Toxic substances in the environment affecting respiratory function of people in Hawaii

Carl P. Hallenborg MD*
Nancy Marsh**
Steven Moser MD***

In this trilogy we have collected data from authors who are concerned with patients with respiratory complaints. Surprisingly there are unique problems in the residents of our State. The full impact of problems known to cause respiratory illnesses, such as asbestosis, will not be known for years to come. Other problems such as the effect of sugarcane burning are just now being identified and may show a parallel to the inhalation of asbestos dust. VOG may be simply an irritant or it may explain in part the high incidence of asthma in our State. Clearly more work needs to be done to explain the pathophysiology, the risk and possible treatment for the consequences on people of these putative toxic substances.

Introduction

Inhaled substances can affect our health adversely, but our knowledge of how much of these do and which of us are affected is incomplete. Although it is insufficient to claim injury by coincidental exposure, we must seek to identify substances that injure us and make sure that such exposure is reduced. The purpose of this article is to review some of those inhaled substances thought to endanger the people of Hawaii.

First, what constitutes an adverse respiratory health effect? Some pollutants in small concentrations affect all adversely. Many more pollutants affect a few of us only under certain circumstances. Both conditions are considered an adverse health effect. For example, nitrogen mustard in minute concentrations can kill people. Asbestos dust in a smoker increases the risk for lung cancer. Accordingly, the Environmental Protection Agency (EPA) has portrayed the burden of pollution as manifested by a spectrum of biological responses such as in Figure 1[1]. In the population exposed, many may show a physiologic effect, pathophysiologic changes and some morbidity and mortality. We presume that the greater number of people exposed, and the higher the dose, then more of them will be adversely affected. The American Thoracic Society in a position statement lists 1) interference with normal activity, 2) episodic respiratory illness, 3) incapacitating illnesses, 4) permanent respiratory injury and 5) progressive respiratory dysfunction, as clinically important in the determination of

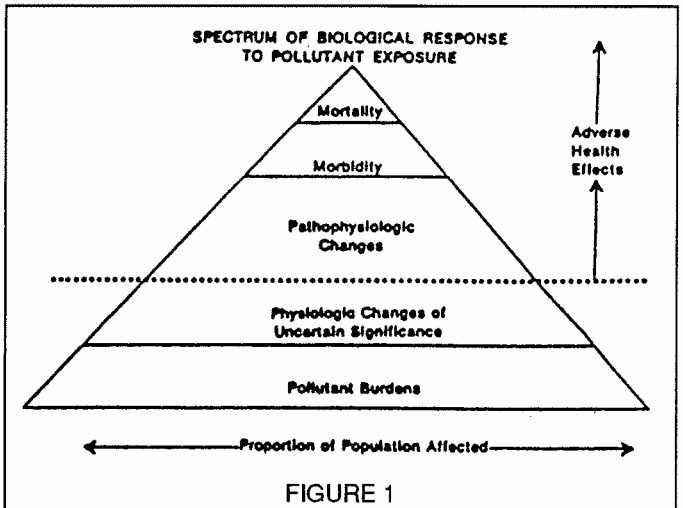

FIGURE 1
Spectrum of biological response to environmental toxin

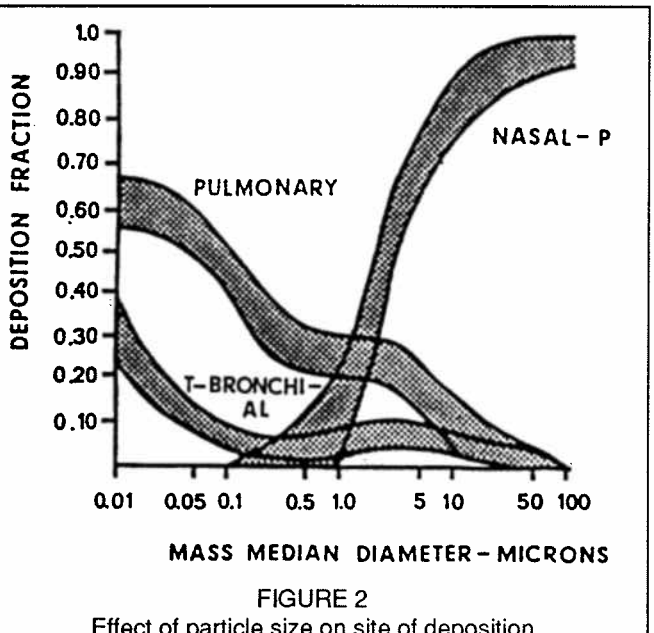

FIGURE 2
Effect of particle size on site of deposition

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* Chief, Pulmonary Division, Dept. of Medicine
Assistant Professor
John A. Burns School of Medicine

