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FINAL REPORT

OZONE TOXICITY EFFECTS CONSEQUENT TO PROLONGED, HIGH INTENSITY EXERCISE IN TRAINED ENDURANCE ATHLETES

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ABSTRACT

The purpose of the present investigation was: (1) to investigate the effects of ozone (O_3) exposure combined with high ventilation volumes incurred during training and competitive simulation protocols; and (2) to study selected ventilatory and respiratory metabolism parameters and subjective symptomatology which could suggest mechanisms involved in previously observed decrements in maximal aerobic performance following O_3 exposure. Ten well trained distance runners, age 21-31 years, with normal pulmonary function, served as subjects. Each subject was exposed on six occasions for 1 h to either filtered air or to O_3 concentrations of 0.20 or 0.35 parts per million (ppm), while riding on a bicycle ergometer at workloads simulating either, a 1 h steady-state training bout, or a 30 min warm-up followed immediately by a 30 min competitive bout. Workloads were set such that the mean ventilation ($\dot{V}_E$) for 1 h was approximately 80 $\ell \cdot min^{-1}$. Standard pulmonary function (PF) tests and periodic observations of exercise respiratory metabolism, heart rate (HR), and $\dot{V}_E$ were obtained. Following each protocol subjects completed a subjective symptoms form. Statistical analyses revealed no significant difference between the training and competitive simulations on PF, but a significant effect across O_3 concentration for FVC, $FEV_{1.0}$ and FEF_{25-75} for all comparisons between FA, 0.20 ppm O_3 and 0.35 ppm O_3, was observed. Significant effects across O_3 concentration for the training protocols for all comparisons of respiratory frequency (F_R) and comparisons between FA and 0.35 and 0.20 and 0.35 ppm O_3 for tidal volume (V_T), were observed. No significant O_3 effect was observed for exercise $\dot{V}o_2$, HR, $\dot{V}_E$, or $\dot{V}_A$ responses, suggesting no alteration in pulmonary gas exchange or O_2 transport or delivery. Subjective symptoms increased as a function of O_3 concentration, and following the competitive protocols, four subjects consequent to the 0.20 ppm O_3 and nine at the 0.35 ppm O_3 exposures, respectively, indicated that they could not have performed maximally. Three subjects were unable to complete both the training and competitive simulation rides at 0.35 ppm O_3, while a fourth failed to complete the competitive ride, only at this concentration. These observations indicate that high mean $\dot{V}_E$ ($\sim$80 $\ell \cdot min^{-1}$) incurred during training and competition simulation resulted in an increased susceptability of endurance athletes to the toxic effects of O_3 exposure. Further, these findings suggest that the O_3 concentrations utilized did not result in any decrement in pulmonary gas exchange and/or oxygen delivery, and that observed performance decrements were the result of physiologically induced subjective limitations of respiratory discomfort.

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Disclaimer

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SUMMARY AND CONCLUSIONS

While training and competing, aerobic endurance athletes routinely engage in prolonged exercise which elicits high mean ventilation rates for periods of an hour or more. Consistent with the effective dose concept, it would be expected that such exercise would result in an increased susceptibility to the toxic effects of ozone exposure. Previous studies have suggested that exposure to ozone at concentrations routinely observed in polluted urban environments results in decreased maximal aerobic performance. The purpose of the present investigation was: (1) to investigate the effects of ozone exposure combined with high ventilation volumes incurred during trainng and competitive simulation protocols; and (2) to study selected ventilatory and respiratory metabolism parameters and subjective symptomatology which could suggest mechanisms involved in previously observed decrements in maximal aerobic performance following ozone exposure. Ten well trained distance runners, age 21-31 years, with normal pulmonary function, served as subjects. Each subject was exposed on six occasions for one hour to either filtered air or to ozone concentrations of 0.20 or 0.35 parts per million, while riding on a bicycle ergometer at workloads simulating either a one-hour steady-state training bout, or a 30 minute warm-up followed immediately by a 30 minute competitive bout. Workloads were set such that the mean ventilation for one hour was approximately 80 $\ell \cdot min^{-1}$. Standard pulmonary function tests and periodic observations of exercise respiratory metabolism, heart rate, and ventilation were obtained. Following each protocol subjects completed a subjective symptoms form. Statistical analyses revealed no significant difference between the training and competitive simulations on pulmonary function, but a significant effect across ozone concentration for FVC, $FEV_{1.0}$, and FEF_{25-75} for all comparisons between filtered air, 0.20 ppm and 0.35 ppm ozone, was observed. Significant effects across ozone concentration for the training protocols for all comparisons of respiratory frequency and comparisons between filtered air and 0.35 ppm and 0.20 and 0.35 ppm ozone for tidal volume were observed. No significant ozone effect was observed for exercise oxygen uptake, heart rate, expired ventilation or alveolar ventilation responses, suggesting no alteration in pulmonary gas exchange or oxygen transport and delivery. Subjective symptoms increased as a function of ozone concentration, and following the competitive protocols, four subjects consequent to the 0.20 ppm ozone and nine at the 0.35 ppm ozone exposures, respectively, indicated that they could not have performed maximally. Three

subjects were unable to complete both the training and competitive simulation rides at 0.35 ppm ozone, while a fourth failed to complete the competitive ride, only, at this concentration. It was concluded that: (1) high mean ventilation rates incurred during training and competition appear to result in an increased susceptibility of endurance athletes to the toxic effects of ozone exposure, in that the athletes demonstrated pulmonary function impairment and altered exercise ventilatory pattern at 0.20 ppm, a level not previously found to induce effects in nonathletes working at the same relative intensity; (2) the ozone concentrations utilized did not result in any decrement in pulmonary gas exchange and/or oxygen delivery, and that observed performance decrements were the result of physiologically induced subjective limitations of respiratory discomfort; (3) the role of increased airway resistance in affecting pulmonary function measurements appeared to be diminished, possibly as a result of the high workloads utilized in this investigation; and (4) as endurance athletes of international caliber would be capable of sustaining ventilation volumes approximately 20 percent higher than our subjects, significant ozone toxicity might well be anticipated at concentrations less than 0.20 ppm in this subpopulation.

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 first and second stage smog alert levels.
2. The ozone effective dose, as well as ozone concentration alone, should be utilized to identify the acute toxicity threshold and to quantify the degree of impairment at higher levels.
3. Further investigations of highly trained endurance athletes exposed to ozone at concentrations of 0.20 ppm or lower should be conducted to examine further the apparent enhanced ozone sensitivity of this sub-population.
4. Further investigations should be conducted to determine whether preexposure to ozone results in acute physiological decrement which would result in a decreased maximal aerobic capacity.
5. Investigations should be undertaken to determine whether the performance decrements observed in the present experiment can be reduced, as is pulmonary function impairment following several repeated daily exposures to ozone.
6. Investigations should be undertaken to determine if subjects with normal resting pulmonary function but with history of asthma, are more susceptible to the acute toxic effects of ozone.
7. Investigations should be undertaken to determine experimentally what role a reduction in FVC, as a result of a decrease in inspiratory capacity, has on $FEV_{1.0}$ and FEF_{25-75} at rest and after exercise.

BODY OF REPORT

INTRODUCTION

General Overview of Ozone Toxicity Effects. Ozone (O_3), an ubiquitous constituent of the upper atmosphere and toxic contaminant predominant in the photochemical smog of numerous metropolitan areas, is among the most potent oxidizing agents in the atmosphere (Jaffe, 1968; Stokinger & Coffin, 1968). O_3 has potent zootoxic properties, reacting readily with various cellular constituents, i.e., coenzymes, amino acids, lipids, and SH ligands, and can potentially disrupt biochemical and physiological function at tissue sites where the greatest amount of O_3 absorption occurs in ambient or experimental exposures (Menzel, 1970; Stokinger & Coffin, 1968).

As with other pollutants, experimental exposures of animals to levels of O_3 above those maximally seen in ambient air have provided considerable qualitative information concerning the pathophysiological changes accompanying acute and chronic inhalation of the gas (Committee on Medical Biological Effects of Environmental Pollutants, 1977; DeLucia, et al, 1975; Fairchild, 1963). Ordinarily, however, especially where oxidant concentrations near ambient alert levels have been administered, the effects of O_3 intoxication have been attributed to direct oxidative lesions localized in the respiratory tract and blood (Jaffe, 1968; Stokinger & Coffin, 1968).

Acute Toxic Effects of Ozone Inhalation in Humans. Ozone was originally of interest to human physiologists because of its actions as a radiomimetic gas and presence in the improperly filtered cabins of high flying aircraft (Bennett, 1962; Clamann & Bancroft, 1959). Subsequently, and in part because humans are subject to occasional acute peak levels due to the cyclic nature of O_3's genesis (both seasonal and diurnal), laboratory studies have focused on short-term effects of O_3 exposures. As noted in Table 1, interest first centered on toxic reactions of humans at rest while exposed to O_3 levels rarely, if ever, encountered in the ambient environment (Goldsmith & Nadel, 1969; Young et al, 1964). In the latter investigation, a 2-h resting exposure to 0.60 and 0.80 ppm O_3 by mouthpiece resulted in decreases in lung diffusing capacity to CO (DL_{CO}), forced expiratory volume, 1 sec., ($FEV_{1.0}$) and vital capacity (VC). These objective alterations were in some cases accompanied by complaints of substernal soreness, tracheal irritation and/or cough. The authors suggested that DL_{CO} was altered by alveolar thickening due to edema, while VC was diminished as a result of a sub-

TABLE 1. Summary of Major Findings of Acute O_3 Toxicity Studies

AUTHORS	EXPOSURE DURATION	CONCENTRATION (ppm)	REST OR EXERCISE*	MAJOR FINDINGS
Young et al (1964)	2 hrs	0.6-0.8	R	Decreased VC, $FEV_{0.75}$, and DL_{CO}
Goldsmith (1969)	1 hr	0.1, 0.4, 0.6, 1.0	R	Increased airway resistance with 1.0 ppm
Bates et al (1972)	2 hrs	0.75	R and E	Exercise potentiated O_3 effect in producing PF changes and subjective symptoms
Hazucha et al (1973)	2 hrs	0.37, 0.75	IE	RV increased, indicating early small airway effect
Buckley et al (1975)	2.75 hrs	0.5	IE	Blood biochemical changes with exposure and mild exercise
Folinsbee et al (1975)	2 hrs	0.37, 0.50, 0.75	R and IE	Increased f_R during exercise after O_3 exposure, with dose response
Hackney et al (1975)	2-4 hrs	0.25, 0.37, 0.50	IE	Certain individuals may be O_3 "reactors," i.e., more sensitive than others
Silverman et al (1976)	2 hrs	0.37, 0.5, 0.75	R and IE	PE impairment more closely related to O_3 effective dose (product of O_3 concentration, $\dot{V}_E$, and exposure time) than concentration, alone
DeLucia & Adams (1977)	1 hr	0.15, 0.30	R and CE	Demonstrated a dose response to both the level of O_3 and the level of exercise in PF and exercise ventilatory pattern. No blood biochemical changes
Folinsbee et al (1978)	2 hrs	0.1, 0.3, 0.5	R and IE	Using heavy workloads, confirmed observations of Silverman et al, re O_3 effective dose
Savin & Adams (1979)	31 min	0.15, 0.3	CE	Observed no PF impairment or reduced performance in brief maximum graded exercise test
Adams et al (1981)	30-80 min	0.2, 0.3, 0.4	CE	Using CE, mouthpiece exposures, observed similar PF impairment as a function of O_3 effective dose as Folinsbee et al (1978)

*R indicates rest; IE indicates intermittent exercise; CE indicates continuous exercise. See Appendix for identification of other abbreviations.

jective limitation to maximal inspiration, and $FEV_{1.0}$ was decreased due to possible airway narrowing.

