EXECUTIVE SUMMARY

THE EFFECT OF HEAVY SUSTAINED EXERCISE IN COMBINATION WITH LOW LEVELS OF OZONE CONCENTRATION IN INDUCING ACUTE PULMONARY FUNCTION IMPAIRMENT IN HUMANS: INTERACTION OF AMBIENT HEAT AND MULTIPLE POLLUTANT EXPOSURES

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INTRODUCTION

Ozone is an extremely toxic constituent predominant in the photochemical smog of numerous California urban areas. Because of its demonstrated biochemical and morphological effects on the lungs of animals acutely and chronically exposed to ambient smog alert levels, and its association with an increased rate of hospital admissions for respiratory ailments, governmental agencies have attempted to set appropriate standards of air quality. Unfortunately, there are limited data relating specific levels of a given pollutant to a particular physiological outcome, especially during exercise when the total amount of pollutant inhalation in a given time is dependent both on the ambient concentration and the ventilatory pattern characteristic of enhanced metabolic demand. The latter is particulary important, in that moderate to very heavy physical activity necessitates an increased ventilation and rate of pollutant inhalation of 5 to 15 times that at rest. Further, in addition to vigorous voluntary exercise becoming increasingly universal in the adult population, primarily for improved health/fitness, there are still numerous outdoor occupations that require vigorous activity over prolonged periods, including construction labor, refuse collection, and postal delivery.

While there is a reasonably sufficient data base for quantitating the pulmonary function response of healthy young adult males exercising when exposed to ozone, there is a paucity of similar objective data relative to perhaps more sensitive subpopulations, including females, children, and older adults. Further, since significant photochemical smog episodes, in which ozone concentrations sufficient to effect acute toxic effects, are frequently accompanied by ambient heat stress and/or above health standard levels of other pollutants, it is essential to study these combinations under controlled laboratory conditions.

In this research investigation, eight separate projects were designed collectively to examine (1) the efficacy of the ozone effective dose concept (expressed as the product of ozone concentration, ventilation minute volume, and exposure duration), in predicting the acute ozone toxicity response in young adult males; (2) the relative ozone toxicity response of young adult females, clinically normal middle-aged males, and highly trained endurance athletes, compared to young adult males at the same effective dose; and (3) the

possible interactive effects of ozone inhalation in the presence of ambient heat and nitrogen dioxide, which are often observed in concert with ozone on the occurrence of photochemical smog alerts.

METHODOLOGY

One hundred six human subjects, ages 19-68 years, undertook sustained bicycle ergometer exercise, ranging from moderate to very heavy intensity, which elicited average minute ventilation volumes between 4 and 12 times greater than that at rest for periods of from 30 to 100 minutes. Subjects were exposed to filtered air and to ozone concentrations ranging from 0.12 to 0.40 ppm, and in one study to 0.60 ppm nitrogen dioxide and to 0.60 ppm nitrogen dioxide plus 0.30 ppm ozone. Exposures were conducted at moderate temperature and humidity, except in one study in which ten young adult females were exposed to filtered air and to 0.15 ppm and 0.30 ppm ozone in both moderate (24°C) and at hot (35°C) conditions. Altogether, a total of 434 exposures were completed.

Measurement of standard pulmonary function tests pre and postexposure, and periodic observations of exercise ventilation, respiratory metabolism, and heart rate were obtained. Following each protocol, subjects completed a subjective symptoms form.

RESULTS

A brief statement of the purpose, experimental design, and principal results of each of the eight studies follows:

1. Refinement of the Ozone Effective Dose Concept. Ozone effective dose, expressed as the simple product of ozone concentration, exposure duration, and minute ventilation volume, predicts acute toxicity effects better than ozone concentration alone. However, there is strong evidence of the latter's greater importance, but the means to express this incongruity remains unresolved. In an attempt to resolve this problem, we exposed ten young adult males on twelve occasions to filtered air, or to one of three ozone concentrations (0.20, 0.30, and 0.40 ppm) at two exercise intensities for varied periods (30-100 min). Statistical analyses revealed that pulmonary function impairment and altered exercise ventilatory pattern (i.e., shallow, rapid breathing), was more closely related to ozone effective dose than ozone concentration alone. However, ozone concentration was found to contribute more to the prediction than either exposure time or minute ventilation volumes. It was shown that the best fit of predicted pulmonary function impairment was a function described by an exponential expression of ozone concentration and the product of minute ventilation volume and exposure time.

2. Effects of Exercise Continuity on Acute Ozone Toxicity. To compare the effect of continuous exercise to that of intermittent exercise, six aerobically trained adult male subjects were exposed to 0.40 ppm ozone during four bouts of exercise that were either 1 hour continuous exercise, or two hours

intermittent exercise, but matched for total ventilation volume and ozone effective dose. Statistical analysis revealed no significant differences in pulmonary function impairment between the 1 hour continuous and 2 hours intermittent exercise protocols. However, alterations in exercise ventilatory pattern and subjective symptoms were somewhat more pronounced during the 1 hour continuous exercise protocols at both levels of total ventilation, although without assessment of filtered air control exposures, these enhanced responses with continuous exercise could not be definitively attributed to differences between the two exercise modes.

