asked to report respiratory illness in any household member & to indicate presence or absence of cough, wheezing or bringing up sputum (all indicative of lower respiratory disease); and signs of upper respiratory disease. Concentrations of NO were determined by monitoring a total of 83 gas-cooking homes & 50 electric-cooking homes for NO_2 & NO over periods of 24 hours. In addition, 53 outdoor air samples were taken in the vicinity of these households. Continuous monitoring for 3-day periods in 46 homes in order to measure instantaneous variations in indoor NO_2 & NO levels in relation to cooking times.	Health: Diaries and verbal questions about cough, phlegm, shortness of breath, wheezing, bringing up sputum, stuffiness, runny nose, head-ache, sore throat & other "cold" & lower respiratory infection symptoms. 821 of the 1952 persons in the study population had FVC & FEV_{75} measured. No description was given as to when the measurements were made. Pollutants: NO_2 & NO were monitored indoors in randomly selected homes.	The incidence of mothers/women with respiratory disease in electric cooking was slightly higher than for women in gas-cooking homes. The differences in incidence between the women in the two types of homes was not significant. The incidence of respiratory illness in the 83 gas-cooking households that were monitored for NO_2 was tested to determine whether the households having NO_2 levels above the median reported higher incidence. No difference in incidence was seen. Authors stated that the respondents might have had difficulty distinguishing between upper & lower respiratory infection. The pulmonary function tests were administered only to volunteers & there might have been some self-selection.

9 Speizer, F.E., Ferris, B., Bishop, Y.M.N.& Spengler, J.	1980	8,120 white children 6 through 10 years of age living in 6 cities.	For response: Significant decrement in pulmonary function based on spirometry test results due to exposures to different indoor pollutants. Decrement was based on difference in long function expected based on height & age.	Health: FVC & FEV_1. Pollutant: Questionnaire responses about type of cooking fuel (mostly gas or electric), home heating fuel, air conditioning, and presence or absence of adult smokers in household; NO_2 measurements. Other: Age, height, sex & city.	Gas cookers had an effect (significant association) on respiratory disease before age 2, but not on diagnosed bronchitis or respiratory illness in the year prior to the study. Parental smoking, sex of the child & city-cohort, but not age at time of reporting were also associated with respiratory disease before age 2. Home heating & FEV, were significantly associated as were gas cookers & lower FEV_1. Measurements taken in homes over 24-hour periods showed NO_2 4 to 7 times higher in homes with gas, not electric stoves but well below national 24-hour standards.
10 Weiss, S.T., Tager, I.B., Speizer, F.E.& Rosner, B.	1980	650 children aged 4-10 years were randomly selected from parochial & public schools in East Boston.	In this study of early-life risk factors for development of chronic obstructive airway disease, interviews determined what illnesses a child had been diagnosed by a doctor as having & compared the diagnoses with reported symptoms.	Health: History of respiratory illness as reported at interview (cough, wheeze, phlegm, colds, bronchitis, asthma, hay fever, eczema, etc.), FVC, FEV_1 & FEF_{25-75}. Pollutant: Cigarette smoking exposure as reported at interview.	Authors found significant excess of respiratory illness in children with persistent wheeze. Also found significant associations of persistent wheeze with histories of acute lower respiratory illness, history of atopic disease, & current parental smoking habits. Parental cigarette smoking was linearly related to occurrence of persistent wheeze & lower degrees of mean FEF. Regression identified mother's current

					smoking status & current persistent wheeze as significant predictors of FEF mean normalized score. Father's current smoking pattern did not predict the score; nor did children's personal smoking, doctor's diagnosis of asthma & past history of lower respiratory illness.
11 Hasselblad, V., Humble, C.G., Graham, M.G.& Anderson, H.S.	1981	16,689 white children 6 to 13 years old from 7 geographic areas.	For selection into study: Children between 5 to 13 years & attending elementary school in 7 selected communities were asked to participate. Asthmatic children (based on history) were excluded, as were nonwhites, and as were any children who were not free of respiratory symptoms for at least 2 of the 3 pulmonary function test periods. For response: Statistically significant reduction in FEV_{75} in children with smokers or gas cookers in their homes as opposed to children without either one or both pollution sources.	Health: FEV_{75}, medical history, presence or absence of cough, cold or sore throat during pulmonary function testing. Pollutants: Number of smokers in each child's household; presence or absence of gas cookers. Other: Location, sex, age, height, season of pulmonary function test (because such tests have been shown to vary according to season), education of head of household.	Age and height correlated well with FEV_{75}, as did sex. Educational attainment of household head did not affect FEV values. FEV varied significantly among communities and no pollutant explained more than 8% of the variation. Authors concluded the community variation might be the result of machine or technician variability. The other major significant factor in FEV variability was maternal smoking habits. It explained 0.1% of the variance. Father's smoking habits showed no effect. A significant decrease in older girls' FEV was associated with presence of gas cookers. Authors concluded that the decreases in FEV, although small, were biologically significant.

12 Samet, J.M., Bishop, Y., Speizer, F.E., Spengler, J.D.& Ferris, B.G.	1981	Total number of visits to a hospital's emergency room in March, April, October & November of 1974-1977 (records abstracted).	Initially abstractors categorized visits into: Asthma, emphysema &/or chronic bronchitis, pneumonia, lower respiratory infection, upper respiratory infection, other respiratory disease, cardiac disease, cardiac & respiratory disease, trauma and miscellaneous. Eventually, because of small numbers in some categories, they were combined to all respiratory diseases, all diseases but trauma, & all diseases. Looked for statistically significant increases in numbers of respiratory disease visits on days with increased pollution.	Health: Diagnosis in hospital records of respiratory or cardiac disease, trauma or miscellaneous. Pollutants: TSP, SO_2, NO_2, CO & O_3. Other: Age, race, sex, date of hospital visit, & temperature.	TSP exceeded then Federal standard 76 of 488 study days. SO_2 exceeded the standard 2 days. All pollutants varied over a wide range. Two analysis techniques were used. The first assessed statistical significance of the morbidity index deviation from the expected value of zero. There were no significant results. The second analysis, linear regression between emergency room visit indices & pollutant variables, identified a small, significant effect of unlagged TSP & of unlagged SO_2 on the respiratory disease index. However, TSP days above federal standard were not associated with excess respiratory disease visits. Authors conclude results demonstrate at most a limited association.
13 Comstock, G.W., Meyer, M.B., Helsing, K.J.& Tockman, M.S.	1981	Records of 1724 residents of Washington Co., Maryland who had participated in two studies of respiratory symptoms and ventilatory function. One	For health: Ventilatory function testing was completed on half the subjects in the questionnaire study and virtually all those in the longitudinal study. Data were adjusted for age, sex & height. For response: Significant differences in ventilatory function between smokers & non-	Health: FEV_1 & FVC & respiratory symptoms. Household exposures: Smoking histories of adult household members; use of gas as a cooking fuel, air conditioning, number of adults & children in the household & the number of rooms. Smoking was categorized as "never	There is definite tendency for persons with another smoker in the household to have impaired ventilatory function; none of the observed differences achieved significance. Men whose household had gas cooking were at greater risk of having each of the respiratory symptoms than those with electric