Bates and colleagues (1972) found an increase in pulmonary resistance, decreases in maximum static recoil pressure and flow rate to 50 percent VC, and a trend of decrease for DL_{CO} when 10 subjects were exposed to 0.75 ppm O_3 in a chamber for two hours. Subsequently, other investigators have demonstrated impaired pulmonary function (PF) at O_3 concentrations in excess of 0.50 ppm (Folinsbee et al, 1975; Folinsbee et al, 1978a; Hackney et al, 1975; Silverman et al, 1976).

The Role of Exercise in Enhancing Acute Ozone Toxicity. The potentiating effects of exercise on acute O_3 toxicity, originally noted with rats by Stokinger et al (1956), was first observed in humans at 0.75 ppm by Bates and colleagues (1972). Subsequently, others (Folinsbee et al, 1975; Hazucha et al, 1973; Silverman et al, 1976) have observed greater O_3 toxicity effects consequent to 2-h exposures at 0.75 ppm with alternate periods of 15 min light exercise ($\dot{V}_E$ increased 2-1/2 times rest) and rest, i.e., with intermittent exercise (IE). Further, in similar 2-h IE exposures, pulmonary function (PF) decrements were also observed at 0.37 ppm, a level that caused no effect in resting exposures (Hackney et al, 1975; Hazucha et al, 1973; Silverman et al, 1976). More recently, DeLucia and Adams (1977) observed PF decrements and exercise ventilatory pattern alterations during continuous, heavy exercise ($\dot{V}_E$ increased 6 times rest) for 1-h while exposed to 0.30 ppm O_3 and at 0.15 ppm in two particularly sensitive subjects. The latter concluded that exercise can increase O_3 toxicity for a given concentration, exposure time product by: 1) reducing the role of the upper respiratory tract in absorbing O_3 due to increased ventilatory flow rates primarily via the oral inspiratory route, 2) increasing the uniformity of ventilation throughout the lungs, and 3) replacing reacted O_3 at a faster rate.

DeLucia and Adams' observations are also of significance with respect to the existence of toxicity effects consequent to rather brief exposure at O_3 levels more routinely observed. For example, while peak 1 h concentrations exceeding 0.50 ppm have been recorded at certain locations in the Los Angeles Basin (Hackney et al, 1975; Mosher et al, 1970), the average daily maximum 1 h concentration during September ranges from 0.26 ppm in inland areas to less than 0.10 ppm at monitoring stations adjacent to the Pacific Ocean (Air Quality and Meteorology, 1979). Further, while light IE exposures employed heretofore by others

may appropriately simulate the enhanced metabolic $\dot{V}_E$ component of the O_3 toxicity effect consequent to a regular day's activity pattern for an average urban citizen who engages in periods of walking interspersed with rest, many occupational or recreational pursuits entail sustained periods of moderate to heavy metabolic demand. This substantially increases $\dot{V}_E$ and the total amount of O_3 inhaled in a given time at a particular ambient concentration.

Folinsbee et al (1975) were the first to examine systematically the effects of O_3 inhalation on exercise ventilatory pattern and respiratory metabolism parameters during submaximal IE exposures. The major response was an increased F_R consequent to O_3 exposure, which was accompanied by a near concomitant decreased V_T, as $\dot{V}_E$ remained essentially constant. Neither HR or $\dot{V}o_2$ were altered systematically by O_3 exposure. Subsequently, DeLucia and Adams (1977) also observed no significant alteration with O_3 inhalation in HR, $\dot{V}o_2$, or $\dot{V}_E$ in subjects exercising continuously (CE) at workloads up to 65% $\dot{V}o_2$ max for 60 min. Further, increased F_R and decreased V_T at the 65% $\dot{V}o_2$ max workload were noted, but were not statistically significant until 60 min, and then only at the 0.30 ppm exposure. More recent studies, utilizing CE (Adams et al, 1981) and IE ranging from light to heavy (Folinsbee et al, 1978a), have demonstrated altered exercise ventilatory pattern ($\uparrow F_R$, $\downarrow V_T$) when subjects were exposed to 0.30 ppm O_3, or higher. Again, exercise $\dot{V}_E$, HR and $\dot{V}o_2$ were not significantly altered from FA control in these exposures. These observations suggest that the shallower breathing pattern effected by O_3 exposure during exercise is associated with a reduced inspiratory reserve (as indicated by much greater reduction in FVC than increase in RV). The greater deadspace volume (V_D) does not appear to adversely affect O_2 exchange, as $\dot{V}o_2$ remains constant, as does HR, throughout work intensities ranging from light (15-20% of $\dot{V}o_2$ max) to moderately heavy (65%).

The Effective Dose Concept. Hackney et al, (1975) were apparently the first to advance a dose-response relationship with respect to an enhanced PF decrement as a function of O_3 concentration. Silverman et al (1976) emphasized that PF impairment was more closely related (as a second order polynomial function) to the effective dose of O_3, as calculated from the product of concentration, exposure time and $\dot{V}_E$. However, their observations were limited to light IE protocols of 1 or 2 h duration at O_3 concentrations of 0.37, 0.50, and 0.75 ppm. Subsequently, Folinsbee et al (1978a) extended the effective dose concept in evaluating both rest and IE protocols of 2 h duration in filtered air (FA) and

at three levels of O_3 concentration (0.10, 0.30 and 0.50 ppm). Further, their exercise workloads varied in intensity, entailing approximately 3, 5 and 7 times resting $\dot{V}_E$. Again, PF declined as a second order polynomial function of the effective dose of O_3. More recently, we (Adams et al, 1981) have observed similar PF impairment as a function of O_3 effective dose in young adult male subjects exercising continuously for 30-80 min in FA and at 0.2, 0.3 and 0.4 ppm O_3.

An important recurring question is the validity of comparison of O_3 toxicity consequent to chamber exposures at rest or with light IE to the CE mode with obligatory oral inhalation method employed in our laboratory. Recently we (Adams et al, 1981) observed that the percent $FEV_{1.0}$ decrement as a function of O_3 effective dose, at least within the range of 0 to 1,200 ppm·ℓ, identifies the degree of O_3 toxicity as approximately equal for our CE exposures to that observed in IE exposures by others. It was also suggested that the spontaneous shift from nasal breathing at rest, in light IE and recovery, to primarily oral breathing at heavier workloads noted by Folinsbee et al (1978a), does not substantially affect O_3 toxicity in humans within $\dot{V}_E$ ranging from 10 to 70 $\ell \cdot min^{-1}$. Previous work with anaesthesized dogs (Yokoyama & Frank, 1972) indicates that O_3 uptake is higher when administered orally than nasally, especially at flow rates typical of resting $\dot{V}_E$ (i.e., the nasal passages are less effective O_3 "scrubbers" at higher flow rates typical of exercise). Hence, it would appear that the mouthpiece obligatory oral inhalation method used in combination with the CE mode can be used interchangeably with the IE chamber method in the study of O_3 toxicity, although definitive comparison using the same subjects exposed in the same laboratory remains to be done.

Folinsbee et al (1975) were the first to demonstrate that exercise ventilatory pattern responses consequent to light IE O_3 exposures were closely related to the effective dose of O_3 inspired. Subsequently, utilizing both resting, as well as heavier exercise protocols, they again observed an increased F_R and decreased V_T with increasing O_3 effective dose (Folinsbee et al, 1978a). More recently, we (Adams et al, 1981) have observed similar alterations in exercise ventilatory pattern in subjects negotiating 30-80 min CE protocols, which again, were more closely related to O_3 effective dose than to O_3 concentration, alone.

<u>Minimum Ozone Concentration Levels for Detection of Acute Toxicity Effects in Active Man</u>. Although, the O_3 effective dose (as enhanced by exercise $\dot{V}_E$

for a given O_3 concentration - time product) predicts more accurately the degree of PF impairment than does O_3 concentration alone, the latter has consistently been shown by multiple regression analysis to be preeminent amongst the three effective dose components (Adams et al, 1981; Folinsbee et al, 1978a; Silverman et al, 1976). That is, as first noted by Silverman et al (1976), for any given effective dose, exposure to a high concentration for a short period has more effect than longer exposure at a lower concentration. This would imply that there is not only a threshold O_3 effective dose (as denoted by the consistently observed second order polynomial relationship to PF impairment), but that there is also a minimum O_3 concentration at which PF impairment will be effected for a given exposure time and activity level.