** Medical Student IV
John A. Burns School of Medicine

*** Internist Nephrologist
1883 Mill Street
Wailuku, Maui

adverse respiratory effect. Not stated but inherently obvious is that individuals such as asthmatics may be more sensitive to inhaled pollutants than others.

In order to identify a possible adverse health effect, we must identify the offending substance, how it gains access to the individual, and the mechanism of injury. Steps can be taken to minimize exposure, to identify those exposed, and to treat affected individuals or whole populations.

Many pollutants have been identified. Pollutants gain access to the respiratory tree according to particle size[2]. In Figure 2 we see that the smaller the particle size the more likely it is to gain access to the lower reaches of the respiratory tract. Thus, particles of size < 1 micron are likely to reach small bronchioles and the pulmonary parenchyma. Although hundreds of pollutants are known to cause problems, certain ones are more prevalent and should be considered in the differential diagnosis in certain medical situations and are worthy of attention below[3].

Problems of current concern in Hawaii include exposure to asbestos, the burning of sugarcane, and VOG. We will look at each problem from the point of view of the offending substance, the population at risk, the potential for injury and the implication that further study may be needed. Table 1 summarizes the approach to the subject. Question marks indicate data that are suspected but not proven.

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1. Asbestos related disease in Hawaii

The effect of asbestos dust on the health of man has been extensively studied in the terms of the offending agent, the pathogenesis and the markers of injury. Briefly, inhalation of asbestos dust over a prolonged period of time causes a retention of dust in the lung. This dust burden in the susceptible host causes pleural thickening and pulmonary fibrosis and increases the risk of bronchogenic and pleural cancer[1].

An industry in Hawaii that utilized asbestos (shipbuilding) existed long before effective control over exposure was established. In addition the use of asbestos in numerous applications (eg home building, brake linings), affected thousands of residents of Hawaii, making them at risk for asbestos-related disease. As many as 8,000 persons were employed at Pearl Harbor during World War II; they were directly exposed. Some brought asbestos-laden clothing home to be laundered by their families.

There is no specific treatment for asbestosis. The fibrosis of the lung initiated by the burden of dust in the susceptible host is relentless and not affected by cessation of exposure nor by medication. Bronchogenic carcinoma of the lung of any etiology has a poor prognosis. A solitary nodule, in the absence of metastases, is a candidate for resection. Pleural-based cancer, mesothelioma, is not treatable.

The diagnosis of asbestosis and asbestos associated malignancy is most often a cause for compensation. The diagnosis should be entertained in the patient with dyspnea or cough of unknown etiology. Such a patient must have a well-documented history of exposure over a considerable period of time, followed by a lag period of 15 to 20 years. This requires an extensive environmental and occupational history be taken.

A careful evaluation of the chest roentgenogram is the next step. Fifty percent of patients with a significant history of exposure will demonstrate at least some pleural changes. It is debatable whether pleural changes alone indicate pulmonary affect. Such changes indicate a susceptible host; however long-term follow-up is necessary in order to define disability. Pulmonary changes, such as bibasilar fibrosis and other more extensive involvement are not specific.

Perhaps the greater benefit of taking serial chest roentgenograms would be the earlier diagnosis of bronchogenic carcinoma at a stage which may be treatable. Accordingly, a patient with documented extensive exposure to asbestos dust should have periodic chest roentgenograms.

Pulmonary function tests are a critical part of the evaluation. Spirometry is also indicated in order to identify obstruction. Obstruction not helped by bronchodilators is supportive of the diagnosis. Lung volume tests may show a restrictive process (Total lung capacity less than 80% of predicted.) Diffusing Lung Capacity for Oxygen (DLCO) is decreased in pulmonary fibrosis and may be the first indication of pulmonary asbestosis.