		study was a comparison of 3 standardized questionnaires on respiratory history or with sections on respiratory history. The second study was a longitudinal study of white men who participated in a census of smokers and non-smokers.	smokers and homes with gas vs. electric cooking.	smoked", "former smoker", and "current smokers".	cooking, although the risks achieved significance ($p<0.05$) only for chronic cough, wheeze & dyspnea greater than grade 3 among men who had never smoked. Among women there was no evidence that exposure to gas cooking was associated with a greater risk of having respiratory symptoms than exposure to other cooking fuels. The presence of another smoker in the house other than the subject was not associated with increased respiratory symptoms & only slightly associated with impaired ventilatory function.
14 Richards, W., Azen, S.P., Weiss, J., Stocking, S.& Church, J.	1981	12 children. All children presenting at the Emergency Room of Childrens Hospital of Los Angeles (CHLA) with asthma from 1/8/79-31/1/80.	For asthma: Attending physician's & principal investigator's diagnoses and respiratory history. For response: Emergency room visits for asthma and hospital admissions for asthma.	Health: Emergency room visits for asthma; hospital admissions for asthma. Excluded asthma precipitated by a viral cold. Pollutants: Coefficient of haze (COH), Hydrocarbons (HC), NO, NO_2, SO_2, O_3, SO_4, TSP. Other: Temperature, relative humidity, wind speed and allergens. Five pollutant monitoring stations and 3 meteorological stations and one allergen collection station in the Los Angeles (study) area.	Increases in asthma emergency room visits and hospitalizations correlated significantly with increased NO, COH, HC, wind conditions (heat & humid), & allergen counts. Significant correlations were also found with decreases in ambient levels of O_3, SO_2, temperature & relative humidity. Among 12 hospitalized asthmatic patients morning peak flow levels were significantly lower during a 10-day peak pollution period than during 2 control periods of low pollution. However, neither differences in clinical symptoms of these patients nor

					need for additional medication were observed.
15 Lan, S.P., Shy, C.	1981	5416 white, long-term residents of one of four selected geographic areas in the New York city area. Subjects volunteered to complete respiratory history questionnaires that had been sent home through their children in selected public elementary schools. All children in the selected schools were asked to take questionnaires home.	For illness: Positive responses to questions about current respiratory illness. For response: Significantly larger numbers of people with chronic respiratory disease (CRD) living in more highly polluted areas.	Health: Positive history of respiratory illness diagnoses or symptoms as reported in questionnaire. Pollutant: SO_2, TSP, respirable suspended particulate matter (RSP), suspended sulphates (SS) & suspended nitrates (SN). Other: Cigarette smoking, age, level of education of head of household, & number of people living in home (plus size of home).	This study was a reanalysis of some data from the CHESS study (by US EPA) of 1972. Data quality were improved by careful editing of raw data & confirmation of air pollution data using other monitoring sources than had been originally used. Authors concluded, after analyzing confounding variables, that smoking was the most important factor in determining the level of severity of CRD. The effect of air pollution showed differential patterns among the smokers & non-smokers. Among smokers, no air pollution effect was observed. Among non-smokers a significant difference was observed among females as it was in males (however, the trend was not significant in males).
16 Silverman, F., Pengelly, L.D., Mintz, S., Kerigan, A.T., Hosein, H.R.,	1982	54 subjects; 36 asthmatics & 18 healthy non-asthmatics. All subjects were non-smokers, had	For asthma: Postive history, physical exam & laboratory tests. For healty subjects: Negative history of asthma & limited pulmonary function	Health: Daily diary of asthma symptoms, subjective well-being, medications used, possible exposures & daily activity pattern. Lung function tests (spirometry, using a vitalo-	At the time of publication data were still being collected in the field. Authors, therefore, gave a preliminary report on the pollutant results, especially as concerned the

Corey, P.& Goldsmith, C.H.		no smokers in the home, no gas stoves, no fireplace in use & resided near air monitoring stations.	tests indicating non-asthmatic, healthy status.	graph) performed on each subject at the beginning and end of each day. Pollutants: Outdoor fixed sites and personal & indoor samples monitoring SO_2, NO_2 & particulates. Sampling carried out Monday-Friday for 4 weeks (2 in summer & 2 in winter). Samplers run 8 hours each day.	various tiers of monitoring used. They found differences between fixed location, indoor, outdoor & personal monitoring. Intercorrelations of pollutant levels among these methods of estimation were relatively weak. Authors support personal samplers if possible or a well-designed outdoor network, indoor sampling & activity diary.
17 Freziers, R.G., Coulson, A.H., Katz, R.M., Detels, R., Seigel, S.C.& Rachelefsky, G.S.	1982	34 asthmatics	For asthma: All subjects sellected from patients attending a clinic of allergists. Clinic physicians reviewed patients' files and selected those with atopic asthma. Potential volunteers then received an isoproterenol challenge & if FEV_1 after challenge indicated $\geq$20% reversibility, they were accepted into the study. For response: Increased medication use and symptoms correlated with changes in sulphates.	Health: Medication changes, asthmatic symptoms and peak flow readings as self-reported twice daily. Peak flow readings were excluded from analysis because of suspect reliability. Pollutants: Sulphate, SO_2, & total oxidant. SO_2 & total oxidant varied collinearly with sulphate & were excluded from most analyses. Other: Pollen, mold, temperature and dew point.	Sulphate appeared to cause more bronchial reactivity, in comparison to SO_2 or total oxidants, as has been supported in other studies. 3 asthmatics were very sensitive to sulphate, 4 subjects appeared to improve as sulphate levels increased & the remaining subjects responded sometimes positively & sometimes negatively. Authors concluded that as many as 9% of asthmatics may be sensitive to increased levels of sulphate in ambient air and that reduction of sulphate levels to below 10$\mu g/m^3$ would significantly reduce the frequency and severity of symptoms & need for medication.

18 Melia, R.J.W., Florey, C. du V.E., Morris, R.W., Goldstein, B.D., Clark, D.& John, H.H.	1982 Part I	Pilot study: 40 homes with gas or electric cookers were monitored. Main study: 183 homes with gas cookers were monitored.	The study were designed to monitor differences in NO_2 levels in different areas of homes and the interrelationship of NO_2, temperature & humidity. In the pilot study the homes had either gas or electric cookers. In the main study all homes had gas cookers. Homes were selected by asking selected classes of school children about the cookers in their homes & requesting families to volunteer. Samplers were placed in bedrooms & living rooms.	Pollutants: NO_2. Other: Temperature, humidity, electric or gas cookers. All measured in different rooms in the houses simultaneously.	Pilot study: In both the living room & bedroom the mean level of NO_2 was higher in homes with gas cookers than with electric cookers. No significant difference between homes with different cookers in temperature or humidity. Main study: Bedroom NO_2 levels tended to be lower than levels in the living room. NO_2 levels in the bedroom were positively associated with use of gas fires for main heating or paraffin heaters anywhere. Use of cooker for heating was associated with high levels of NO_2. Temperature was related to type of heating & of house. Humidity was not related to any factors.
19 Melia, R.J.W., Florey, C. du V.E., Morris, R.W., Goldstein, B.D., John, H.H., Clark, D., Craighead, I.B.& MacKinlay, J.C.	1982 Part II	183 homes with gas cookers & with children 5-6 years old. 191 children in the 5-6 year age group.	For response: Statistically significant increase in respiratory illness in children in homes with high NO_2 levels.	Health: Symptoms of respiratory illness chronicled in a self-administered questionnaire completed by the mother about the 5-6 year old children in the house. Pollutants: NO_2 monitored in child's bedroom or living room, number of cigarette smokers in home. Other: Humidity & temperature.	After allowing for effects of age, sex, social class, number of cigarette smokers in the home, temperature & relative humidity, no statistically significant relation was found between the prevalence of having one or more respiratory conditions & weekly average levels of NO_2 in the bedroom or living room. However, the prevalence of having one or more respiratory conditions tended to be highest in homes with