The latter is of significance since photochemical air pollution occurs widely, because O_3 concentration has been correlated with hospital admissions for respiratory disease (Paproski & Walker, 1974), and because those who pursue rather routine occupational and recreational physical activity patterns reach O_3 effective dose levels effecting acute toxicity response within 1-h when exposed to O_3 concentrations within the first stage alert range (0.20 - 0.35 ppm). For these and similar reasons, governmental agencies have attempted to set appropriate standards of air quality, but unfortunately, there are only limited data relating to a given O_3 concentration for short-term exposures to PF decrement during exercise when the total amount of O_3 inhaled in a given time is dependent both on the ambient concentration and the increased ventilation characteristic of enhanced metabolic demand. Recently, however, important advances have been made, in that Folinsbee et al (1978a) observed that the O_3 concentration at which no PF impairment occurred, varied according to the level of activity. That is, in 2-h exposures when subjects remained at rest, a PF impairment effect occurred only at 0.50 ppm. At the highest IE workload ($\dot{V}_E$ = 70 $\ell \cdot min^{-1}$) no PF effect was observed at 0.10 ppm, while at 0.30 ppm, a moderate IE workload ($\dot{V}_E$ = 50 $\ell \cdot min^{-1}$) elicited an effect. Working independently on a similar attempt to identify a threshold O_3 concentration using a CE mode (Adams et al, 1981), we observed that there was no significant PF decrement consequent to 60 min exposure at 0.20 ppm O_3 when exercise $\dot{V}_E$ was maintained at 63 $\ell \cdot min^{-1}$. On the other hand, after 60 min exercise at the same workload while exposed to 0.30 ppm, there was significant impairment in several PF parameters. Hence, it would appear that the threshold O_3 concentration for subjects exercising at moderate intensity during short-term exposures (<2-h), lies between 0.20 and 0.30

ppm, although DeLucia & Adams (1977) observed PF impairment in two particularly sensitive subjects exposed to 0.15 ppm while exercising continuously for 1-h at a mean $\dot{V}_E$ of 65 $\ell \cdot min^{-1}$.

Effect of Ozone Inhalation on Endurance Performance. Even before laboratory data relating the additional adverse effect of elevated $\dot{V}_E$ during exercise were available, O_3 was implicated as a detriment to maximal endurance performance by Wayne et al (1967). These investigators found that the level of oxidant present 1 h before a cross country race correlated closely with diminished performance. Carbon monoxide (CO) level, temperature, and humidity showed no correlation to performance. The authors suggested that maximal exertion could have been limited by some physiological effect of the pollutant, or perhaps by the increased discomfort of performance in the polluted environment. Subsequently, Drinkwater et al (1974) and Raven et al (1974) found no decrement in maximum oxygen uptake ($\dot{V}o_2max$) when giving peroxyacetyl nitrate (PAN) and CO, singly or in combination. Other photochemical air pollutants, including nitrogen dioxide (NO_2) and sulfur dioxide (SO_2) have also been studied during exposures to occasionally observed ambient levels, singly and in combination with O_3. The addition of 0.30 ppm NO_2 did not produce any additional effect on PF response to that noted in either 2 or 4-h exposures to O_3, alone (Hackney et al, 1975). Further, even when one hour of moderate exercise ($\dot{V}_E$ = 33 $\ell \cdot min^{-1}$) was included in a 2-h exposure to 0.62 ppm NO_2, no significant PF impairment was observed (Folinsbee et al, 1978b). Hazucha & Bates (1975) observed no effect of 0.37 ppm SO_2 on PF consequent to 2-h IE exposures, but the addition of 0.37 ppm SO_2 to 0.37 ppm O_3 considerably accentuated the PF effect observed during O_3, alone, exposures. However, this observation has not been verified in subsequent studies (Bedi et al, 1979; Bell et al, 1977), and it appears likely that this presumed synergism was confounded by the lack of control of particulate levels and of relative humidity and temperature (Bedi et al, 1979). Thus, while further study is needed relative to the possible potentiation of other air pollutant consitutents in combination with O_3 at concentrations typical of smog alert levels, it seems evident that it is O_3, particularly at observed ambient smog alert concentrations, which has the principal physiological effect and thus, alters submaximal and maximal exercise response.

Maximal oxygen uptake ($\dot{V}o_2max$), the physiological noninvasive parameter most closely related to maximum endurance performance, was shown by Folinsbee and associates (1977) to decrease significantly (10%) after a 2-h light IE exposure

to 0.75 ppm O_3. It is uncertain whether the $\dot{V}o_2max$ decrement was actually due to reduced O_2 pick-up, transport or delivery capacity, as it was accompanied by decreases in maximum attained workload, maximum $\dot{V}_E$, V_T, and HR_{max}. The authors concluded that the reduced $\dot{V}o_2max$ was a consequence of ventilatory limitation of maximum effort, probably related to respiratory discomfort. Subsequently Horvath et al (1979) contended that it was difficult to determine whether this decrement in work capacity was due to the quantity of O_3 inhaled, or to the time exposed to O_3. These investigators observed significantly reduced PF responses following 2-h resting exposure to both 0.50 and 0.75 ppm O_3, but they found no significant change in maximum exercise performance, $\dot{V}o_2$ max, $\dot{V}_E$ max, and HR max. Hence, at O_3 concentrations in excess of ambient levels normally seen, i.e., >0.50 ppm, increased $\dot{V}_E$ consequent to light IE and thus, the total effective dose of O_3 during exposure to 2-h, plays a significant role in inducing post-exposure maximum exercise decrement.

At O_3 concentrations characteristic of ambient smog alert levels, the effect of O_3 inhalation on exercise performance is less definitive. Man In t Veld and Zeedijk (1972) found no effect on cardiorespiratory response and PF of athletes during 20 min of progressive bicycle exercise up to a load of 300 W (1836 $kpm \cdot min^{-1}$) while exposed to 0.30 ppm O_3. The importance of exposure time and $\dot{V}_E$, even with O_3 concentration at 0.38 ppm, was demonstrated in a recent study in which no significant decrement in performance, $\dot{V}o_2max$, or PF were observed consequent to a 31 min multistage, progressively graded exercise test to $\dot{V}o_2max$ (Savin & Adams, 1979). As shown in Fig.1, the peak $\dot{V}_E$ exceeded 150 $\ell \cdot min^{-1}$, but the mean $\dot{V}_E$ (64 $\ell \cdot min^{-1}$) was not reached until 20 min of exercise (i.e., 26 min of exposure, as the protocol entailed an initial 6 min resting phase). However, DeLucia and Adams (1977) observed significantly altered exercise ventilatory patterns ($\downarrow V_T$ and $\uparrow F_R$) during 60 min exposure to a lower O_3 concentration (0.30 ppm) during continuous exercise at a steady-state $\dot{V}_E$ of 65 $\ell \cdot min^{-1}$, but not until 45 min. Further, it was also observed that prolonged, moderately heavy exercise may become intolerable, in that it was necessary to reduce the workload approximately 20% during the final 15 min of a 60 min ride at 65% $\dot{V}o_2max$ when two particularly sensitive subjects were exposed to 0.30 ppm O_3 (DeLucia and Adams, 1977).

It seems evident, then, that $\dot{V}o_2max$ and endurance exercise performance are compromised when O_3 concentration and the effective dose are of sufficient magnitude to elicit toxic effects. However, there is some question as to the mecha-

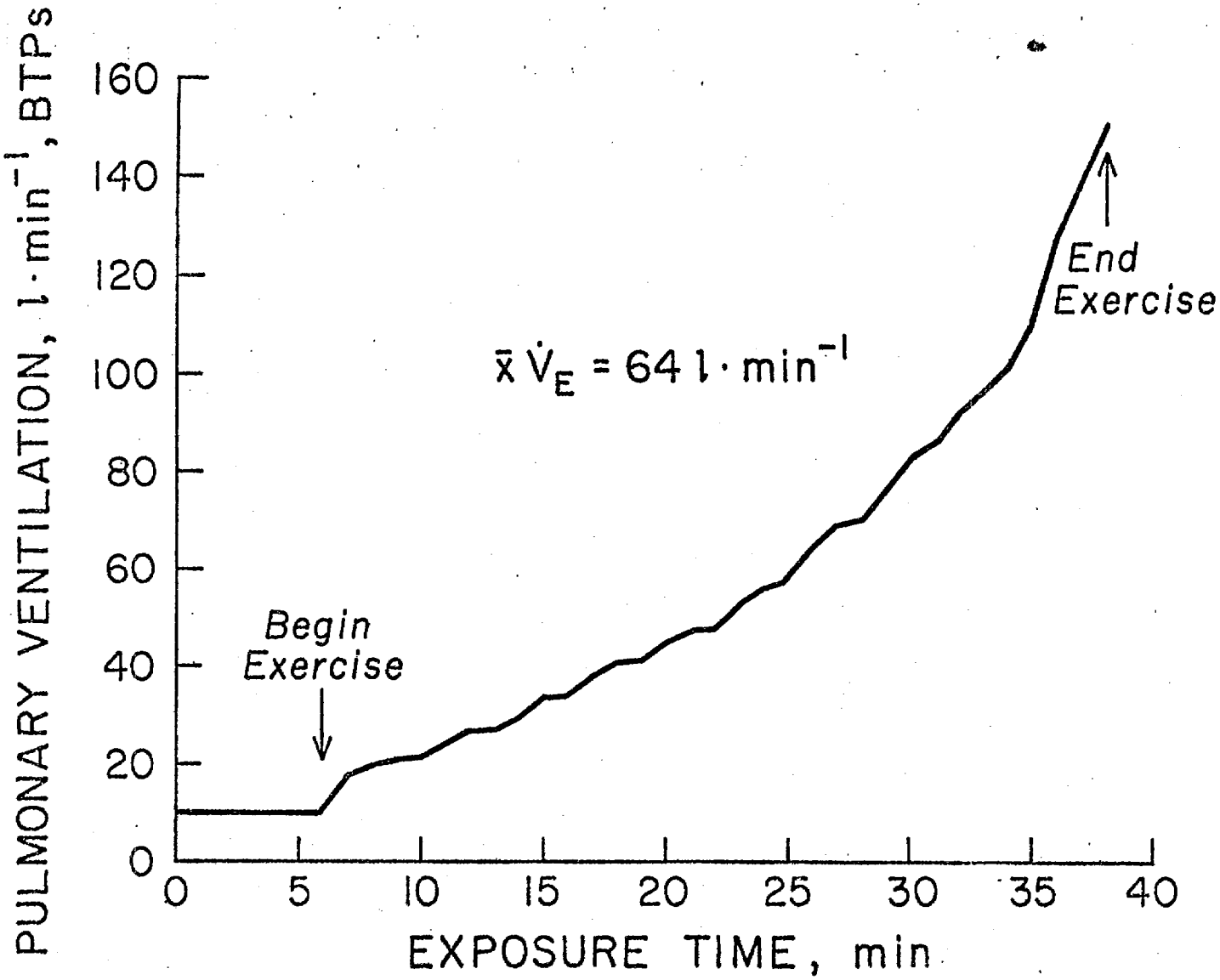

FIG. 1. Group mean $\dot{V}_E$ response to maximum graded exercise.