The clinical diagnosis of asbestosis is not easy. No single finding is specific nor is it necessary for all findings to be in place in order to establish the diagnosis. A reasonable consensus to the approach for a clinical diagnosis is provided by the American Thoracic Society[2]. (See appendix)

We have followed many patients with documented heavy exposure to asbestos occurring over a 20-year period prior to evaluation. Data is presented here on 74 patients. Each patient had a history of exposure (including a history of smoking), 4 views of the chest by roentgenogram and pulmonary function

CRITERIA FOR THE CLINICAL DIAGNOSIS OF ASBESTOSIS

1. A reliable history of exposure.
2. An appropriate time interval between exposure and detection.
3. Clinical criteria:
   a) Chest roentgenographic evidence of type "s", "t", "u", small irregular opacifications in profusion 1/1 or greater.
   b) A restrictive pattern of lung impairment with a forced vital capacity below the lower limit of normal.
   c) A diffusing capacity below the lower limit of normal.
   d) Bilateral date or pan-inspiratory crackles at the posterior lung bases not cleared by cough.

(Accepted by the American Thoracic Society)

TABLE I

Patients	N	Pleural Asbestosis N	(%)	Pulmonary Asbestosis N	(%)
Non-smokers	45	22	(49)	23	(51)
Mild	8	7	(88)	4	(50)
Moderate	8	3	(38)	2	(25)
Heavy	13	9	(69)	10	(77)
	74				

Smoking history in relation to diagnosis of asbestosis in 74 patients with a documented history of exposure to asbestos dust. Percentages indicate number of positive findings.

TABLE II

Asbestos Exposure	N	Pleural Asbestosis N	(%)	Pulmonary Asbestosis N	(%)
Mild	9	4	(44)	4	(44)
Moderate	26	15	(58)	14	(54)
Heavy	40	22	(55)	23	(58)
	75				

Degree of asbestos exposure in relation to diagnosis of asbestosis in 74 patients. Percentages indicate number of findings.

tests. A history of smoking was graded as mild (<10 pack-years), moderate (10-20 pack-years), and heavy (>20 pack-years). The exposure to asbestos was graded as mild (<10 years), moderate (10-20 years) and heavy (>20 years). Pleural asbestosis was defined as demonstrating any evidence of thickening of the pleura; pulmonary asbestosis was defined as changes indicating fibrosis on the chest roentgenogram and/or reduction of DLCO.

Table I compares our diagnosis of pleural and pulmonary asbestosis with history of smoking. Pleural changes are frequently seen but are not related to the amount of smoking. Pulmonary asbestosis appears more often in heavy smokers; this may indicate a synergistic effect. However, it is a known fact that smoking per se damages the lung.

Table II pits our diagnosis of asbestosis against the amount of asbestos exposure. Pleural and parenchymal changes are common and are not a function of the amount of exposure. Once a threshold of exposure has been established, the patient is ultimately at risk for asbestos-related disease.

These data are being presented to show that patients exposed to asbestos in Hawaii are indeed affected and that this is a health hazard in Hawaii. There is no doubt that asbestos dust should be avoided whenever possible. There is no evidence that a brief exposure is dangerous, however an extensive evaluation of the critical degree of exposure is expensive and not warranted.

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Sugarcane burning in Hawaii: A possible health hazard

The question has been raised whether incidental as well as chronic exposure to burning of sugarcane is detrimental to one's health. On the North Shore area of Oahu, residents living near a sugarcane factory have been exposed for many years to the smoke, fumes and debris that result from burning the leaves of the sugarcane. These inhabitants who live in close proximity have complaints of respiratory dysfunction such as dyspnea, coughing and wheezing; several have died of

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respiratory disease. Many still residing there have inquired about the possible connection between their symptoms and the burning of cane close by.

As part of the procedure in harvesting, the rows of cane are set on fire so that the excess leafage is burned away. The burning of the cane results in airborne suspended particles that may act as irritants to respiratory tract tissue, and thereby promote increased susceptibility to carcinogens.