					high levels of NO_2 & lowest in homes with low levels. Significant positive association was found between prevalence of respiratory conditions & relative humidity.
20 Aderele, W.I.	1982	380 children, aged 10 mos.-13 yrs., who were diagnosed asthmatics.	For asthma: Criteria for diagnosis and grading severity were reported in another journal article. For response: History and some skin sensitivity tests.	Health: History of asthma; sensitivity to skin tests. Environmental: Tobacco smoke, fuel smoke, general housing conditions, animal dander. Other: Food, rainy season (study conducted in Nigeria), exercise and infection.	Large percentage of asthmatics gave positive history of asthma in the family; reaction to skin tests for housedust, feathers, ascaris & D. Pteronyssinus; exercise & nighttime. There was an association between severity of asthma & smoking habits of fathers and siblings (amount of smoking not quantified).
21 Perry, G.S., Chai, H., Dickey, D.W., Jones, R.H., Kinsman, R.A., Morrill, C.G., Spector, S.L.& Weiser, P.C.	1983	41 asthmatics participated but analysis was only on the data of 24 of the 41 who had at least 60% complete data for the study period. All subjects were non-smokers.	For asthma: Confirmation of perennial asthma symptoms, methacholine inhalation challenge, twice-daily PEFR's for 5 to 7 days, medical history, physical examination, prick tests to allergens, chest X-ray, EKG and Panic-Fear Personality Scale. For response: Statistically significant increase in symptoms, bronchodilator usage or decrease in PEFR during time periods when air pollutant concentrations increased.	Health: Twice daily self-reported asthmatic attack symptoms. Twice daily self-measured PEF. Continuously recorded usage of as-needed aerosolized bronchodilators by nebulizer chronologs. Pollutants: Coarse & fine fractions of inhaled particulate matter (total mass, sulphates & nitrates), SO_2, CO & O_3. Other: Temperature & barometric pressure.	During the time of the study there were very few days in which high levels of suspended particulates were recorded. Analysis included use of the Korn-Whittemore statistical model to include the factor of the high dependence between asthma status in successive observation periods. Only fine nitrates were associated (p-value=.0229) with increased symptom reports & aerosol bronchodilator usage.

					Authors concluded lack of results due to lack of days with high pollution concentrations.
22 Wagner, C.J., Danziger, R.E.& Nelson, H.S.	1983	12 bronchial asthmatics who gave a history of weather-related aggravation of symptoms.	For asthma: Patients at an allergy clinic diagnosed as having asthma by the clinic physicians (details not given). Apparently some were extrinsic & some were intrinsic asthmatics. Volunteered after authors advertised for asthmatic volunteers with weather-related symptoms. For response: Peak flow readings taken on a Mini-Wright Peak Flow Meter that were significantly different during weather changes and during changes in levels of positive ions.	Health: Peak flow readings taken daily at 0800, 1200, 1700 and 2200 hours. Meteorologic: Temperature, barometric pressure, wind velocity & measurable precipitation obtained daily from one location. Ion: Positive & negative ions measured at same times as peak flow measured. Highest value during a 10-minute sampling was used for analysis.	There were no asthmatic attacks in the study population during the study period. There were 3 storm fronts during the study period. It was concluded that the increase of asthma symptoms associated with the passage of weather fronts (which are preceeded by any increase in positive small air ions) is not a result of sensitivity to positive small air ions.
23 Goldstein, I.F.& Cuzick, J.	1983	Visits to emergency rooms at hospitals for asthma in 3 New York City hospitals (1969-1977) and in one hospital in New Orleans (1953-1968 & 1969-1977).	For asthma: Any diagnosis recorded as an asthmatic attack in the emergency rooms log books, regardless of type of asthma. For response: Significant increase in emergency room visits for asthma on various days of the week or seasons.	Health: diagnosed asthmatic attack. Other: Day of the week, season.	In New York City there is an excess of visits on Sundays and Mondays for adults in all seasons, the excess being somewhat larger in autumn. For children there is also a pronounced excess for Sundays but not a consistent one for Mondays. In New Orleans there is no particular day-of-the-week pattern, with the exception of winter, in which Monday had a larger number of visits.

				The difference between day-of-the-week pattern of visits for the 2 cities is highly statistically significant. Authors conclude these pattern differences indicate a different environmental etiologic agent acting on the 2 populations. In New York they suggest there is a triggering agent in the home environment but that the agent is indoors & outdoors in New Orleans.
24 Holguin, A.H., <u>et al.</u>	52 asthmatics; 21 living in one area, 31 living in a second area.	<u>For asthma</u>: Positive respiratory history, pulmonary function tests, EKG, chest X-rays, physical exam and blood test for IgE serum immunoglobolin. <u>For response</u>: After defining asthmatic attack for each individual, increased numbers of asthmatic attacks on days of increased pollutant concentrations.	<u>Health</u>: Daily symptomatology and medication use, thrice-daily peak expiratory flow rate. <u>Pollutants</u>: O_3, NO_x, CO, SO_2, TSP, sulphates & nitrates monitored at 2 fixed sites and one mobile station that monitored individual, selected homes indoors & outdoors for one week at a time. O_3 & TSP monitored for 12 hours in selected subject's breathing zones. <u>Other</u>: Temperature, humidity, wind velocity & direction and hourly activity pattern.	CO and SO_2 were not included in the analysis because the concentrations were very low. Of 52 subjects, one's data were excluded due to unreliability. One was excluded because the subject had asthmatic attacks daily. 8 were excluded because they had< 5 attacks during 6 months. Results showed a statistically significant increase in asthmatic attacks when O_3 increased and this was enhanced when temperature simultaneously decreaed. NO_2 and relative humidity had no influence on significance. Pollens significantly affected som subjects but not the group as a whole. If the 8 subjects with< 5 attacks were included in the model with the 42, the results were still significant.

