in mortality from this disease. The application of such principles in New Zealand, helped enormously by the decision of government on the recommendation of the Asthma Task Force to provide peak expiratory flow meters free of charge to patients, has been associated with a recent downward trend in the asthma mortality rates, particularly in young people. An interesting feature of this trend has been that the previously considerably increased mortality rates among the Maori and Polynesian races have fallen to equal the mortality rates in Europe. If the recent increase in asthma mortality in the United States is real, and the consensus view is that it is real, especially in black subjects and among young people, then such strategies could be used equally effectively in the United States as in New Zealand. While we wait final confirmation of the reality of the reported trends in morbidity and mortality caused by asthma and explanations for these trends, management of asthma, especially its inflammatory component, can be taken more seriously and lives can be saved.

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Sulfur dioxide and asthma—A double-edged sword?

SO₂ is a ubiquitous air pollutant produced by combustion and processing of sulfur containing fossil fuels. It is thus a major constituent of polluted urban air. In addition, SO₂ is widely used in industry with an estimated 500,000 workers in the United States regularly exposed in settings ranging from smelters and paper-pulp mills to wineries and food-processing plants.

The first suggestion that SO₂ might produce important adverse effects on human health came from observations of increases in mortality in association with several episodes of severe air pollution that occurred in the middle of this century. Although information about the specific pollutants present during these episodes is incomplete, the best estimates suggest that the concentrations of SO₂ were quite high. For example, during a severe episode of polluted fog in London in 1952, the maximal average concentration of SO₂ during 24 hours was estimated at 1.5 ppm, more than 10 times the current standard set by the United States EPA. The excess deaths attributable to pollution during these episodes were generally clustered among patients with preexisting cardiopulmonary disease, suggesting that the pollutants present during these episodes may be exerting their adverse effects on the lung. Patients with asthma were found to be especially susceptible to these episodes of pollution. For example, in one study, 88% of patients with asthma experienced exacerbations during the pollution episode that occurred in Donora, Pa., in 1948.8 Stimulated by these associations between air pollution and respiratory morbidity and mortality, investigators have examined the effects of SO₂ on several species of animals, including mice, guinea pigs, rats, dogs, cats, donkeys, and monkeys. The two most important effects observed have been an increase in airflow resistance and an alteration in mucous secretion.24 Acute inhalation of SO₂ has been reported to increase, rapidly, the airflow resistance in dogs, cats, and guinea pigs. Generally, this effect has only occurred after inhalation of concentrations of SO₂ > 5 ppm, well in excess of the concentrations encountered in polluted outdoor air. The one exception to this statement is a report of a statistically significant increase in pulmonary resistance in guinea pigs exposed to concentrations of SO₂ < 1 ppm.2 This response, although it was statistically significant, was quite small. The same investigator found that 46 ppm of SO₂ was required to increase resistance by 50% above baseline. In general, SO₂ has not caused morphologic evidence of lower respiratory injury in animals unless it was inhaled in high concentrations (>25 ppm). Thus, extrapolation from these experiments in normal healthy animals would not predict an important acute effect of SO₂ on airflow resistance in the concentrations encountered in polluted air (generally <1 ppm).

Several studies have examined the effects of acute inhalation of SO₂ on normal human subjects. In most of these studies, inhalation of concentrations >5 ppm was demonstrated to cause small but significant decrements in airway function.8 9 10 Occasional "sensitive" subjects were found to respond in a similar fashion to concentrations as low as 1 ppm.2 11 12 Because these effects were small, and usually required inhalation of concentrations of SO₂ well in excess of those encountered in polluted outdoor air, these results were interpreted to imply that SO₂ itself was not likely to be responsible for the adverse health effects of air pollution.

However, studies from several different laboratories have now demonstrated that concentrations of SO₂ that have little or no effect on normal healthy subjects can produce marked, symptomatic bronchoconstriction in subjects with asthma.13 14 The bronchoconstrictor effect of SO₂ is greatly potentiated by exercise. Thus, exercising subjects with even mild asthma routinely develop bronchoconstriction when they inhale concentrations of SO₂ > 0.4 ppm during moderate or heavy exercise. This effect occurs after periods of exposure as brief as 2 minutes and is associated with symptoms typical of an acute exacerbation of asthma.14 15 As with all stimuli to acute bronchoconstriction, airflow obstruction and symptoms usually remit spontaneously but can persist for periods in-

Abbreviations used

SO₂: Sulfur dioxide
OSHA: Occupational Safety and Health Administration
EPA: Environmental Protection Agency