Previous studies have shown that these particles are biogenic silica fibers[1] that, when inhaled, may lead to lung cancers similar to those caused by asbestos fibers. The silica fibers are being released in the sugarcane growing regions of the United States, as well as in a number of foreign countries, during the worldwide practice of open-field burning of cane leaves and cane "trash." Epidemiological studies done in these areas suggest a relationship between biogenic silica exposure and cancer. The evidence for these fibers as an etiological agent in cancer comes from several sources worldwide.

In 1976, Das et al[2] documented 5 cases of rare mesothelioma in persons who were involved with sugarcane farming, or an allied trade, but who had had no previous exposure to asbestos (Mesothelioma is an uncommon neoplastic condition having a well-established association with exposure to asbestos[3]. Its incidence has been reported to range between 0.02% and 0.2% of all autopsies[4]).

In a 1983 laboratory study by R. H. Newman of the Imperical Cancer Research Fund in England[1], the presence of silica fibers resembling asbestos fibers was noted in the ash of sugarcane leaves burned in the harvesting process. In a report published in 1986[5], Newman found the biogenic silica to be 0.85 um in diameter and 10 to 300 um long, which is within the size range of asbestos fibers that are carcinogenic. Newman argued that there was significant evidence worldwide (China, India, Iran, Africa, Australia, and Louisiana) to suggest strongly that "siliceous plant fibres, with dimensions similar to asbestos, are involved in the causation of mesothelioma and lung cancer in sugarcane workers."

In the United States, a Louisiana State University study done in 1982[6] showed a direct correlation between that state's high incidence of lung cancer and sugarcane farming. Rothschild and Mulvey interviewed the next of kin of 284 persons (randomly chosen) who had died of lung cancer during 1971 to 1977 in Southern Louisiana. Of the deceased, 38% had been employed for at least 6 months as sugarcane farm workers (statistically significant for $p < 0.0001$) compared to 20% in the matched controls. After adjustment for smoking, the relative risk estimate of lung cancer mortality for sugarcane farm workers was 2.4 (95% confidence limits, 1.7 to 3.6). The sugarcane farmers who died of lung cancer had worked for longer periods in the sugarcane farm industry than did those sugarcane farmers in whom lung cancer did not develop ($p = 0.006$). Two of the deceased sugarcane farmers with no discernible exposure to asbestos were found at autopsy to have had mesothelioma.

According to a 1979 study by Rothschild et al[7], many of the regions in Louisiana that grow sugarcane show high mortality due to lung cancer. In the continental US, sugarcane production is a major industry in only 2 states other than Louisiana: Florida and Texas. Two of the 3 sugarcane-growing counties of Florida have a high mortality due to lung cancer. In Texas, none of the 3 counties has this high a mortality rate. However, sugarcane farming in Texas was started only after 1970. Thus, sufficient time may not have elapsed for the disease to be manifested.

A study of Florida sugar operations conducted by the National Institute for Occupational Safety and Health (NIOSH)[8] in 1985 showed that when sugarcane is burned, silica is released into the atmosphere in the form of fibers ranging from 3.5 to 65 um long (mean = 12 um). The samples in the study contained as many as 58,000 inorganic fibers per cubic meter of cane-smoke-polluted air and 300,000 fibers per cubic meter in the air during the harvesting of the burned crop. More than half of the fibers in one sample were purely or mainly silica in composition. In 1984, NIOSH had stated in regard to asbestos that there is no safe concentration of exposure to asbestos, but recommended that exposure to asbestos fibers greater than 5 um in length not exceed 100,000 fibers per cubic meter of air[9].

The Hawaiian Planters Association has estimated pre-harvest burning of cane fields in Hawaii annually consumes between 1.7 and 2.5 billion cubic feet of trash. If only 1% of the resulting ash from these burnings consists of asbestos-like, fine, biogenic fibers, it may well constitute a health threat to residents in the cane areas.

Accordingly, inhabitants of the North Shore who live in close proximity to sugarcane fields were asked and agreed to be part of our study in 1984, 1985, and 1986.

The experiment

Fourteen residents living within a 3-block radius of a sugarcane factory were given health and breathing questionnaires to determine their past, present, and family medical histories (especially a full account of respiratory symptoms), their cigarette smoking habits, lifestyle, years of exposure and degree of exposure to sugarcane burning and other environmental hazards. These residents then underwent a physical exam; chest radiographs were obtained.