APPENDIX B

RESPIRATORY ILLNESS AND AIR POLLUTION

ENVIRONMENTAL CHAMBER STUDIES

RESPIRATORY ILLNESS AND AIR POLLUTION
B. ENVIRONMENTAL CHAMBER STUDIES

AUTHOR	YEAR PUB.	SAMPLE SIZE	DIAGNOSTIC CRITERIA	VARIABLES	RESULTS
32 Jaeger, M.J., Tribble, D.& Wittig, H.J.	1979	80 subjects; 40 healthy non-smokers & 40 subjects suffering from mild to moderat asthma.	For health: Normals were screened by history, physical examination & preliminary lung function testing that determined they were free of pulmonary dysfunction. Asthmatics were selected because known to have mild disease & had not had asthma attacks during three months prior to the study. Response: Significant decrease in pulmonary function after exposure to SO_2.	Health: CV, closing capacity (CC), RV, FRC, Raw, FVC, FEV_1, MMFR and single breath N_2 washout. Pollutant: Exposure to .5 ppm SO_2 in a chamber for 3 hours. Other: Purified air, temperature, humidity. Spirometry tests were performed 2 minutes, 30 minutes, 1, 2 and 3 hours after entering the chamber.	In normals the VC, FEV_1 & MMFR increase with time during exposure to air & to SO_2. Increases occur gradually during the first 2 hours of exposure & decrease slightly during the 3rd. Time effect is significant for FEV_1 & MMFR. No difference in time course when subjects exposed to SO_2 as compared to air. In asthmatics the FEV_1 & MMFR changes with time are more pronounced than in normals. Time course on air & on SO_2 shows no difference. Average values of MMFR are lower during SO_2 than air exposure. Authors conclude exposure to .5 ppm SO_2 for 3 hours has no detectable effect on pulmonary function except for a small decrease in MMFR.

33 Sheppard, D., Saisho, A., Nadel, J.A.& Boushey, H.A.	1981	13 subjects with mild asthma and non-smokers; 7 subjects in one study and 6 in the second study.	For asthma: History of recurrent wheezing, chest tightness & reversible airway obstruction documented by a physician. Pulmonary function screening tests. For response: Significant bronchoconstriction after exposure to SO_2 during excercise to determine the exercise effect on SO_2-induced bronchoconstriction. In a second set of studies the authors compared bronchoconstriction produced by breathing SO_2 during exercise with that produced by hyperventilation with SO_2.	Health: V_{tg}, R_{aw} & SR_{aw} for both studies. Pollutants: 1st study - .5 ppm SO_2 breathed while exercising followed by .5 ppm SO_2 breathed while resting; next .25 ppm SO_2 breathed during exercise & rest & finally .10 ppm SO_2 breathed during exercise & at rest. 2nd study - one day subjects were exposed to 1 ppm SO_2 during exercise; the next day they were exposed to 1 ppm SO_2 while hyperventilating. Other: Amount of exercise & hyperventilation, temperature & humidity.	Neither inhalation of .50 ppm SO_2 at rest nor exercise or hyperventilation alone had an effect on SR_{aw}. Inhalation of SO_2 during exercise significantly increased SRaw. In the 2 most responsive subjects, inhalation of .1 ppm of SO_2 during exercise also significantly increased SRaw. When subjects took larger breaths inhaling SO_2 during hyperventilation to more closely match the volume of breaths taken after exercise the time courses of SO_2-induced bronchoconstriction after hyperventilaton & after exercise were nearly identical. SRaw increased by the same amount over varying times whether SO_2 was inhaled during exercise or hyperventilation. Authors conclude exercise increases SO_2-induced bronchoconstriction.
34 Linn, W.S., Bailey, R.M.,	1982	24 asthmatics for one-hour chamber exposure	For asthma: Physcian confirmation & 10% reduction in FEV_1 after methacholine challenge.	Health: Airway resistance (R_{aw}), thoracic gas volume (V_{tg}) & specific airway resistance ($SR_{aw} = R_{aw} \times V_{tg}$), FVC, FEV_1,	This study had subjects exposed in a chamber in situations similar to real life, including mild exer-

Shamoo, D.A., Venet, T.G.,, Wightman, L.H.& Hackney, J.D.		per week for three weeks.	For response: Statistically significant increase in symptoms or airway resistance or decrease in FVC, FEV_1 or V_{tg} after exposure to SO_2.	scores of subject-reported symptomatology. Pollutants: SO_2 (at .25 and .50 ppm) & minimal NO. Other: Humidity, temperature.	cise. Exposure was not directly thru a mouthpiece as in previous studies. No measures of response showed statistically significant variation attributable to SO_2, although small significant increases in resistance attributable to exercise were found. Contrasts with significant results in chamber studies in which SO_2 exposure was by mouthpiece only.
35 Koenig, J.Q., Pierson, W.E., Horike, M.& Frank, R.	1982	8 atopic adolescents, with sinusitis or atopic dermatitis but without extrinsic asthma.	For atopy: No history of wheezing, no drugs or hospitalization for asthma. Lower respiratory tract hypersensitivity confirmed by exercise-induced bronchospasm after a standardized exercise challenge test and by positive responses to a methacholine challenge test. For response: Statistically significant decreases in FEV_1, $V_{max\ 50}$ & $V_{max\ 75}$ and increases in R_T & FRC.	Health: Total respiratory resistance (R_T), functinal residual capacity (FRC). FEV_1, maximum flow calculated at 50% vital capacity ($V_{max\ 50}$), maximum flow calculated at 75% vital capacity ($V_{max\ 75}$), vital capacity (VC), FVC & exercise-induced bronchospasm. Pollutants: NaCl droplets alone, NaCl & SO_2 (1 ppm), SO_2 alone -- each combination or single pollutant was injected in a chamber for 30 minutes while subjects exercised moderately. Exposures through a mouthspiece. Other: Relative humidity & temperature.	Exposures to either SO_2 alone or SO_2 in combination with NaCl droplets produced statistically significant changes in R_T, FEV_1, $V_{max\ 50}$ & $V_{max\ 75}$. Exposures to air with NaCl alone produced no changes. Results indicate that inhalation of 1 ppm SO_2 by atopic adolescents can produce exercise-induced bronchospasm.

36 Snashall, P.O.& Baldwin, C.	1982	11 normal, health subjects. 4 asthmatics (3 extrinsic asthmatics and 1 intrinsic asthmatic).	For asthma: Positive family history, positive cutaneous sensitivity tests to several allergens. Unspecified as to how intrinsic asthmatic chosen except for history of late onset asthma. For response: Statistically significant decrease in sG_{aw}.	Health: R_{aw}, V_{tg} & specific conductance (sG_{aw}). Pollutants: SO_2 (8 ppm) in chamber for 30 seconds (1 asthmatic), one minute (other 3 asthmatics) or 3 minutes (all normals). Other: Propranolol (100 mg) for normals one hour prior to SO_2 inhalation. Either atropine methonitrate or sodium cromoglycate inhaled in aerosol form for 5 minutes 20 minutes prior to SO_2 exposure.	After SO_2 inhalation in controls, sG_{aw} decreased in all subjects. Atropine & SCG significantly inhibited the SO_2 response. With atropine the degree of inhibition was inversely related to the subjects responsiveness to the SO_2 inhalation. In all asthmatic subjects atropine did not inhibit the SO_2 response; SCG had an effect similar to that seen in normal subjects. Authors concluded that results indicate that vagal efferent mechanisms are involved in bronchial response to SO_2 in normal subjects, but such mechanisms are not important in hyperreactivity to SO_2 in asthmatics. The mechanism of inhibition with SCG is unknown.
37 Tan, W.C., Cripps, E., Douglas, N.& Sudlow, M.F.	1982	8 normal, health subjects. 7 atopics. 22 asthmatics.	For atopy: Positive response to house dust mite extract & at least one other common environmental agent in skin prick tests. Positive history of seasonal or perennial rhinitis but not of any episodic wheeze. FEV_1 & FVC were within normal	Health: TGV, R_{aw} and sG_{aw}. Pollutants: SO_2 in concentrations ranging from 0-20 ppm for 5 minutes. Other: Aerosol of ipratropium bromide administered 60 minutes prior to SO_2 exposure in 7 atopic and 9 asthmatic sub-	sG_{aw} decreased significantly in atopic and asthmatic subjects but not in normals after SO_2 exposure. Prior inhalation of disodium cromoglycate significantly decreased the response to SO_2 in atopics &