(Savin and Adams, JAP, 1979)

nism(s) involved. For example, both Wayne et al (1967) and Folinsbee et al (1977) have suggested that respiratory discomfort may cause the decrease in exercise performance. Alternatively, PF and exercise ventilatory pattern changes consequent to significant O_3 inhalation, could effect physiological limitations to endurance exercise performance. For example, increases in RV combined with increased F_R and decreased V_T, would be expected to result in an increased V_D/V_T ratio and a decreased alveolar ventilation ($\dot{V}_A$). Consequently, a reduction in ventilation perfusion ratio ($\dot{V}_A/\dot{Q}$) and arterial saturation with oxygen (SaO_2) would result. These alterations, in turn, would lead to a decreased O_2 delivery to the tissues. Holub et al (1979) observed a 3.7% reduction in SaO_2 in four healthy subjects exposed to 0.4 ppm O_3 combined with IE for 2¼ h. Measurements in one subject indicated altered distribution of inspired gas which would support an increased V_D/V_T ratio. Additionally, increases in internal airway resistance not only increase the energy cost of breathing but may actually limit ventilatory capacity and aerobic work tolerance. Dressendorfer et al (1977) have demonstrated significant reductions in $\dot{V}_E$max, $\dot{V}o_2$max, and maximal work time on a bicycle ergometer as a result of increased external airway resistance. Finally, others have presented evidence suggesting how O_3 could impair oxygen transport via crossing the lung air-blood barrier and interfering with the optimum functioning of the red blood cell (Buckley et al, 1975; Kindya and Chan, 1976; Menzel et al, 1975). However, this evidence is circumstantial, especially at ambient smog alert levels (DeLucia and Adams, 1977).

Statement of the Problem. Endurance athletes are considered by many to evidence the most healthy cardiorespiratory system in the general population. They routinely train at intensities of 70% of $\dot{V}o_2$ max or higher (which necessitate steady-state $\dot{V}_E$ in excess of 75 $\ell \cdot min^{-1}$) for periods of 1 h, or longer. This $\dot{V}_E$ is substantially higher than that utilized in a previous investigation (62 $\ell \cdot min^{-1}$), in which no PF impairment was observed consequent to a 60 min exposure at 0.20 ppm, but for which a tendency to reduced $FEV_{1.0}$ (-4.8%) was noted at 75 min (Adams et al, 1981). The primary purpose of the present investigation was to examine the effect of the high $\dot{V}_E$ characteristic of prolonged aerobic activity in highly trained endurance athletes on acute O_3 toxicity at levels representing the first stage alert range (i.e., 0.20 and 0.35 ppm).

Further, we have observed in pilot work that these athletes experience a similar average $\dot{V}_E$ for 1-h, in which the first 30 min is spent in a typical pre-competition warm-up and the final 30 min at a very high, sustained workload

similar to that experienced in competition. Thus, it was envisioned that this protocol could be used as a comparison to the similar mean $\dot{V}_E$ steady-state training protocol to determine if the competitive simulation $\dot{V}_E$ pattern induced an enhanced acute O_3 toxicity effect. A final purpose of the present study was to determine what effect exposure to O_3 over the first stage alert range had on simulated competitive aerobic endurance performance.

METHODOLOGY

Pilot Work. In order to achieve the objectives of the present study, it was necessary to devise a competitive endurance exercise simulation. Via questioning of competitive runners, a 60 min exposure was formulated, which entailed 30 min of warm-up, followed immediately by 30 min of exercise at a workload approximating competitive effort (i.e., approximately 85% $\dot{V}o_2$ max). Figure 2 depicts this mimicked competitive scenario in terms of $\dot{V}_E$ response from pilot work with three subjects.

Subject Description and Base-line Measurements. Ten Caucasian males, whose basic anthropometry, $\dot{V}o_2$ max, and pulmonary function are given in Table 2, served as subjects (Institutional Human Use Committee approval and signed individual informed consent were obtained). All subjects were, or had recently been engaged in competitive endurance running, and all were actively involved in an aerobic training program at the time of testing. Individual intensity of training was not modified significantly during the course of the experiment. However, since bicycle ergometry was the exercise mode employed, runners were asked to incorporate bicycle ergometry was the exercise mode employed, runners were asked to incorporate several bicycle riding sessions in their normal training program. None of the subjects smoked, and all had pulmonary function within normal limits.

Each subject first completed an orientation to all testing procedures. Base-line pulmonary function and basic anthropometry, including body composition via hydrostatic weighing, were measured during another session. To attenuate habituation effects, and to establish individual steady-state $\dot{V}_E$ response to various workloads, each subject completed a total of 120 min of bicycle ergometer riding in 3 or 4 sessions while breathing FA through the mouthpiece delivery system employed in the experimental protocols.

$\dot{V}o_2$ max was assessed via a progressive increment protocol, utilizing a Monark bicycle ergometer. With pedal frequency maintained at 60 rpm, the initial

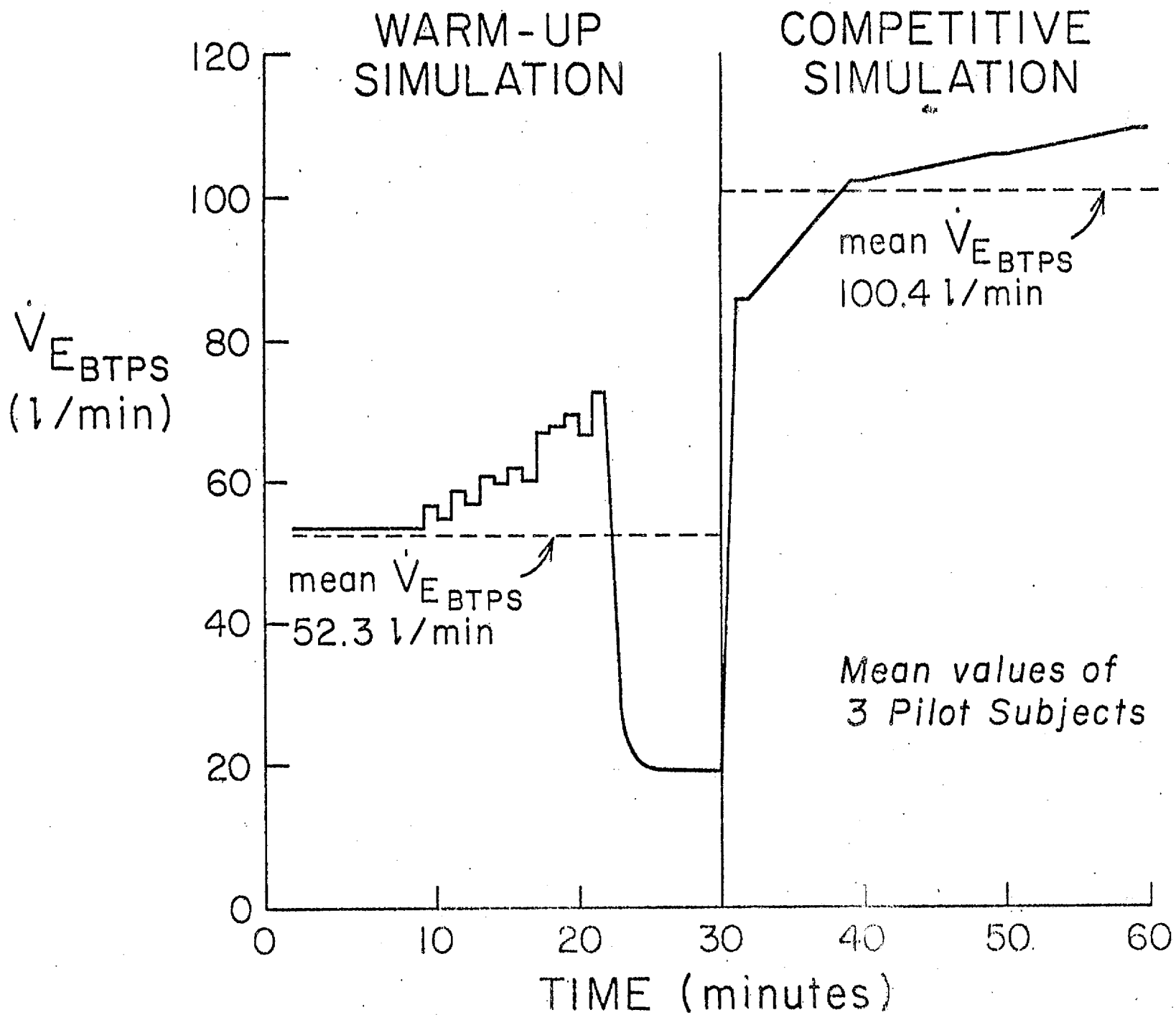

FIG. 2. Description of the Competitive Simulation Exposure in Terms of $\dot{V}_E$ Response.

TABLE 2. Subject's Anthropometry, $\dot{V}o_2$ max, and Pulmonary Function

Subject #	Age, yrs	Ht, cm	Wt, kg	Body fat, % BW	$\dot{V}o_2$ max, $\ell \cdot min^{-1}$	RV, ℓ	FVC, ℓ	TLC, ℓ	$FEV_{1.0}$ $\ell \cdot sec^{-1}$	$\frac{FEV_{1.0}}{FVC}$, %	FEF 25-75% $\ell \cdot sec^{-1}$
1	27	179	65.0	9.31	4.57	1.72	5.92	7.64	4.68	79.1	4.46
2	22	185	77.0	6.05	4.81	1.64	7.17	8.81	5.16	72.0	3.95
3	23	179	73.2	11.2	4.62	1.28	5.44	6.72	4.52	83.1	4.55
4	19	188	69.3	4.33	4.34	1.52	6.96	8.48	5.43	78.0	4.99
5	21	193	74.5	8.93	4.95	1.54	7.01	8.55	5.42	77.3	4.56
6	23	185	71.6	20.2	4.59	1.25	6.05	7.30	4.98	82.3	5.50
7	26	177	67.1	14.5	4.24	0.98	5.30	6.28	4.01	75.7	3.45
8	23	179	70.0	10.3	4.58	1.37	6.06	7.43	4.47	73.8	3.77
9	20	179	66.1	11.7	4.63	0.97	5.64	6.61	4.67	82.7	5.00
10	31	181	72.3	12.5	4.34	1.38	5.30	6.68	4.33	81.7	4.82
Mean	24	183	70.6	10.9	4.57	1.37	6.09	7.45	4.77	78.6	4.51
S.D.	4	5	3.84	4.45	0.22	0.25	0.72	0.91	0.47	3.91	0.63

load was set at 3.0 kp, increased to 4.0 kp, and then by 0.5 kp increments at 2-min intervals until voluntary exhaustion. During the heaviest workload attempted, subjects were encouraged to increase the pedal frequency above 60 rpm, with cessation occurring when pedal frequency dropped significantly below 60 rpm.