Pulmonary function tests were performed to determine the type and degree of physiologic impairment resulting from a particular disease process. These were used in the early detection of lung disease and the assessment of its severity and progression[10]. In our study, a spirogram was used to measure the forced vital capacity (FVC) of the residents. The volume of the FVC exhaled in the first second constitutes the 1-second forced expiratory volume (FEV 1), which was also measured. From the FEV, the rate of flow of the exhaled air was computed. The standard against which this is compared is the forced expiratory flow of 25 to 75% of the FVC (FEF 25-75%). The forced expiratory flow for 50% of the FVC (FEF 50%) was also computed. The total lung capacity (TLC) and residual volume (RV) were determined by the helium dilution technique. The diffusing capacity (DLCO) was measured by a single breath test using carbon monoxide (see Table 1 and Figure 1).

The onset of symptomatic asbestosis is uncommon until at least 20 to 30 years after exposure[11]. Because the actual years

TABLE 1

Pulmonary function test values taken over a period of 3 years in terms of percentage of residents living near a sugarcane factory (values corrected for age and smoking).

	FEV 1	FEF 50%	FEF 25-75%	TLC	VC	
DLCO						
Normal	86%	7%	0%	14%	57%	21%
Reduced	14%	93%	100%	86%	43%	79%

	RV
	—
Normal	7%
Slightly Elevated	86%
Elevated	7%

of exposure varied from 4 to 40 years, not all the residents examined had signs or symptoms of respiratory problems. However, more than half the residents complained of dyspnea and a nonproductive, irritating cough; the two most frequent initial symptoms of asbestosis[11]. Auscultation of the chest revealed some end-respiratory wheezing on forced expiration in about a third of the residents. Chest roentgenograms were unremarkable, showing no pleural plaques. In asbestosis, the plaques usually are bilateral and have to be relatively extensive, or contain abundant calcium, in order to be visualized[11].

There is evidence that the earliest effects of the exposure to asbestos dust affects primarily the small airways in the peripheral parts of the lung; therefore, this may not be detected on routine pulmonary function tests[11,12]. However, the data (Table I) does show that the majority of the residents have a restrictive condition, demonstrated by normal values for FEV 1 and reduced values for TLC and DLCO. Although the FEF 25-75% is a sensitive guide to the presence of airway obstruction, flow rates may be reduced in restrictive lung disease secondary to a low vital capacity[10]. Almost half of the residents had a reduced vital capacity. Also, decrements in FEF 25-75% and FEF 50% reflected the presence of small airway disease.

The characteristic functional abnormalities in asbestosis are reduction in vital capacity (43% in our study) and in total lung capacity (86% in our study), a normal, or sometimes slightly elevated, residual volume (total 93% in our study), and reduction in diffusing capacity (79%) for carbon monoxide[12]. The pulmonary function test data seems to indicate a possible development of a restrictive lung disease, conceivably asbestosis. More important, however, than the functional definition of an advancing disease is its detection at an early stage. Diffusing capacity seems to relate closely to the degree of disability from asbestosis, and attempts to detect the disease at a pre-symptomatic stage have concentrated on the measurement of this, as well as of vital capacity. An alarming 79% of the residents had a decreased DLCO. However, impaired diffusion is more strongly related to smoking than to the intensity of exposure to asbestos[11]; 64% of the residents were or had been smoking cigarettes.

It appears that the pulmonary function test data does not show clearly the presence of asbestosis; however, it does suggest the presence of some lung disease, with reductions mainly in FEF 50%, FEF 25-27%, TLC, DLCO, as well as a slightly elevated RV.