			limits. For asthma: Recent history of episodic wheezing & dyspnea. Positive responses to skin prick tests to house dust mite & other allergens. Evidence of an increase in FEV_1 of greater than 20% after inhaling a sympathomimetic bronchodilator. For response: Statistically significant decrease in sG_{aw}.	jects. Placebo (lactose) or disodium cromoglycate at 6-hour intervals 24 hours before SO_2 exposure in 6 normals, 5 atopics & 18 asthmatics. Aerosol clemastine (or placebo of saline) given to 7 asthmatics 10 minutes before inhalation to 10 ppm SO_2.	asthmatics. Prior treatment with inhaled ipratropium bromide blocked response in atopics, but the effect was variable in asthmatics. Prior treatment with inhaled clemastine also reduced response in asthmatics without causing a change in sG_{aw}. Concluded that non-allergic bronchial hyperactivity to SO_2 was increased in atopics & asthmatics & that mediator release, in addition to vagal reflex, has a role in such bronchoconstriction.
38 Kirkpatrick, M.B., Sheppard, D., Nadel, J.A.& Boushey, H.A.	1982	6 asthmatics	For asthma: Airway hyperreactivity demonstrated by histamine bronchoprovocation or reversible airflow obstruction demonstrated by spirometry; history of episodic cough, wheezing & dyspnea; physical examination; pulmonary function tests. For response: Measured V_{tg} and R_{aw} to calculate SR_{aw}. A significant change in SR_{aw} after exposure to SO_2.	Health: SR_{aw}. Pollutants: .5 ppm SO_2 inhaled nasally, orally, or oronasally while exercising for 5 minutes. Other: Humidity.	Breathing humidified air plus SO_2 through a mouthpiece or by facemask during exercise significantly increased SR_{aw} in all 6 subjects. Breathing same combination by facemask with mouth occluded significantly increased SR_{aw} in 5 out of 6 subjects. Inhalation through mouthpiece did not significantly increase SR_{aw} over facemask breath-

					ing but was significantly greater than breathing by facemask with the mouth occluded. Conclude that although nasal breathing partially protected against SO_2 bronchoconstriction, both oral & oronasal breathing of low concentrations during exercise can cause significant bronchoconstriction in asthmatics.
39 Orehek, J., Massari, J.P., Gayrard, P., Grimaud, C.& Charpin, J.	1976	20 asthmatics	For asthma: Unspecified. For response: Increase in initial SR_{aw} after NO_2 exposure and enhanced bronchoconstrictor effect of carbachol.	Health: TGV, SR_{aw}. Pollutants: NO_2 at 0.1 ppm for one hour prior to carbachol inhalation. Other: Carbachol (0.1% nebulized solution in 0.9% saline) administered for 2-4 minutes several times until at least a 100% increase in SR_{aw} over initial, pre-carbachol inhalation was measured.	NO_2 induced a slight but significant increase in initial SR_{aw} and enhanced bronchoconstrictor effect of carbachol in 13 subjects. NO_2 had no such effects in 7 subjects. In 4 subjects, exposure to a higher concentration of NO_2 (0.2 ppm) yielded variable results. Very low levels of NO_2 can adversely affect some asthmatics.
40 Kerr, H.D., Kulle, T.J., Mcilhany, M.L.&	1979	13 asthmatics. 7 chronic bronchitics. 10 normal,	Asthma defined as a medical history of episodes of breathlessness, wheezing and cough lasting for hours to days fol-	Health: Self-reported symptoms of cough, sputum, irritation of mucous membranes & chest discomfort. Forced vital	Minimal reporting of symptoms which did not correlate with functional changes. More asthmatics

Swidersky, P.		healthy subjects.	lowed by intervals of complete remission. Chronic bronchitis defined as a medical history of daily cough with sputum production persisting for 3 or more consecutive months for a period of 2 or more consecutive years. For response: Statistically significant decrement in pulmonary function after exposure to NO_2.	capacity (FVC), R_{aw}, V_{tg}, functional residual capacity (FRC), specific airway conductance ($SG_{aw}=1/R_{aw}/V_{tg}$), total lung capacity (TLC), residual volume (RV), forced expiratory volume (FEV_1), & mid-expiratory flow rate (MEFR). Pollutants: 0.50 ppm NO_2 for 2 hours accompanied with light exercise. Other: Temperature & humdidity.	than bronchitics reported symptoms. Significant pulmonary changes after exposure to NO_2 were observed in decreased quasistatic compliance for all subjects. FRC increased significantly for the 20 asthmatics & chronic bronchitics. When asthmatics and bronchitics were analyzed as separate groups, there were no significant changes with exposure. No significant decrement of lung function in asthmatics or bronchitics after 2 hour exposure to .50 ppp NO_2.
41 Orehek, J., Grimaldi, F., Muls, E., Durand, J., Vialda, A.& Charpin, J.	1981	7 allergic patients.	Allergy confirmed by skin tests to grass pollen. Response was to be indicated by a significant increase in specific airway resistance (SR_{aw}).	Health: SR_{aw}. Pollutants: 207 $\mu g/m^3$. NO_2 exposure for one hours. Inhalation of grass pollen after NO_2 exposure.	No significant change in baseline SR_{aw} or in response to antigen was observed after NO_2 exposure.
42 Wagner, H.M., von Nieding, G.& Beuthan, A.	1982	11 healthy male volunteers; 2 smokers, 9 non-smokers.	For health: Not described. For response: Significant change in pulmonary function after exposure to selected pollutants in a chamber.	Health: TGV, $R_{t,N}$, R_{aw} and respiratory gas change for oxygen & CO & blood composition, serum electrolytes, & enzymes in blood.	As compared to initial values before exposure there was a significant increase of R_{aw} and decrease of PaO_2 at the end