Experimental Design. A graphic illustration of the six experimental protocols is depicted in Figure 3. In exposures 1, 3 and 5, the subjects exercised at a continuous, steady-state workload necessitating $\dot{V}_E \cong 80\ \ell \cdot min^{-1}$, for 60 min. In exposures 2, 4 and 6, which were designed as a competitive exercise simulation, the subjects first performed a typical pre-race warm-up for 30 min. More specifically, the first 30 min entailed riding at a moderate workload (~50% $\dot{V}o_2$ max) for 10 min, followed by a series of seven 1 min "sprints" at progressively increasing workloads (up to 90% $\dot{V}o_2$max), with 1 min resting recovery between each. The remaining time (7 min) in this 30 min period was spent in resting recovery. The final 30 min was consummated at a sustained high work intensity (85% $\dot{V}o_2$ max), typical of a competitive aerobic endurance effort.

Each of the exercise conditions - steady-state and competitive simulation - were accomplished in FA, as well as in exposures to 0.20 and 0.35 ppm O_3. The order of experimental protocols was randomized for each subject, with a minimum of 3 days intervening between treatments. Subjects were not informed whether they were receiving O_3, and in order to prevent olfactory detection, 0.30 ppm O_3 was generated for 1-2 min prior to initiating all experimental protocols. After each protocol, subjects completed a subjective symptoms questionaire, indicating whether they had received O_3 and, if so, at what concentration. Additionally, following each competitive simulation ride, subjects were asked if they would have been able to perform maximally in a competitive situation, taking into account their subjective symptoms.

All experimental treatments were completed in a room, 3.0 m x 2.4 m x 3.7 m, in which dry bulb temperature and relative humidity were maintained within 22-25° C and 35-50%, respectively. To facilitate convective and evaporative cooling, a constant airflow of 2.5 m/sec was directed at the subject's anterior surface via an industrial grade floor fan.

Pulmonary Function Measurements. A short battery of PF tests was administered immediately prior to each experimental protocol and repeated within 10 min following exercise. Residual volume was determined utilizing a modified Collins 9-liter spirometer by the O_2 rebreathing method (Wilmore, 1969), with initial and equilibrium N_2 readings taken on an Ohio 700 digital N_2 analyzer. At

FIGURE 1

EXERCISE CONDITION → / AIR MIXTURE ↓	← 60 min → STEADY-STATE EXERCISE	← 30 min → "WARM-UP"	← 30 min → COMPETITIVE EXERCISE SIMULATION
FA	1 $\dot{V}_E \cong 80$ l/min	2 $\bar{X}\dot{V}_E \cong 55$ l/min	$\bar{X}\dot{V}_E \cong 105$ l/min
0.20 ppm O_3	3 960	4	960
0.35 ppm O_3	5 1680	6	1680

FIG. 3. Description of the Experimental Design.

least two determinations each of forced vital capacity (FVC) were made on a Collins 10-liter Stead-Wells Spirometer assembly of the Basic Clinical Spirometer Module, No. 03000, with simultaneous measurement of flow volume loops on a Hewlett-Packard x-y recorder, NO. 7045A. Forced expiratory volume at 1_s ($FEV_{1.0}$) and forced expiratory flow rate during the middle half of FVC (FEF 25-75%) were calculated from the spirometric tracings.

Ozone Administration and Monitoring. Specific air mixtures during all experimental protocols were inhaled by subjects through a mouthpiece system previously described (DeLucia and Adams, 1977). A schematic diagram of the blow-by exposure system employed is depicted in Figure 4. Air filtered through a Mine Safety Appliances C-B-R filter was drawn through a Rotron CHE-1 pump at a flow of approximately 600 $\ell \cdot min^{-1}$. From the exhaust port of the Rotron pump, the air was pumped into a 0.91-m Teflon-lined aluminum tube, and underwent turbulent mixing at the tangential junction of 5.1-cm diameter aluminum tubing into the major 15.2 cm diameter aluminum tube. Such mixing was necessary to obtain O_3 dilution to the low levels used in this experiment, since concentrated O_3 created from silent arc discharge (Sander Ozonizer, type II) of compressed gaseous O_2 was introduced proximal to the turbulent mix. At the distal end of the 0.91-m tube, O_3- containing air was directed from an exhaust port to a Teflon-coated Hans Rudolph respiratory valve, via a 0.91-m length of fluoroflex Teflon tubing. Subatmospheric pressures generated during the inspiratory phase of breathing resulted in the flow of the O_3-air mixture into the respiratory valve. Positive expiratory pressures shut the fenestrations on the diaphragm on the inspiratory side of the valve, allowing flow of expired air unidirectionally into a 5 stainless steel mixing and sampling chamber to a Parkinson-Cowan (PC) gas meter, type CD-4. Expired air was thence routed into the distal portion of the mixing tube and, along with the pumped air mixture not inspired by the subject, exhausted via a 10-cm ID Flexaust CWC neoprene hose to the laboratory outside air ventilation outlet. Airflow resistance encountered in the breathing circuit, although not measured, was not significant at the flow rates incurred by the subjects.

O_3 concentration was routinely determined by sampled air from the inspiratory side of the Hans-Rudolph valve, drawn through a 0.64-cm Teflon tube connected to a Dasibi O_3 meter. The digital reading of O_3 concentration in ppm was compared on several occasions to that determined by UV absorption photometric method (DeMore et al, 1976) at the University of California, Davis, Primate Cen-

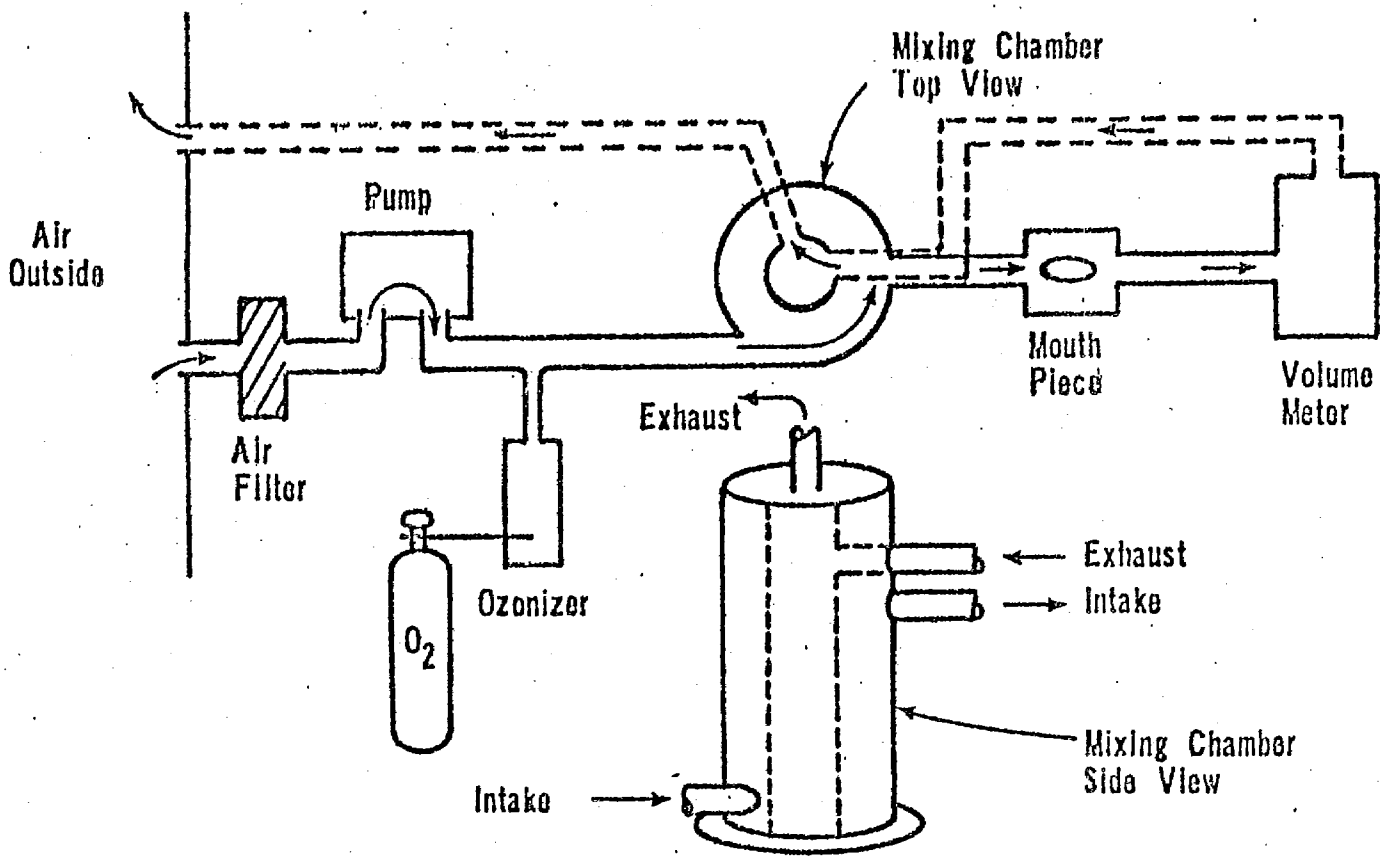

FIG. 4. SCHEMATIC DIAGRAM OF THE O_3 EXPOSURE SYSTEM EMPLOYED.

ter. The O_3 containing air from the sampling point on the inspired side of the respiratory valve to the subject was not likely reduced in concentration by passage through the respiratory valve diaphragms which, although of silicon rubber, did not show typical deterioration indicative of reactivity with the oxidant.