3. Effects of Inspiratory Route on Physiologic Responses to Ozone. To compare the effects of our obligatory oral inhalation method to the ad-lib breathing permitted in chamber exposures, we studied the pulmonary function and subjective symptom responses of six aerobically trained subjects exposed to 0.40 ppm ozone on five occasions. Each exercised continuously at one of two work loads, but with the minute ventilation, exposure time product similar for all protocols. Four exposures were randomly delivered with a Hans-Rudolph respiratory valve attached to a silicone facemask, with inspiratory route effected with and without a noseclip. Statistical analysis revealed no significant differences across conditions in pulmonary function or subjective symptoms. The fifth exposure, delivered via the same respiratory valve, but without the facemask, revealed significantly greater pulmonary function decrements than that observed for the respiratory valve, facemask with noseclip exposure. The latter suggests partial ozone reactivity to the facemask and clean shaven facial surface of the subjects.

4. Comparison of Aerobically Trained and Nontrained Young Adult Females' Physiologic Responses to Ozone. To determine the effects of aerobic training on the physiologic response of young adult females upon exposure to ozone, 40 subjects completed 1 hour continuous exercise exposures. Work intensities - light, moderate and heavy - while exposed to filtered air, or to 0.20, 0.30, and 0.40 ppm ozone, were used. Both the aerobically trained and nontrained groups demonstrated significant pulmonary function impairment and a greater number of reported subjective symptoms in the ozone exposures compared to filtered air, but there were no statistically significant differences between the groups' responses. The equivalent minute ventilation volume imposed on both groups was elicited at absolute work loads approximately 10% less for the trained group. Thus, were the nontrained subjects to jog or ride a bicycle at the same submaximal speed as their trained counterparts in the prevailing photochemical smog condition, they would incur a greater minute ventilation and hence, a greater ozone effective dose and acute toxicity response. Both groups of females incurred greater pulmonary function impairment at the ozone effective dose imposed than that observed in earlier studies for young adult males.

5. Comparison of Aerobically Trained and Nontrained Middle-Aged Males' Physiologic Responses to Ozone. The purpose of this investigation was to determine if pulmonary function impairment and alterations in exercise ventilatory pattern consequent to 1 hour of continuous exercise while exposed to ozone were different in a group of aerobically trained middle-aged males, as compared to their nontrained counterparts. Comparisons were made at two exercise intensities necessitating equivalent minute ventilation volumes while exposed to filtered air and to 0.30 and 0.40 ppm ozone. Both groups demonstrated a trend

toward pulmonary function impairment and altered exercise ventilatory pattern when exposed to ozone, but only a few differences were significantly different from filtered air control. Further, their pulmonary function impairment was actually somewhat less - though not statistically significant from that incurred by young adult males at similar ozone effective doses. There were no significant differences between the responses to ozone inhalation of the trained and nontrained groups, although if the latter had attempted to walk, jog, or bicycle at the same speed, their minute ventilation (and thus the ozone effective dose) would have been about 30 percent greater.

6. Endurance Performance and Ozone Toxicity Responses of Competitive Athletes During Low Level Exposures. Ten highly trained endurance athletes were studied to determine the effects of exposure to low ozone concentrations on pulmonary function and simulated competitive endurance performance. Each subject was randomly exposed to filtered air, and to 0.12, 0.18, and 0.24 ppm ozone while performing a 1 hour competitive simulation protocol on a bicycle ergometer. Endurance performance was evaluated by the number of subjects unable to complete rides and associated decreases in ride times. Statistically significant decreases in pulmonary function and competitive simulation ride time were observed following the 0.18 and 0.24 ppm ozone exposures. All subjects completed the filtered air exposure competitive simulation ride, whereas one, five, and seven subjects did not complete the 0.12, 0.18, and 0.24 ppm ozone exposures, respectively. No significant ozone effect was observed on exercise respiratory metabolism or ventilatory pattern. The number of subjective symptoms reported increased significantly following the 0.18 and 0.24 ppm ozone protocols. These data indicate that endurance performance decrements following low level ozone exposure are the result of physiologically induced breathing discomfort.

7. Combined Effects of Ozone and Ambient Heat on Exercising Females. To study the possible interaction of ozone and ambient heat, which often occur in concert during summer photochemical smog episodes, we exposed ten aerobically trained young adult females for 1 hour to filtered air and to 0.15 and 0.30 ppm ozone, in both moderate (24°C) and hot (35°C) conditions, while exercising continuously at a heavy work load. Exposure to 0.30 ppm ozone induced significant pulmonary function impairment and altered exercise ventilatory pattern, while exposure to 0.15 ppm ozone produced a trend toward pulmonary function decrement. Significant interactions of ozone and ambient heat were obtained for exercise ventilatory patterns, while pulmonary function impairment displayed a trend toward an ozone/temperature interaction. Subjective discomfort increased with both ozone and heat exposure, such that three subjects ceased exercise prematurely when ozone and ambient heat were combined. These results indicate that accentuation of subjective limitations and certain physiological alterations by ambient heat coinciding with photochemical oxidant episodes, impairs exercise performance.