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cess of 1 hour if they are untreated. For many subjects with mild asthma, the exacerbations induced by ambient concentrations of SO2 in the laboratory are as severe as, or more severe than, any exacerbations that they experience from stimuli outside the laboratory. The concentrations required to produce these effects (≥0.4 ppm) can be exceeded in air in the vicinity of point sources of SO2 emission and in indoor air of homes heated with kerosene space heaters. Much higher concentrations are encountered in the workplace in which the present standard set by the United States OSHA allows exposure up to 5 ppm as a time-weighted average during an 8-hour workshift. It is thus clear that exposure to SO2 in indoor and outdoor ambient air and in the workplace can be an important cause of acute symptomatic bronchoconstriction in patients with asthma. As noted above, the present OSHA standard, designed to protect healthy workers, allows exposure to concentrations of SO2 more than an order of magnitude higher than those known to cause symptomatic exacerbations of asthma. Unfortunately, the present primary National Ambient Air Quality Standard for SO2, the standard set by the United States EPA to protect even the most sensitive segments of the population, is also inadequate. This standard is based on a 24-hour averaging time, whereas symptomatic SO2-induced bronchoconstriction occurs after exposure as short as 2 minutes in duration.

The article by Riedel et al.11 suggests another possible interaction between SO2 and asthma. In their study, guinea pigs exposed to SO2 or filtered air for 8 hours daily on 5 consecutive days were also exposed to an aerosol of ovalbumin on the third through fifth days. Animals exposed to all three concentrations of SO2 were subsequently found to be more likely to develop bronchoconstriction on reexposure to ovalbumin on the third through fifth days. Animals exposed to all three concentrations of SO2 exposure appeared to result in higher concentrations of IgG antibodies against ovalbumin in both S02 exposure. It is now clear that in addition to initiating classic reflex responses, airway aberrant nerves are the source of a variety of peptide mediators that can alter the function of both macrophages and lymphocytes.45

Forty years ago SO2 was considered one of the leading causes of adverse respiratory effects of air pollution. During the next three decades, a large number of studies in several mammalian species, including healthy humans, led most scientists to conclude that the concentrations of this pollutant present in ambient air were probably benign. The present OSHA and EPA standards were established from that data base. It is now clear that this erroneous conclusion was based on a failure to study the appropriate population and that the acute adverse effects of near ambient concentrations of SO2 on patients with asthma can be quite profound. If the effects of repeated exposures to low concentrations of SO2 reported by Riedel et al.11 are confirmed and extended to other species (especially humans) interest in this common pollutant as a cause of adverse respiratory effects of air pollution may yet come full circle.

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Original articles

The relationship of serum IgA concentration to human immunodeficiency virus (HIV) infection: A cross-sectional study of HIV-seropositive individuals detected by screening in the United States Air Force

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Serum immunoglobulins were measured in 107 patients with human immunodeficiency virus seropositivity. Each patient was categorized by the Walter Reed staging classification and serum concentrations of immunoglobulins were compared with patient staging. Serum IgM concentrations were normal in all but nine patients. Serum IgG concentrations were elevated in 74 of 107 patients, with no significant differences noted between different stages of disease severity. Serum IgA concentrations were elevated in 38 of 107 patients, with a significant relationship noted between increasing staging category and increasing serum IgA concentration (p = 0.0001). Serum IgA concentrations in patients with human immunodeficiency virus seropositivity may be a useful marker of immunologic progression of disease. (J ALLERGY CLIN IMMUNOL 1988;82:965-70.)

AIDS is caused by infection with HIV. The Department of Defense has initiated a program to screen all military personnel for HIV seropositivity; every HIV-seropositive member of the United States Air Force is referred to WHMC for evaluation. This evaluation includes a detailed analysis of each patient's immune status, a serologic survey for concomitant viral infections, and a complete epidemiologic profile. Redfield et al. recently described a staging classification for HIV infection. We would like to report our experience applying this classification to patients seen at WHMC in various stages of HIV infection. We found a direct relationship between serum IgA concentrations and progression of infection as defined by Redfield et al. This prompted a more thorough evaluation of the role of serum IgA in HIV infection, and raised the possibility that serum IgA concentrations may be predictive for the development of AIDS.

MATERIAL AND METHODS

Patients

All patients admitted to WHMC between October 1985 and August 1986 with positive ELISA and Western blot results to HIV were evaluated clinically and by the following laboratory parameters: complete blood and platelet count; chemistry profile; quantitative immunoglobulins performed