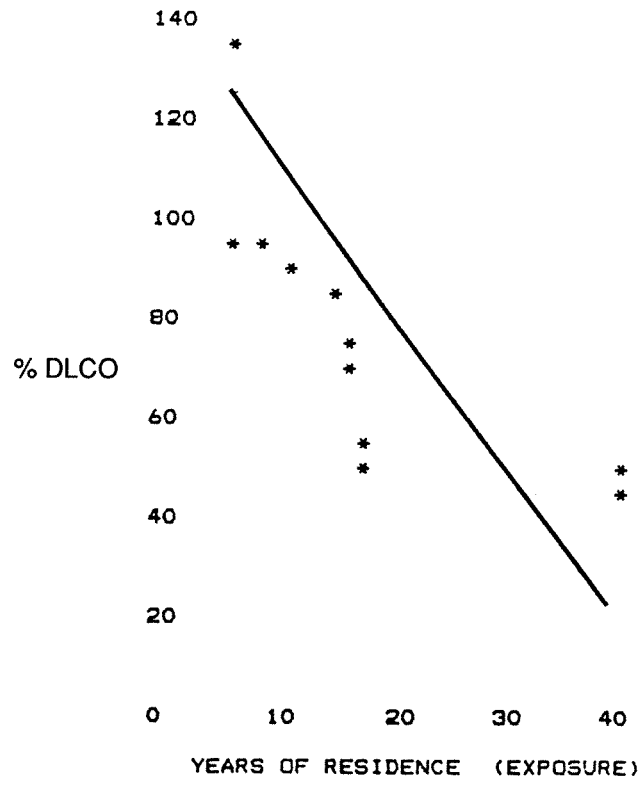
The physical exam, and symptoms of coughing and dyspnea, indicated a respiratory problem among a good number of residents living in the area near the sugarcane factory. With the exception of one person, they had had no known previous exposure to asbestos. Several residents noted that their respiratory problems began after moving to the North Shore area, and some experienced an improvement upon living away from the area.

There did not appear to be a positive correlation between the severity of symptoms and the number of years of residence (exposure) in the area in all of the residents. On the other hand, there seemed to be a positive correlation with the decrease in values in the pulmonary function tests had the number of years of residence (exposure in the area, especially in DLCO (Fig. 1).

No significant changes in pulmonary funciton test values during the 3 years of testing of each resident were observed. However, it is advisable for those with likely constant expo-

FIGURE 1

Number of years of residence (exposure) near a sugarcane factory vs % DLCO for each resident



Values are an average taken over a 3-year time period.

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sure to asbestos-like particles to be tested yearly, since even a brief exposure, for as short a period as 2 to 6 months, may produce asbestosis or pleural disease more than 20 to 30 years later[11].

There may or may not be a connection between sugarcane burning and the occurrence of respiratory disorders in the nearby residents, but further testing done for long periods of time, utilizing a larger cohort of residents, should provide a more accurate indication of a possible health hazard in Hawaii, as well as elsewhere.

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The effects of "VOG"* on respiration

Most physicians and their patients on the island of Hawaii believe there is an increase in the morbidity and mortality of patients with asthma and that this is due to the frequent and continuous eruptions of the Kilauea Volcano. Subsequent to an eruption, asthmatics make more frequent visits to their physicians, emergency rooms, and often require hospitalization. There have been 6 deaths due to asthma on the Island of Hawaii this past year (1990), more frequent than the national average. However, spot reviews of emergency room records conducted by the CDC in 1982 and a questionnaire conducted by the Hawaii State Department of Health (DoH) failed to document this widespread clinical impression.

The volcanic emissions, measured at the site, consist primarily of CO_2, water vapor, and SO_2. Sulfur dioxide, or SO_2, is the most abundant, potentially noxious, gas and it has been emitted at the rate of 300-1000 tons per day during this 3-year-long eruption. Levels of SO_2 in the populated areas were below the standards set by the DoH.

On the other hand, volcanic eruptions have been a known hazard from the ancient times of the Roman empire when Mount Vesuvius buried cities such as Pompeii. Few health professionals know, however, that volcanoes are also a current health hazard. As many as 55,000 people have died in the 20th century and countless more have suffered lesser effects. The best and most recent studies involved the unexpected eruptions of Mount St. Helens in 1980 in the Pacific Northwest. This was studied in detail by Dr. Sonia Buist and her colleagues.

From her studies it is clear that scientific methods previously had not been used and the effects were underestimated. Other volcanoes have caused different kinds of problems, depending on the type of eruption and the character of the emissions[1].

The characteristics of the emissions from Kilauea have been delineated[2]; the emissions contain H_2O (87%), SO_2 (12%), CO_2 (8%), as well as minute concentrations of H_2S and CO (carbon monoxide).