8. Physiological Effects of Nitrogen Dioxide and Nitrogen Dioxide Plus Ozone Consequent to Heavy, Sustained Exercise. The purpose of this study was two-fold: (1) To determine the effects of exposure to 0.60 ppm nitrogen dioxide on pulmonary function consequent to heavy, sustained exercise; and (2) to determine the combined effects of exposure to 0.30 ppm ozone and 0.60 ppm nitrogen dioxide on pulmonary function under the same exercise conditions. Ten

aerobically trained young adult males will be exposed for 1 hour to filtered air, 0.60 ppm nitrogen dioxide, 0.30 ppm ozone, and to 0.60 ppm nitrogen dioxide plus 0.30 ppm ozone. Preliminary analysis of the complete data set available on five subjects indicates no appreciable difference in pulmonary function, exercise ventilatory pattern or subjective symptom responses between the filtered air and 0.60 ppm nitrogen dioxide exposures. The responses to the 0.30 ppm ozone exposure were substantially different from those observed for the filtered air and nitrogen dioxide exposures, but essentially the same as those for the 0.30 ppm ozone and 0.60 ppm nitrogen dioxide in combination exposure.

CONCLUSIONS

From the results of the above studies we have drawn the following conclusions:

1. In predicting the acute toxic effects of ozone inhalation upon exposure to substantially different concentrations, greater weighting must be given the ozone concentration than either exposure time or minute ventilation volume.

2. There is no statistically significant difference in pulmonary function impairment when employing 1 hour continuous exercise and 2 hours intermittent exercise in ozone exposures at the same total ventilation volume and effective dose.

3. Exposure via obligatory mouthpiece inhalation to 0.40 ppm ozone during moderate and heavy exercise does not result in significantly different pulmonary function or subjective symptom responses than those observed in ad-lib (mouth and/or nose) breathing exposures.

4. Nontrained young adult females do not evidence any substantial difference in their response to ozone inhalation at the same ventilation volume and effective dose when compared to aerobically trained females.

5. Young adult females evidence greater physiologic response to ozone at the same effective dose than do their male counterparts. This difference appears to be primarily associated with the mean lung size difference between the sexes, which is approximately 1 and 1/2 times larger for the male.

6. Middle-aged males, whether aerobically trained or nontrained, incur approximately the same toxic response to ozone, as do their young adult male counterparts. The possibility remains, however, that more elderly subjects are more sensitive to ozone inhalation at the same effective dose.

7. Because of the extremely high ventilation rates incurred in competitive simulation protocols, endurance athletes exposed to ozone for 1 hour at concentrations of 0.18 ppm, experience pulmonary function impairment and performance decrements induced primarily by breathing discomfort.

8. Since ozone toxicity is a function of the total effective dose, those athletes engaged in competition not necessitating high ventilation volumes, will not in general, be adversely affected.

9. Trained young adult females experience impaired work performance due to accentuation of subjective symptoms and certain physiological alterations occurring when ambient heat and ozone exposure coincide, although the mechanisms remain unclear.

10. Exposure for 1 hour to high ambient levels of nitrogen dioxide while engaged in heavy continuous exercise does not induce physiologic responses comparable to those incurred in exposure to photochemical smog alert levels of ozone.

RECOMMENDATIONS

1. Further investigations of subjects exercising continuously at intensities characteristic of increasingly popular aerobic training programs should be conducted at ozone concentrations characteristic of those approaching and including the first stage smog alert level.

2. Since subjective symptoms and alterations in exercise breathing pattern affect one's desire and ability to work and appear to precede other responses to ozone inhalation, studies should be conducted in which these parameters are carefully monitored at ozone concentrations and effective doses that fail to elicit statistically significant pulmonary function impairment.

3. A systematic study of the apparent greater sensitivity to ozone evidenced by the young adult female compared to her male counterparts should be effected. Comparative exposures should be at the same ozone concentration at both the same absolute effective dose and also at a lower effective dose for the female in proportion to her reduced lung size compared to the male's.

4. More apparently healthy elderly individuals should be studied to ascertain if they represent a particularly sensitive sub-population to the acute effects of ozone inhalation. Prolonged (in excess of 1 hour), low intensity exercise, simulating the activity entailed in walking or playing 18 holes of golf, should be utilized.

5. The role of very high ventilation rates incurred by elite endurance athletes, such as marathon runners and race walkers, should be studied in combination with ozone exposures at concentrations at or below the current Federal Air Quality Standard (i.e., $\leq$0.12 ppm).

6. Additional study of the causes of premature cessation of work performance in exercising females when exposed to ozone and ambient heat, not seen in filtered air exposures to ambient heat alone or in exposures to ozone alone, is warranted.

7. Study of the time decay of the initial ozone exposure hypersensitivity effect upon the physiologic effects incurred on reexposure to ozone within 1 to 5 days, should be undertaken. This has implications for those setting health effects standards, as well as those who conduct laboratory studies in which there are advantages to repeatedly exposing subjects.