Exercise Measurements. Pulmonary ventilation was measured continuously on a Hewlett-Packard 7402A recorder via a potentiometer attached to a Parkinson-Cowan high-speed gas meter (Type CD4). Respiratory metabolism was determined via expired air volume (PC meter) and percent O_2 and CO_2 by a semiautomated sampling method incorporating a manually rotated three-way valve sampling system (Wilmore & Costill, 1974), and utilizing Applied Electrochemistry S-3A and Beckman LB-2 gas analyzers. Expired air volumes and respiratory metabolism values were calculated according to procedures outlined by Consolazio et al (1963). Heart rate was determined from the elapsed time between four consecutive R waves read from an ECG tracing taken every 10th min. Respiratory metabolism measurements were taken every tenth minute and ventilatory pattern measurements every fifth minute, as the previous computer data acquisition study had indicated these intervals satisfactory for detecting any significant change in response in clinically normal subjects.

Alveolar ventilation was determined by breath changes in fraction of CO_2 at the mouth, which were monitored for 45 seconds during each 1 minute $\dot{V}o_2$ measurement, and recorded on the second channel of the 7402A recorder. Samples were drawn directly from the mouthpiece and diverted into the head of the CO_2 analyzer via a solenoid driven 3-way stopcock with minimum deadspace. End tidal CO_2 fraction ($F_{ET}CO_2$) was corrected to alveolar values using the alveolar gas equation as given by Jones and associates (1975). Alveolar ventilation ($\dot{V}_A$) was calculated using the corrected end-tidal CO_2 fraction ($FET_{corr}CO_2$) via the following equation:

$$\dot{V}_A = \frac{\dot{V}_E(BTPS) \times F_{ECO_2}}{F_{ET_{corr}}CO_2}$$

where: $\dot{V}_{E(BTPS)}$ is the expiratory minute volume in BTPS and F_{ECO2} is the expiratory CO_2 fraction. Functional deadspace (V_D) was calculated via the following equation:

$$V_D = V_T - (\dot{V}_A/F_R)$$

Respiratory frequency (F_R) was determined by counting the number of deflections in the breath by breath changes in CO_2 for 30 seconds and then multiplying by 2.

Statistical Procedures. Duplicate PF measurements were corrected to BTPS and averaged for pre- and postexposure. The postexposure value for each parameter was subtracted from the preexposure value to obtain differences representing the treatment effect for each protocol. Values for $\dot{V}o_2$, $\dot{V}_E$, F_R, V_T, V_D, $\dot{V}_A$, and HR obtained during the last minute of exercise were subtracted from those obtained in the 10th min of the steady-state, training simulation protocols, and from the 36th min of competitive simulation protocols.

To determine if the O_3 exposures resulted in statistically significant alterations in exercise physiological response from that for the FA control exposure, a one-way ANOVA with repeated measures, was applied. A two-way ANOVA with repeated measures across air mixtures and exercise protocol was applied to the PF data. Upon obtaining a significant F from ANOVA, the Duncan multiple range test (Edwards, 1960) was used to determine the means between which significant differences existed. A significance level set at $P \leq .05$ was applied in all statistical analyses.

RESULTS

Individual and group data for the subjects anthropometry and pulmonary function, given in Table 2, showed a mean $\dot{V}o_2$ max of 4.57 $\ell \cdot min^{-1}$. Their mean VC and TLC can be seen to be well above that of the normally active male population, although this is expected, in part, because of their atypical body height. Their pulmonary flow rates are unremarkable.

Exercise Response. Because the two 60 min exercise protocols differed in intensity and continuity, cardiorespiratory and ventilatory parameters were analyzed by separate 1-way ANOVAs. The group means, SD, and percent change (as calculated from values at 60 min minus those at 10 min, divided by the values at 10 min for the continuous, training simulation protocol; and values at 60 min minus those at 36 min, divided by the values at 36 min for the competitive simulation protocol) for the exercise cardiorespiratory and ventilatory variables are summarized in Tables 3 and 4. Group mean differences (last min value minus 10th min and 36th min values for the training and competitive simulation protocols, respectively), together with the F values, are given in Table 5. While, in general, the absolute differences are greater for the competitive protocols, this is

TABLE 3. Exercise Cardiorespiratory, $\dot{V}_E$, and Respiratory Frequency Responses

Continuous	HR, beats·min^{-1}		$\dot{V}O_2$, ℓ·min^{-1}		$\dot{V}_E$, ℓ·min^{-1}, BTPS		F_R, breaths·min^{-1}	
FA	10 min	60 min	10 min	60 min	10 min	60 min	10 min	60 min
$\bar{x}$	143	154	2.93	3.10	76.7	79.8	31.4	33.8
SD	16	17	0.14	0.23	5.8	8.8	3.2	4.2
Δ		7.7%		5.8%		4.0%		7.6%
0.2 ppm O_3								
$\bar{x}$	143	151	2.96	3.09	76.0	80.8	31.6	39.4
SD	15	17	0.21	0.32	9.1	8.0	4.7	8.0
Δ		5.6%		4.4%		6.3%		24.7%
0.35 ppm O_3								
$\bar{x}$	141	148	2.98	3.14	76.2	82.7	31.7	45.9
SD	17	18	0.22	0.27	7.5	10.8	3.0	8.5
Δ		5.0%		5.4%		8.5%		44.8%
Competitive								
FA	36 min	60 min	36 min	60 min	36 min	60 min	36 min	60 min
$\bar{x}$	161	173	3.53	3.81	96.8	112.6	36.1	44.2
SD	16	15	0.30	0.39	8.2	7.6	5.5	8.0
Δ		7.4%		7.9%		16.3%		22.4%
0.20 ppm O_3								
$\bar{x}$	160	172	3.58	3.81	96.0	111.7	36.9	47.6
SD	16	16	0.15	0.24	7.0	9.0	6.4	8.6
Δ		7.5%		6.4%		16.3%		29.0%
0.35 ppm O_3								
$\bar{x}$	158	168	3.58	3.84	97.2	116.7	39.9	52.6
SD	16	18	0.22	0.20	7.7	12.4	8.0	9.6
Δ		6.3%		7.3%		20.1%		31.8%

TABLE 4. Exercise Ventilatory Responses

Continuous

	V_T, ℓ		V_D, ℓ		V_D/V_T		$\dot{V}_A$, ℓ·min^{-1}, BTPS	
FA	10 min	60 min	10 min	60 min	10 min	60 min	10 min	60 min
$\bar{x}$	2.46	2.39	0.73	0.76	0.30	0.32	53.8	54.0
SD	0.28	0.36	0.11	0.20	0.05	0.09	6.9	9.5
Δ		-2.8%		4.1%		6.7%		0.4%
0.2 ppm O_3								
$\bar{x}$	2.42	2.14	0.78	0.76	0.32	0.36	51.3	52.9
SD	0.26	0.35	0.08	0.24	0.06	0.10	7.7	10.5
Δ		-11.6%		-2.6%		12.5%		3.1%
0.35 ppm O_3								
$\bar{x}$	2.42	1.84	0.81	0.67	0.33	0.37	50.5	51.7
SD	0.30	0.32	0.15	0.16	0.06	0.10	5.3	8.6
Δ		-24.0%		-17.3%		12.1%		2.4%

Competitive

FA	36 min	60 min	36 min	60 min	36 min	60 min	36 min	60 min
$\bar{x}$	2.72	2.61	0.98	0.99	0.37	0.39	61.6	68.7
SD	0.36	0.45	0.20	0.32	0.08	0.14	11.0	15.8
Δ		-4.0%		1.0%		5.4%		11.5%
0.20 ppm O_3								
$\bar{x}$	2.66	2.38	0.79	0.80	0.31	0.34	66.4	72.1
SD	0.40	0.34	0.22	0.33	0.11	0.14	10.2	13.1
Δ		-10.5%		1.3%		9.7%		8.6%
0.35 ppm O_3								
$\bar{x}$	2.50	2.26	0.88	0.91	0.36	0.41	62.3	67.9
SD	0.42	0.36	0.17	0.23	0.09	0.12	9.5	12.4
Δ		-9.6%		3.4%		13.9%		9.0%

TABLE 5. Exercise Response Comparisons

	Continuous				Competitive			
Variable	FA	0.2 ppm	0.35 ppm	F Ratio	FA	0.2 ppm	0.35 ppm	F Ratio
HR, beats·min^{-1}	10.6	8.1	7.0	0.42	12.4	11.2	10.2	0.30
$\dot{V}O_2$, ℓ·min^{-1}	0.17	0.13	0.16	0.21	0.29	0.23	0.25	0.14
$\dot{V}_E$, ℓ·min^{-1}	3.1	4.8	6.5	1.17	15.3	15.7	19.5	1.03
F_R, breaths·min^{-1}	2.4	7.8	14.2	19.42*	8.1	10.7	12.7	3.49
V_T, ℓ	-.08	-.28	-.58	10.75*	-.11	- .27	- .24	2.25
V_D, ℓ	.03	-.02	-.14	2.22	.01	.01	.03	0.05
$\dot{V}_A$, ℓ·min^{-1}	0.3	1.6	1.2	0.24	7.1	5.7	5.6	0.12

*Significant at $P<0.05$.

principally a function of metabolism induced by the higher intensity work, as opposed to an O_3 treatment effect. This is apparent, in that the only significant F values were for F_R and V_T for the continuous training simulation protocol. Post-hoc analysis revealed that all individual comparisons were significantly different for F_R, but only those between FA and 0.35, and 0.20 and 0.35 ppm for V_T. Failure of the mean differences for F_R and V_T to reach statistical significance for the competitive protocols is due, in part, to the fact that some subjects were already "responding" to the 0.35 ppm O_3 exposure when the "initial" 36th minute values were obtained (ED = 780 ppm·ℓ, i.e., 0.35 ppm x 30 min x 55 $\ell \cdot min^{-1}$, plus 0.35 ppm x 6 min x 96 $\ell \cdot min^{-1}$). This notion was supported by observation of a significant F from ANOVA of the final minute values across treatment conditions for both F_R and V_T. The percent change in F_R and V_T, as a function of air mixture, is depicted in Figure 5, while that for $\dot{V}_E$ and $\dot{V}_A$ is shown in Figure 6.