				Measurements were taken immediately prior to expsore, after 1 and 2-hour exposures and 1 hour after termination of exposure. Pollutant: NO_2 at 5 ppm, SO_2 at 5 ppm & O_3 at .1 ppm for 2 hours of simultaneous exposure.	of the exposure period. PaO_2 tended to normalize within an hour after exposure but R_{aw} increased. There were no significant changes in biochemical factors.
43 Kleinman, M.T., Bailey, R., Linn, W.S., Anderson, K.R., Whynot, J.D., Shamoo, D.A.& Hackney, J.D.	1983	31 asthmatics	For asthma: Previously physician-diagnosed asthma confirmed at screening examination. Screening included EKG's, lung function tests & bronchoconstrictor challenge. For response: Statistically significant response to bronchial challenge (at varying concentrations) after exposure to .2 ppm NO_2. Response to bronchial challenge measured by FVC and FEV_1 lung function tests.	Health: FEV_1 & FVC tested before and after exposure & R_t & symptoms. Pollutant: .2 ppm NO_2 exposure for 2 hours. Other: Purified air before and after NO_2 exposure & for 2 hours (the same as the NO_2 exposure period). Light exercise for the first 15 minutes of each 30-minute period during the 2 hours. Exposure to pure air or NO_2 took place one time for each with a 3-week separation between.	The R_t showed a 9% increase on NO_2 days compared to a 1% decrease on control days (p=.105). FEV_1 showed small significant declines from pre- to post-tests similar on control & NO_2 days. FVC also decreased pre to post but not significantly. Group mean symptom score changes during exposure were slightly but significantly less favourable on control days than on NO_2 exposure days. Lower respiratory symptoms were responsible for the majority of the difference. Responses to methacholine after control and NO_2 showed greater response after NO_2 but the excess response was small. NO_2 caused a tendency towards greater bronchial reactivity.

44 Hackney, J.D., Linn, W.S., Mohler, J.G., Pedersen, E.E., Breisacher, P.& Russo, A.	1975 Part II	8 male volunteers; 4 normal, healthy men & 4 with a history of hyperreactive airways.	For health: Normals had no history of cough, chest discomfort or wheezing associated with allergy or exposure to air pollution. Hyperreactive men had normal FVC, FEV and closing volume (CV) but had histories of cough, chest discomfort or wheezing associated with allergy or exposure to air polltion. For response: Significant respiratory distress after exposure to O_3 in a chamber but not after exposure to purified air.	Health: FVC, FEV_1, R_t, CV, thoracic gas volume (TGV), R_{aw}, RV, blood carboxyhemoglobin (COHb), static & dynamic lung compliance (C_{st}, C_{dyn}), resting & exercise oxygen consumption (VO_2) & pulmonary diffusing capacity (DL_{CO}) & symptoms. Pollutant: Normals tested 5 days per week for 3 weeks. First 3 week days purified air; last 2 week days to pollutants for 5 hours with pulmonary function tests during the last hour. (1st week, .50 ppm O_3; 2nd week, .50 ppm O_3 & .30 ppm NO_2; 3rd week, .50 ppm O_3 & .30 ppm NO_2 & 30 ppm CO). With hyperreactives, exposure was shortened to 2 hours (1st & 2nd week, .25 ppm O_3; .37 ppm O_3 for one day in 3rd week). Other: Temperature, humidity.	All 4 hyperreactives were significantly affected by .37 ppm O_3. All 4 normals were affected minimally or not at all by .50 ppm O_3. In normals the addition of NO_2 at .30 ppm did not produce additional detectable effects. Addition of CO to the pollution mixture also failed to produce detectable effects other than increases in COHb levels. The results of this study corresponded well with studies by Bates et al. & Hazucha et al..
45 von Nieding, G., Wagner, M., Löllgen, H.,& Krekeler, H.	1977	11 health volunteers for 2-hour chamber exposure. 9 of the 11 had a second 2-hour exposure.	Statistically significant increase in R_{aw} or decrease in PaO_2 after exposure to selected air pollutants.	Health: Airway resistance, arterial oxygen partial pressure (PaO_2). Pollutants: 11 subjects exposed for 2 hours to 5 ppm NO_2, 0.1 ppm O_3 or to a mixture of 5 ppm NO_2 & 0.1 ppm O_3. 9 subjects exposed to mixture of NO_2, O_3 & SO_2 in MAK (maximum allowable concen-	NO_2 & SO_2 inhaled in MAK concentraton for 1 and 2 hours respectively cause significant increase in R_{aw} and decrease of PaO_2. Exposure to a combination of NO_2 & SO_2 does not have a significantly stronger effect than that of each alone. No significantly stronger

				traton for occupation: 5 ppm NO_2, 0.1 ppm O_3 and 5 ppm SO_2) and MIK (maximum allowable concentration in ambient air: 0.05 ppm NO_2, 0.025 ppm O_3, and 0.1 ppm SO_2). Other: Temperature, humidity.	response of R_{aw} or PaO_2 from simultaneous exposure to NO_2, O_3 & SO_2 in MAK concentrations. Inhalation of a mixture of NO_2, SO_2 & O_3 at MIK level shows no signicant response of R_{aw} or PaO_2. If exposure to this mixture is followed by bronchial challenge of 2% acetylcholine there is an increased bronchial reaction.
46 Kagawa, J.	1983	7 healthy male subjects.	For health: No history of chronic respiratory or cardiovascular disease; normal findings on physical examination. For response: Significant decrement in pulmonary function after exposure to pollutants in a chamber.	Health: R_{aw}, V_{tg}, G_{aw}, single breath nitrogen washout (N_2), FVC, FEV_1 & V_{50} & V_{25} & symptoms. Pollutant: Two-hour exposures once per week. Each subject exposed in order, to purified air, .15 ppm O_3, filtered air, .15 ppm SO_2, combination of .15 ppm O_3 & .15 ppm SO_2, filtered air, .15 ppm NO_2, a combination of .15 ppm O_3 & .15 ppm NO_2, filtered air, .15 ppm SO_2 & .15 ppm NO_2, and a combination of .15 ppm O_3, .15 ppm SO_2 & .15 ppm NO_2. Other: Intermittant light exercise.	Almost half the subjects developed cough during deep inspiration and one subject had chest pain during exposure to O_3 alone. G_{aw}/V_{tg} was the most sensitive index to observe changes produced by exposure to any of the pollutants. Significant decreases in G_{aw}/V_{tg} were observed in 6 of 7 subjects exposed to O_3 alone as compared to the G_{aw}/V_{tg} during filtered air exposure. No significant enhancement of effect was observed in the mixture of O_3 & other pollutants although there was a slightly greater decrease of G_{aw}/V_{tg} with the mixture.

47 Linn, W.S., Chang, Y.T.C., Julin, D.A., Spier, C.E., Anzar, U.T., Mazur, S.F., Trim, S.C., Avol, E.L.& Hackney, J.D.	1982	64 volunteers; 21 asthmatics & 43 normals. All were between 18 & 55 years of age, lived in a specified area (Hawthorne, California) & had no medical contraindication to participation.	For health: Volunteers who answered advertisements for subjects. Medical history showed no pulmonary disease for normals. Asthmatics had been diagnosed by physicians and had a positive medical history. Response: Significant change in pulmonary function after exposure to ambient air in a chamber.	Health: FVC, FEV_1, PEFR, TLC, RV, CC, R_t & single breath N_2 & symptoms. Pollutant: Ambient air was monitored for O_3, NO_2, SO_2, CO, total hydrocarbons (THC), TSP, SO_4, NO_3, Na, NH_4, Cl & K. Other: Pollen, spores, temperature & humidity, & purified air & light exercise. Exposures were in an area of known high pollutant concentratins for 2 hours with light exercise (4 15-minute intervals interspersed with 15-minute rest periods). Lung functin tests were performed in the chamber immediately prior to exposure (still breathing exposure atmosphere).	O_3 concentrations were uniformly low. SO_2 concentrations were higher than in a similar study but well below the national standard. TSP, SO_4, NH_4, CO, NO_2 & THC mean levels were moderately low. Temperatures were lower than in other study. Pollen concentrations were lower than in previous study. Asthmatics had higher symptom scores than did normals. Only maximum expiratory flow rate, 75% (V_{max} 75) showed a slight statistically significant decrement with ambient exposure & this test is of questionable physiological importance. Authors conclude that the difference between these results & those of the previous study are due to lower ambient pollutant concentrations during this study.
48 Avol, E.L., Linn, W.S.,	1983	2 studies were conducted during 2 consecutive	For asthma & health: Medical interview, physical examination, EKG & exercise stress	Health: FVC, FEV_1, V_{max} 50%, TLC, R_t, N_2, SaO_2 & a symptom questionnaire.	Two studies' results contrast markedly. In 1980 subjects showed statis-