The most likely cause of respiratory toxicity is SO_2 both by its high concentration and high potential for causing toxic particulate matter such as sulfites and sulfates. The SO_2 interacts with water in sunlight to form an acid H_2SO_4. This has recently been shown through carefully controlled studies to cause respiratory problems in humans. Ostro[3] reports that a group of asthmatics exposed to acid aerosol react in a predictable way in proportion to the increase in the acid (Figure 1). Peak flow meters were used to document end-points. Utell[4] studied only 12 asthmatics but showed clearly that airway conductance significantly dropped after exercise and after a 4-hour exposure to H_2SO_4 450ug/m3 (Figure 2). Furthermore, they were able to document that 450ug/m3 was an important threshold level.

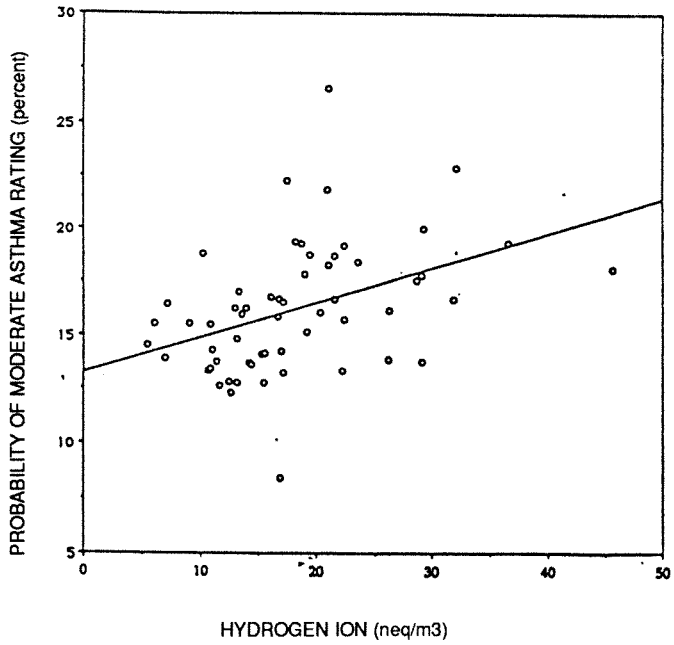

FIGURE 1
Moderate asthma rating versus hydrogen ion, controlling for covariants

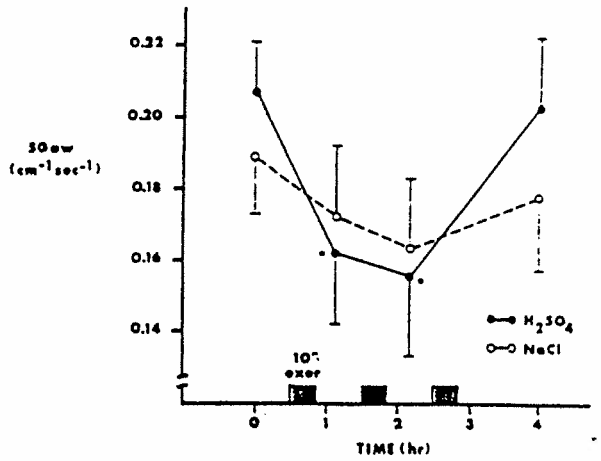

FIGURE 2

Mean values of specific airway conductance (SGaw) before, during, and immediately after the 4-hour exposure to 450 ug/m3 H_2SO_4 and NaC1 aerosols for 12 asthmatics. Significantly greater decrements occurred with H_2SO_4 compared to Nac1 following the first and second exercise periods ($p<0.05$). Bars represent standard error of mean.

We do not know whether sulfur dioxide from Kilauea acts in this way, whether particulates reach toxic levels, or whether these toxic chemicals affect the Hawaiians. Consequently, the Hawaii Lung Association has established monitors as the result of a proposal submitted by Ed Morgan MD and Mr. James Morrow. A longitudinal clinical study has been launched by Drs. Hallenborg, Matthews and Ono. Even if "toxic levels" are not documented by these monitors, it is possible that lower levels of particulates may injure susceptible individuals, such as asthmatics with mild infections or after activity. No one has done such a study previouisly.

*VOG = Volcanic Fog, a colloquialism

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