Subjects exercised at individually prescribed workloads to elicit a mean $\dot{V}_E$ of approximately 80 $\ell \cdot min^{-1}$. The mean $\dot{V}_E$, measured from a continuous recording for both the training and competition simulation procotols, were 77.4 and 77.5 $\ell \cdot min^{-1}$, respectively (F = 0.44). The subjects were exercising at approximately 68% of $\dot{V}o_2$ max for the training simulation protocol and at 84% of $\dot{V}o_2$ max for the last 30 min of the competitive simulation protocol. Each subject completed all rides during the FA and 0.20 ppm O_3 exposures. However, during the 0.35 ppm O_3 exposures, three subjects were unable to complete either the training or the competitive simulation rides, while another subject was unable to complete the competitive ride only.

Pulmonary Function Response. Since the two protocols were designed to elicit the same mean $\dot{V}_E$ and thus, to deliver the same O_3 effective dose, PF data were analyzed by a 2-way repeated measures ANOVA. The groups means, SD, and percent change (as calculated from values obtained immediately postexposure minus preexposure, divided by the preexposure value) for the pulmonary function variables are summarized in Table 6. Group mean differences (postexposure minus preexposure) for the training and competitive simulation protocols are given in Table 7.

The 2-way ANOVA revealed no significant exercise mode effect, but a highly significant (<.0002) treatment main effect for FVC, $FEV_{1.0}$, and FEF_{25-75}. The F ratios for the pulmonary function variables, together with the statistically significant individual mean comparisons by post-hoc analysis, are given in Table 8.

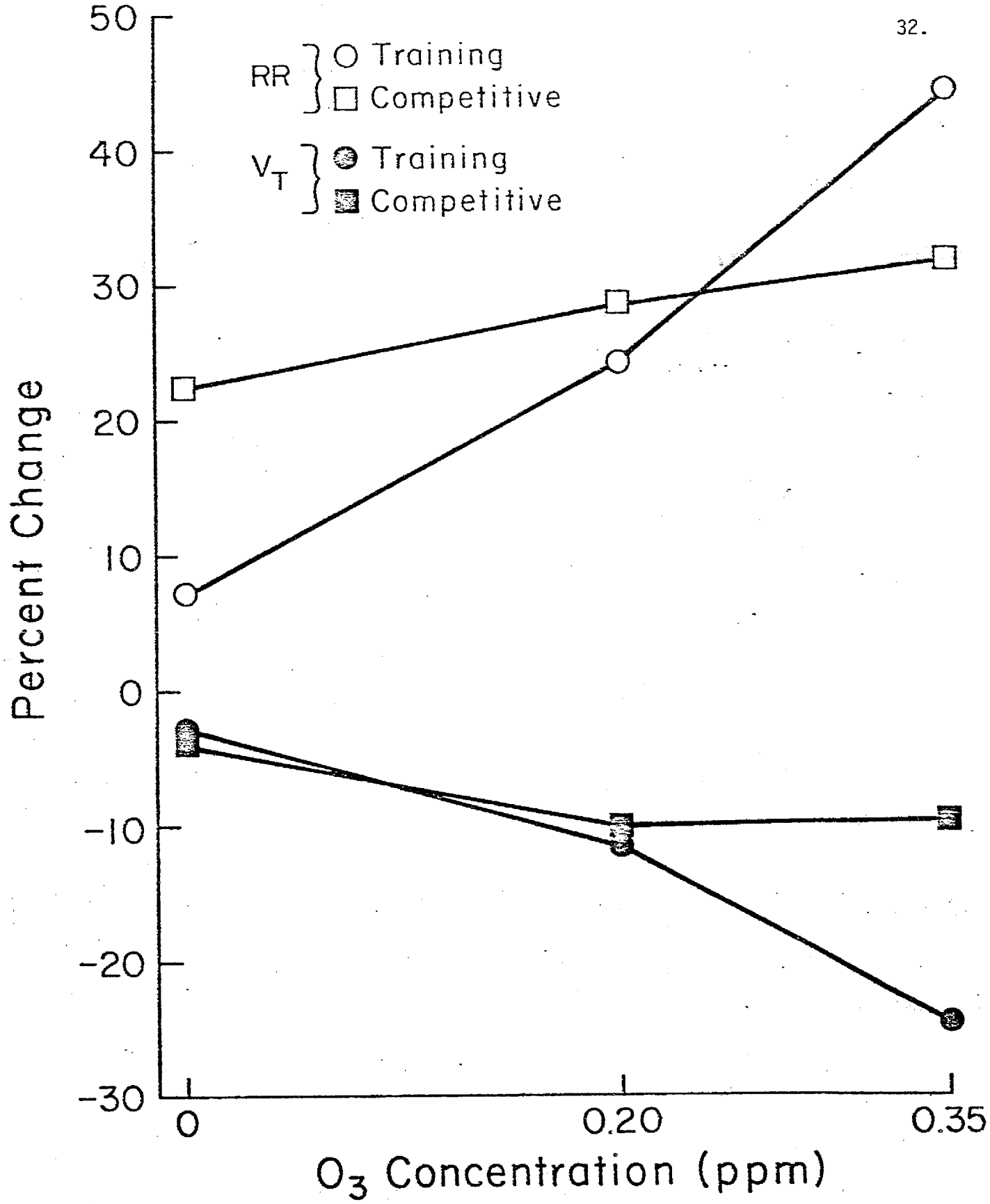

Fig. 5. Percent Change in Exercise Ventilatory Pattern as a Function of O_3 Concentration.

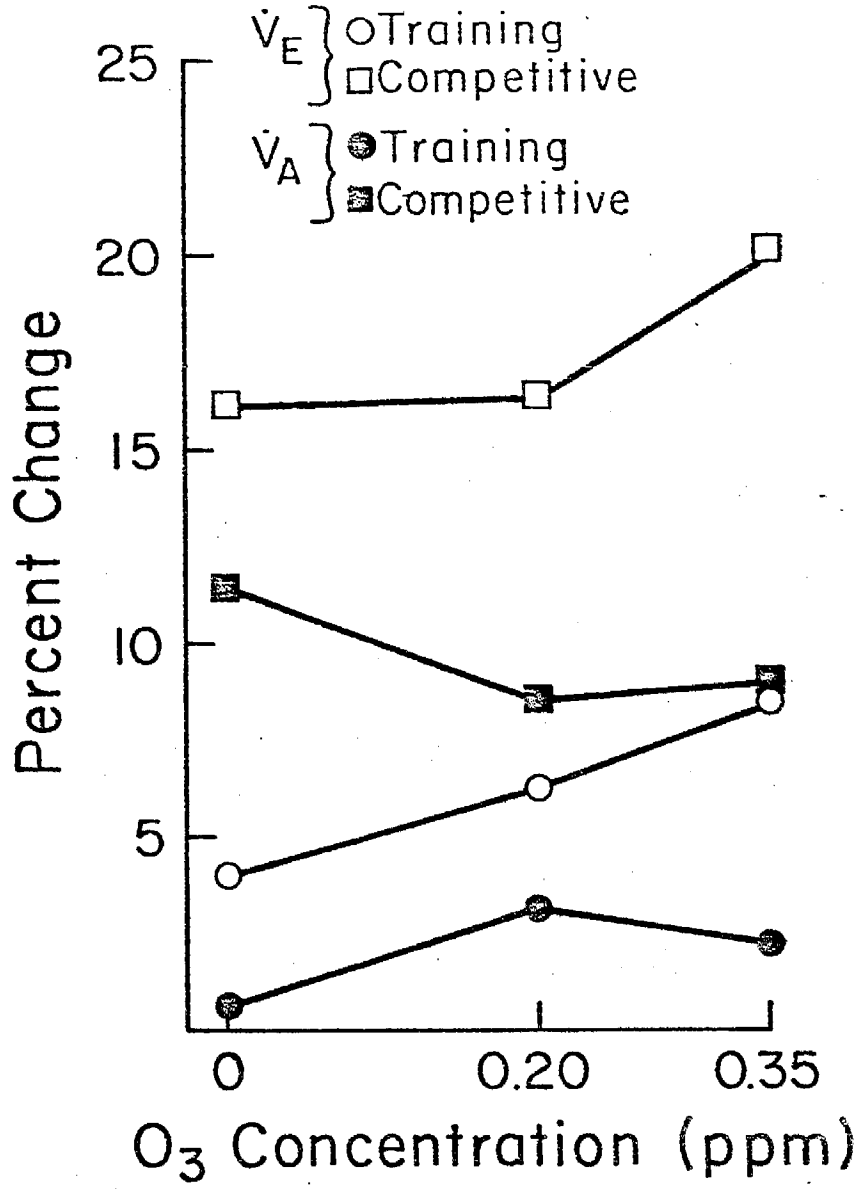

Fig. 6. Percent Change in Exercise Ventilation as a Function of O_3 Concentration.

TABLE 6. Pulmonary Function Responses

	RV, ℓ		FVC, ℓ		$FEV_{1.0}$, ℓ		FEF_{25-75}, ℓ·sec^{-1}	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Continuous								
FA								
$\bar{x}$	1.40	1.51	6.13	6.02	4.75	4.82	4.55	4.68
SD	0.25	0.29	0.75	0.59	0.46	0.42	0.64	0.65
		+7.9%		-1.8%		1.5%		2.8%
0.2 ppm O_3								
$\bar{x}$	1.37	1.47	6.05	5.62	4.74	4.47	4.46	4.28
SD	0.27	0.33	0.76	0.83	0.41	0.47	0.60	0.65
		7.3%		-7.1%		-5.7%		-4.0%
0.35 ppm O_3								
$\bar{x}$	1.35	1.44	6.10	4.98	4.78	3.79	4.44	3.39
SD	0.28	0.32	0.70	0.79	0.51	0.74	0.68	1.12
		6.7%		-18.4%		-20.7%		-23.6%
Competitive								
FA								
$\bar{x}$	1.38	1.45	6.03	6.04	4.83	4.92	4.63	4.91
SD	0.29	0.29	0.70	0.52	0.48	0.44	0.52	0.43
		5.1%		0.2%		1.9%		6.0%
0.20 ppm O_3								
$\bar{x}$	1.39	1.45	6.14	5.56	4.85	4.49	4.51	4.40
SD	0.29	0.31	0.69	0.80	0.45	0.58	0.71	0.76
		4.3%		-9.4%		-7.4%		-2.4%
0.35 ppm O_3								
$\bar{x}$	1.34	1.46	6.11	5.09	4.85	3.97	4.60	3.68
SD	0.26	0.38	0.67	0.74	0.42	0.78	0.63	1.00
		8.9%		-16.7%		-18.1%		-20.0%

TABLE 7. Pulmonary Function Response to Treatments

Variable	Continuous FA	Continuous 0.2 ppm	Continuous 0.35 ppm	Competitive FA	Competitive 0.2 ppm	Competitive 0.35 ppm
RV, ℓ	0.11	0.10	0.09	0.07	0.07	0.12
FVC, ℓ	-0.11	-0.43	-1.13	-0.01	-0.58	-1.02
$FEV_{1.0}$, ℓ	0.08	-0.27	-0.99	0.09	-0.35	-0.88
FEF_{25-75}, $\ell \cdot sec^{-1}$	0.13	-0.18	-1.05	0.28	-0.12	-0.93

TABLE 8. F Ratios and Specific Significant Mean Differences from Post-Hoc Analysis for Pulmonary Function Variables

Variable	F Ratio	Specific Significant Mean Differences*
RV	0.11	Not applicable
FVC	35.25*	FA - 0.35; 0.20-0.35; and FA - 0.20
$FEV_{1.0}$	21.70*	FA - 0.35; 0.20-0.35; and FA - 0.20
FEF_{25-75}	14.40*	FA - 0.35; 0.20-0.35

*Significant at $P<0.05$.