Shamoo, D.A., Venet, T.G.& Hackney, J.D.		summers in the Los Angeles area. 1. 1980: 60 subjects; 7 asthmatics and 53 healthy. 2. 1981: 98 subjects; 50 asthmatics and 48 healthy.	test. For response: Significant differences in pre-exercise and pre-exposure to post-exercise and post-exposure FVC, FEV_1, $V_{max\ 50\%}$, TLC, total resistance of the respiratory tract (R_t), nitrogen wash-out (N_2), & percent saturation of arterial hemoglobin with oxygen (SaO_2).	Pollutant: Chamber had filtered air for one hour prior to subject exercise beginning. When exercising subjects were exposed to either filtered air or ambient air pumped in. The following pollutants were monitored: O_3, SO_2, CO, THC, NO_2, temperature, relative humidity, TSP, NO_3 & SO_4. When analyzing the subject responses were compared based on whether their exposure was to filtered or ambient air.	tically significant reductions in lung function test performance, as well as increases increases in symptoms with ambient air. Ambient exposure concentrations were 0.165 ppm O_3 and 227 $\mu g/m^3$ TSP. Some relationship between increasing O_3 level & increasing severity of response was suggested. In 1981 the subjects showed smaller mean responses than the 1980 group & there was no suggestion of a dose-response relationship with O_3. Mean exposure concentrations were 0.156 ppm O_3 & 166 $\mu g/m^3$ TSP. Authors concluded that short-term effects of moderate exercise vary among individuals & some may develop respiratory irritation.
49 Zeballos, R.J., Shturman-Ellstein, R., McNalley, J.F., Hirsch, J.E.&	1979	2 studies were conducted to determine the role of hyperventilation in exercise-induced	For asthma: American Thoracic Society (ATS) criteria for moderate perennial bronchial asthma which included respiratory history & selected pulmonary function tests.	Health: FVC, FEV_1, FEF_{25-75}, FEF_{75}, R_{aw}, SG_{aw}. Other: Hyperventilation self-induced for 3 minutes; hyperventilation induced by 10	In normal subjects, moderate exercise performed with mouth or nasal breathing did not induce significant post-exercise change. Similar exercise

Souhrada, J.F.		bronchoconstriction. One study involved 3-min. hyperventilation with 7 normal subjects and 9 asthmatic subjects. The second study involved 10-min. hyperventilation with 6 normal subjects & 8 asthmatics. Ages 7-14 years.	For healthy subjects: Absence of history of respiratory or cardiac disease. For response: Statistically significant differences in pulmonary function after exercise-induced hyperventilation or self-induced hyperventilation when breathing exclusively through the nose or the mouth.	minutes of exercise; hyperventilation by a combination of the two. Oral vs. nasal breathing. Level of exercise.	in asthmatics induced significant change in all pulmonary variables. 3-minute voluntary hyperventilation induced no changes in normal subjects with asthmatics, 3-minute oral hyperventilation produced significant changes whereas nasal hyperventilation changes were significantly decreased. 10-minute oral, exercise-induced hyperventilation in normals & asthmatics induced significant decrease in FEF_{25-75}, FEV, FEF_{75} & SG_{aw} immediately or 7-10 minutes after exercise in asthmatics. Mouth breathing potentiated the bronchoconstrictive response.
50 Dahms, T.E., Bolin, J.F.& Slavin, R.G.	1981	10 asthmatics & 10 normals, healthy subjects	Asthma confirmed by prior medical history and positive methacholine challenge test. Response based on significant decreases in FVC, FEV_1, and FEF_{25-75} after exposure to sidestream smoking.	Health: FVC, FEV_1, & mean forced expiratory flow during the middle of FVC (FEF_{25-75}), blood sample for carboxyhemoglobin (COHb) analysis. Spirometry every 15 minutes in the chamber. COHb before and at the end of the hour's exposure. Pollutants: Sidestream cigarette smoke (.15 mg of tar &	All subjects showed .40% increase in COHb after exposure. Asthmatics had significant linear decrease after one hour in FEV_1 (21.4%), FEF_{25-75} (19.2%) & FVC (20%). Alterations readily reversible in all subjects after inhalations of metaproterenol. Controls showed no change in pulmo-

				.15 mg of nicotine) for one hour.	nary function with same exposure.
51 Hackney, J.D., Linn, W.S.& Bell, K.A.	1978	5 normal, healthy subjects, 5 sensitive subjects (with a history of high reactivity to inhaled irritants) & 6 asthmatics were exposed to $(NH_4)_2SO_4$. --- 6 normals & 6 asthmatics were exposed to NH_4HSO_4. --- 6 normals & 6 asthmatics were exposed to H_2SO_4.	<u>For sensitive subjects</u>: A history of response to inhaled irritants. <u>For asthmatics</u>: Not stated. <u>For response</u>: Significant changes in pre- and post-exposure lung function tests. Exposure was simultaneous with moderate exercise.	<u>Health</u>: Not stated. <u>Pollutants</u>: $(NH_4)_2SO_4$, NH_4HSO_4, H_2SO_4. <u>Other</u>: Controlled temperature & humidity.	$(NH_4)_2SO_4$ exposure: Normals had no response at low humidity & mixed response at high. Sensitives had inconsistent variations that were not consistent with adverse exposure effects. Asthmatics had no significant responses. NH_4HSO_4 exposure: No significant changes in normals or asthmatics attributable to varying levels of pollutant. H_2SO_4 exposure: No normals showed exposure-related changes. Asthmatics had no significant group pulmonary changes but 2 possibly significant changes in airway resistance. Authors conclude there is no adverse effect at the levels they studied but further research is suggested.
52 Utell, M.J., Morrow, P.E.& Hyde, R.W.	1982	16 normal, healthy subjects. 17 asthmatics.	<u>For asthma</u>: A demonstrated abnormal increase in SG_{aw} after inhaling carbachol and a positive respiratory history.	<u>Health</u>: SG_{aw}, TLC, maximum expiratory flow volume (MEFV), partial expiratory flow volume (PEFV), FVC & FEV_1 all performed before, during & after	When compared with NaCl, sulphate (1 mg/m^3) produced siginicant reductions in SG_{aw} and flow rates in asthmatics. There were no

