INTRODUCTION

The inhalation of ozone (O₃), a ubiquitous air pollutant, may lead to chronic health effects in well individuals and may exacerbate health problems in people with preexisting lung disease. An important challenge in laboratory studies of human O₃ exposure is the noninvasive determination of adverse alterations in lung function. Whereas forced expired flow and specific airway resistance are well-established indicators of O₃-induced decrements in conducting airway function [3], measurements specific to the peripheral airspaces are lacking. The purpose of the current research was to evaluate a noninvasive measurement of peripheral airspace response that was based on CO₂ capnometry.

Farmery [1] developed a model of the CO₂ expirogram in which the slope of the alveolar plateau is attributed to the continuing accumulation of CO₂ in a well-mixed peripheral region as expiration proceeds. In particular,

\[ \frac{dF}{dV} = \frac{F_M \theta}{(V_M + V_T/2)} \]  

where \( dF/dV \) is the slope of expired CO₂ fraction with respect to expired volume in the plateau region, \( F_M \) is the mean expired CO₂ fraction, \( \theta \) is fraction of the breathing period occupied by expiration, \( V_T \) is the expired tidal volume, and \( V_M \) is the end-expiratory volume of the well-mixed peripheral lung region. In the present research, the effect of O₃ exposure on \( V_M \) for a group of 47 healthy people was determined.

MATERIALS AND METHODS

Twenty-three women and twenty-four men, all healthy nonsmokers between the ages of 18-33, participated in two research sessions in which they exercised for one hour on a bicycle ergometer in order to elicit a total ventilation of 30 liters per minute. While exercising, the subjects breathed through a mouth-only mask through which they were exposed to room air during the first session and air containing 0.3 parts per million O₃ during the second session. The mask was instrumented such that respiratory flow and O₃ concentration could be monitored throughout each breath. The overall uptake of O₃ (OZU) was computed as the integral of the product of the respiratory flow and the respired O₃ concentration.

Measurement of the CO₂ expirogram was duplicated immediately preceding the air or O₃ exposure, 10 minutes following exposure, and 70 minutes following exposure. During this measurement, the subjects were at rest and breathed through a mouthpiece assembly that monitored respiratory flow and respired CO₂ fraction. The subjects were coached to breathe at inspiratory and expiratory flows of 250 ml/sec with an inspiration time of 3 seconds and an expiration time of 5 seconds. A separate value of \( V_M \) was determined for each CO₂ expirogram using equation 1.

RESULTS

The average±sd of the pre-exposure values of \( V_M \) among all subjects in the air and O₃ exposure sessions was 4330±1030 ml. The relatively large variation of \( V_M \) was similar at all 3 measurement times and in both research sessions. Variations associated with the pre-exposure \( V_M \) were evaluated by an ANOVA including a components-of-variance analysis that employed subject and session as random factors. The results indicated that between-subject, between-session, and within subject variations contributed 60%, 0%, and 40% of the total variance, respectively. Moreover, between-subject differences were significant (p<0.001) whereas between-session differences were not significant (p=0.331).

The \( V_M \) values separately averaged for each subject over the two research sessions were significantly correlated with subject height (r=0.596, p<0.001) as well as with subject weight (r=0.425, p=0.003). This is similar to what has been observed for standard lung volumes such as functional residual capacity.

Although \( V_M \) decreased slightly as a result of exercise alone (Fig. 1; Air), a two-tailed Student’s t-test indicated that this effect was not statistically significant at 10 minutes (p=0.226) or 70 minutes post-exposure (p=0.132). On the other hand, the combination of exercise and O₃ (Fig. 1; Ozone) caused a dramatic decrement in \( V_M \) that was significant at 10 minutes post-exposure (p=0.000) and remained...
The slope of the alveolar plateau of expired breath curves is frequently attributed to stratified inhomogeneities due to diffusion limitations or regional inhomogeneities due to mechanical effects. In the case of the CO₂ expirogram, in particular, the accumulation of CO₂ in the peripheral lung during the expired breath is a third source of the alveolar slope. Employing a single-path convection-diffusion model, Huang and associates [2] demonstrated that stratified inhomogeneities are negligible compared to the effect of CO₂ accumulation when the tidal volume is greater than 10 ml/kg; the average tidal volume in the present study was 18 ml/kg. Thus, VMP values computed from equation 1 are due in part to a true, well-mixed, peripheral lung compartment but they must also be affected by regional inhomogeneities. This explains why the average pre-exposure VMP value that we computed was nearly twice as large as a normal functional residual capacity. In spite of the influence of regional inhomogenities, we found that pre-exposure values of VMP were correlated with height and weight, as one would expect if VMP was related to lung size. Moreover, the goal of this study was to use changes in VMP as a marker of physiological response so that baseline contributions of regional inhomogeneity should have a small influence on the results.

We observed a small but insignificant decrease in the average VMP in the air exposure session when exercise alone was the physiological disturbance. However, only 60% of the subjects exhibited negative values of ∆VMP, so that the individual responses were not consistently negative. With the combination of exercise and O₃ exposure, however, there was a significant and dramatic decrement in VMP that was consistently observed in about 85% of the subjects.

The major problem with the measurement of VMP is its large variability. This variability is amplified even more when one is trying to tease out the response in terms of a change in VMP. Although measurements on different days contributed little to the overall variability, differences between subjects and between replicate measurements within the same subject contributed equally to variability. Thus, improvements in the precision of our instrumentation and in the reproducibility of a subject’s breathing maneuver during the expirogram measurement could markedly reduce variability, possibly eliminating some of the (inconsistent) positive changes in VMP that were observed during O₃ exposure.

Finally, we were able to demonstrate that between-subject differences in ∆VMP were related to OZU (Fig. 2). In particular, about 10% of the variation in ∆VMP was explained by differences in OZU. The weakness of this relationship is not surprising for two reasons. First, changes in overall O₃ retention in the respiratory system may not parallel changes in O₃ uptake in the peripheral lung, the site of the ∆VMP response. Second, other subject-specific factors such as antioxidant capacity and cell sensitivity may influence an individual’s response to O₃ exposure.

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REFERENCES