			For response: Significant reduction of SG_{aw} after inhalation of acidic sulphates.	inhalation. Pollutants: Acidic sulphates ($NaCl$, $NaHSO_4$, NH_4HSO_4 & H_2SO_4) inhaled orally at 1 mg/m^3 for normal subjects and at a range of from 1 mg/m^3 to 0.1 mg/m^3 for asthmatics, each inhalation for 16 minutes. NaCl acted as a control. Other: Carbachol inhaled in concentrations of 0.00, 0.025, 0.05, 0.10, 0.25, 0.50 and 1.0% sequentially until SG_{aw} decreased by more than 40% of the control value in asthmatics. No response in normal subjects.	significant reductions in normals after sulphate inhalation. The two most sensitive asthmatics demonstrated airways changes at the 0.1 mg/m^3 sulphate level. To a far more significant degree the bronchoconstrictor action of carbochol was potentiated by sulphates more or less in relation to their acidity in normals & in asthmatics.
53 Golden, J.A., Nadel, J.A.& Boushey, H.A.	1978	8 healthy, non-smoking adult volunteers; 5 women & 3 men.	For health: No history of atopy, asthma or chronic lung disease. Pulmonary function screening tests were all normal including response of an increase in R_{aw} of no more than 2.50 cm. H_2O per liter per sec. after inhaling 10 breaths of 1.6% histamine aerosol. For response: Bronchial reactivity to histamine was assessed before & after exposure to O_3. For pre & post O_3 baselines R_{aw} & TGV were measured. Responses to O_3 exposure and significant differences in pre & post O_3	Health: R_{aw} & TGV measured after histamine challenge prior to O_3 exposure, and after O_3 and a second histamine challenge. R_{aw} was measured again after histamine challenges, 1 day, 1 week, 2 weeks & 3 weeks after the O_3 exposure. Pollutant: O_3 exposure (.6 ppm) in a chamber for 2 hours. Other: Temperature, humidity & histamine (1.6% solution) in aerosol.	Study results showed that brief exposure of healthy subjects to O_3 has little effect on R_{aw} but significantly increases bronchial reactivity to histamine aerosol. For 2 subjects (of the 8), the increase in R_{aw} persisted for more than 1 week after the 2-hour exposure to O_3. Authors concluded that the O_3 exposure produced bronchial hyper-irritability via cholinergic postganglionic pathways, probably by damaging airway epithelium & thereby sensitizing

			exposure to histamine were measured to determine significance.		bronchial irritant receptors. In 4 subjects, pretreatment with atropine sulphate aerosol blocked the R_{aw} increase by histamine after exposure to O_3.
54 Lategola, M.T., Melton, C.E.& Higgings, E.A.	1980, March	Two studies were conducted with varying concentrations of ozone for 2 different time periods. In the first study 27 adults participated. In the second study 28 adults participated. All subjects considered surrogate flight attendants.	Health: All subjects were non-smokers and had a medical examination and were found to be healthy. Response: Significant changes in symptoms (subjective, self-reported), spirometry and results of treadmill tests after exposure to O_3.	Health: Subjective symptoms of chest, heart, throat discomfort or headache; spirometry included FVC, FEV_1, FEF_{25-75} & FEF_{50-75}. During the treadmill test, ECG, heart rate & arrhythmia were monitored. Pollutant: Ozone in the first study at 0.2 ppmv for 4 hours and at 0.3 ppmv for 3 hours in the second study. Other: Constant temperature & humidity; changes in altitude to match a plane in flight; treadmill activity to match flight attendants' work.	In the first study there were no significant differences in symptoms, spirometry or treadmill results between subjects exposed and those not exposed to ozone. In the second study there were no significant differences in treadmill results between ozone-exposed and non-exposed subjects. However, there were significant differences in the symptoms and the spirometry (FVC & FEV_1). Authors conclude the ozone threshold for reversible adverse effects on symptoms & spirometry was reached by 3-hour exposure to 0.3 ppmv. Data also suggested greater symptomatic sensitivity to O_3 in femals.
55 Lategola, M.T., Melton, C.E.&	1980, Sept.	40 male subjects aged 40-59 years,	Health: Physical exam by a physician to confirm good health.	Health: subjective symptoms of throat, chest or heart or eye discomfort or headache;	The only statistically significant O_3/no O_3 difference in symptom mean

Higgings, E.A.	some were smokers, some were non-smokers. All subjects were considered surrogate airline passengers or cockpit crew.	Response: Significant changes in symptoms or pulmonary function before, during and after exposure to O_3.	spirometry included FVC, FEV_1, FEF_{25-75} & FEF_{50-75}. ECG was monitored continuously during exposure. Pollutant: Ozone for 3 hours at 0.30 ppmv. Other: Ambient air exposure for 3 hours; constant temperature & humidity; changes in altitude to match a plane in flight (pre-altitude, altitude, post-altitude).	scores in the smoker group was in the 50-59 year age group at altitude. In non-smokers there was significant difference in the O_3/no O_3 periods in the 40-49 year age group in altitude & post-altitude and in the altitude 40-59 year age group. For all subjects combined the O_3/no O_3 differences at both altitude & post-altitude were significant. For spirometry statistically significant O_3/no O_3 differences were seen in 40-49 year smokers, in FVC, in 40-49 non-smokers in FVC, in 50-59 non-smokers in FVC & FEF_{75-95} and in 40-59 non-smokers in FVC & FEV_1. For all subjects significant differences occurred in FVC, FEV_1 & FEF_{75-95}. Authors concluded that the O_3 threshold for sedentary subjects is right at 0.30 ppmv.

56 Kulle, T.J., Sauder, L.R., Kerr, H.D., Farrell, B.P., Bermel, M.S.& Smith, D.M.	1982	24 volunteer, healthy subjects; 13 males, 11 females; all non-smokers.	For health: No history of chronic respiratory or cardiovascular disease and normal findings on physical examination. For response: Significant decrement in pulmonary function after exposure to pollutants in an environmental chamber.	Health: FVC, FEV_1 & FEV_3. Pollutant: .4 ppm O_3 for 3 hours per day for 3 weeks, interspersed with exposures to filtered air for 3 hours per day. Other: Light exercise each day before end of exposure period for 15 minutes, bronchial challenge.	FVC for the first two days of O_3 exposure was significantly decreased from the control. Days 3, 4 and 5 showed no significant difference. When subjects were re-exposed 7 days following the 5-day repeated exposure, FVC was again significantly decreased. FEV_1 data show trends similar to FVC data. Bronchial challenge tests were conducted and significant increase in reactivity occurred on days 2 and 3 of the O_3 exposure, but no significant differences on the 4th & 5th days. Loss of adaptation as measured by the bronchial challenge test was not demonstrated; unlike FVC, the bronchial reactivity measurement did not show a significant change with re-exposure to O_3 7 days later.

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TITTEL
Respiratory illness and air pollution

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ABSTRACT (max. 300 characters, 5-10 lines.
The effects of various air pollutants, singly or in combination, on respiratory function were studied as early as the 1930's. This report details some of the research in this field, concentrating on results of two research methodologies: Environmental chamber studies and epidemiological cohort studies.

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