The mean percent changes for both exercise modes for the four pulmonary function variables, as a function of O_3 concentration, are depicted in Figure 7.

A summary of the symptomatic response to treatments for the training and competitive protocols is given in Table 9. In spite of the single-blind procedure utilized, the occurrence of symptoms, even at the 0.20 ppm exposures, permitted the subjects to deduce that they had received O_3. In response to the question of whether they would have been able to perform maximally in a competitive situation - given their indicated subjective symptoms - all subjects indicated they could have performed maximally after the FA exposures. Following the 0.20 ppm O_3 exposures, four of ten subjects indicated that they could not have performed maximally, while one was unsure. Following the 0.35 ppm competitive simulation ride, nine subjects (including four who elected to cease exercise before 60 min) stated that they would definitely not have been able to perform maximally in an actual competition, while one subject was unsure.

DISCUSSION

The results of the present investigation demonstrate that exposure of well trained endurance athletes to as low as 0.20 ppm O_3 while engaged in 1 h exercise protocols simulating aerobic training and competition, produces significant acute toxicity effects. Further, these prolonged, high intensity work bouts induced sufficient $\dot{V}_E$, such that exposure to 0.35 ppm O_3 intensified these effects, resulting in additional PF impairment and subject symptom discomfort sufficient to cause premature cessation of exercise performance in four subjects.

Minimum Ozone Concentration Level for the Detection of Acute Toxicity Effects. In acute laboratory chamber exposures ($\leq$ 2 h), numerous investigators have demonstrated that light exercise performed for 15 min, with 15 min rest, intermittently, intensifies PF impairment at a particular O_3 concentration, even as low as 0.37 ppm (Bates et al, 1972; Folinsbee et al, 1975; Hackney et al, 1975; Hazucha et al, 1973), a level that did not elicit an effect in 2 h resting exposures (Hackney et al, 1975; Hazucha et al, 1973; Silverman et al, 1976). Using heavier IE workloads, Folinsbee et al (1978a), observed significant PF impairment consequent to a 2 h exposure to 0.30 ppm O_3, but not at 0.10 ppm. The authors concluded that the threshold acute O_3 toxicity concentration for subjects exercising at moderately severe energy expenditures lies somewhere between 0.10 and 0.30 ppm. The minimum toxicity effect level may be closer to 0.30, in that with 1 h CE protocols at moderately heavy workloads ($\dot{V}_E$ = 63-65 $\ell \cdot min^{-1}$),

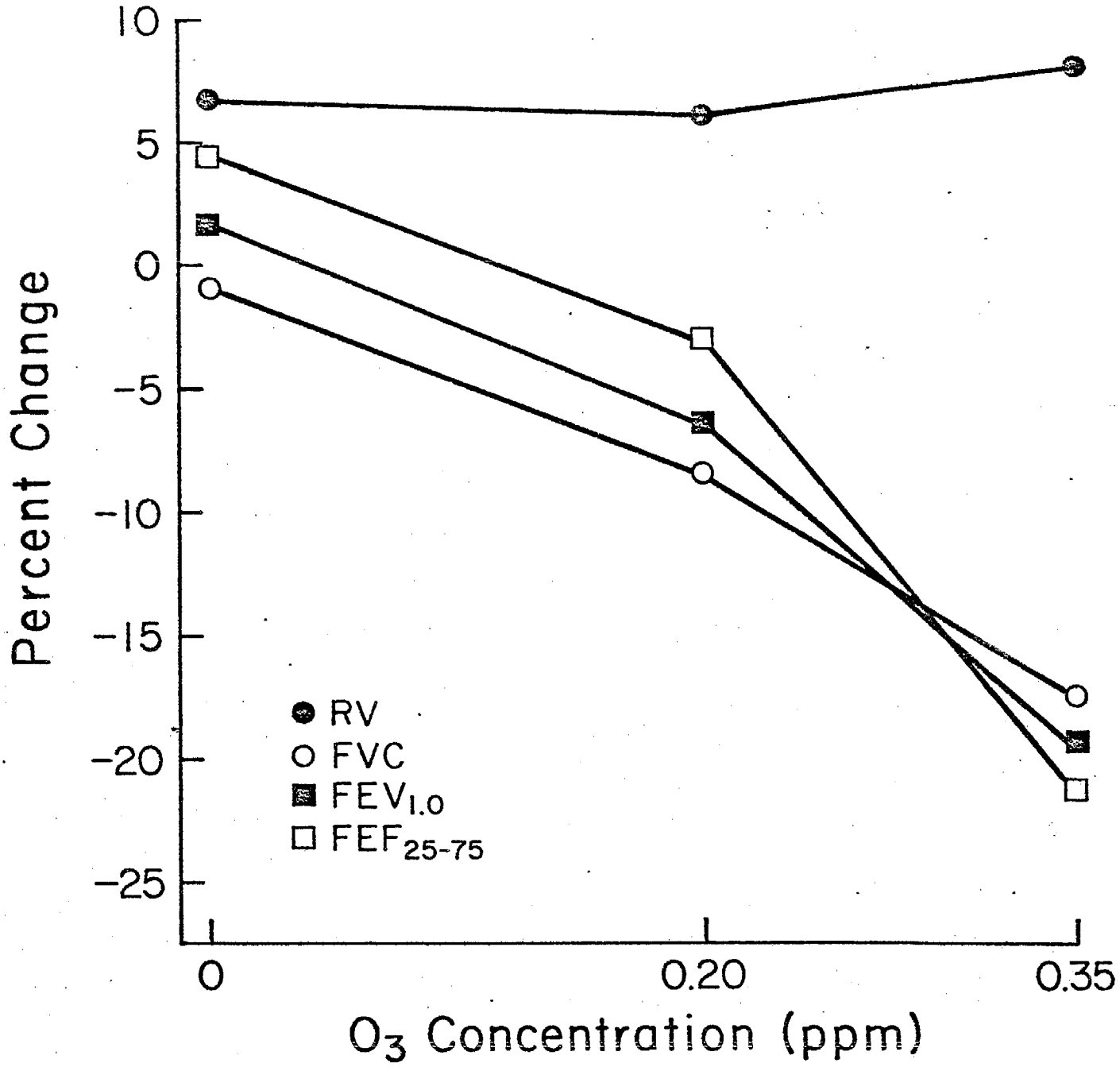

Fig. 7. Percent Change in Pulmonary Function as a Function of O_3 Concentration.

TABLE 9. Symptomatic Response to Treatments

Symptom	Continuous FA	Continuous 0.20 ppm	Continuous 0.35 ppm	Competitive FA	Competitive 0.20 ppm	Competitive 0.35 ppm
Shortness of breath	0	5	8	1	7	9
Cough	1	8	8	0	6	8
Excess sputum	3	4	4	1	5	7
Throat tickle	1	5	6	2	4	6
Raspy throat	1	5	7	3	5	3
Wheezing	0	2	1	0	1	3
Congestion	0	3	3	1	2	3
Headache	0	3	3	1	1	3
Nausea	0	2	6	1	5	5
"Other" symptoms	1	4	6	2	5	5
Total symptoms for treatments	7	41	52	12	41	52
No. of subjects believing they received O_3	0	9	10	1	9	10

Values represent total number of subjects reporting symptoms.

we have observed statistically significant PF impairment and exercise ventilatory pattern alteration consequent to exposure at 0.30 ppm O_3 (Adams et al, 1981; DeLucia & Adams, 1977), while exposures to 0.20 ppm O_3 of up to 1 h duration did not elicit acute toxicity effects. However, a tendency toward PF impairment after 75 min exposure to 0.20 ppm O_3, with 63 $\ell \cdot min^{-1}$ $\dot{V}_E$, was observed (Adams et al, 1981).

In the present study, mean $\dot{V}_E$ for both the continuous, training and competitive simulation protocols was 77.5 $\ell \cdot min^{-1}$, which was sufficient to elicit a significant ($P < .05$) decrement in FVC and $FEV_{1.0}$, as well as a four-fold increase in subjective symptoms (Table 9) during 1 h exposure to 0.20 ppm O_3. Further, significant alteration in exercise ventilatory pattern ($\uparrow F_R$, $\downarrow V_T$) was observed for the training simulation protocol. Hence, it appears that work intensities eliciting $\dot{V}_E \geq 75$ $\ell \cdot min^{-1}$, if sustained for 1 h or longer, are sufficient to lower the threshold for acute O_3 toxicity effects to 0.20 ppm for healthy, well trained young adult males.

Relation of Ozone Toxicity to the Effective Dose Inhaled. Results of the present study provide additional evidence confirming the efficacy of the O_3 effective dose in identifying the degree of the acute toxicity effect. That is, the steady-state $\dot{V}_E$ incurred in the training simulation protocol and the non-steady-state $\dot{V}_E$ effected in the competitive simulation protocol, but with the same mean $\dot{V}_E$ for 1 h and thus, the same effective dose- produced virtually equivalent PF impairment (Tables 5 and 6) and subjective symptoms (Table 9).

In a previous study (Adams et al, 1981), we noted that the percent decrement in $FEV_{1.0}$ as a function of the O_3 effective dose for our CE, obligatory mouthpiece inhalation method was essentially equal to that observed by Folinsbee and others (1978a) in IE, chamber exposures. This comparison is depicted in Figure 8, in which the dashed line represents the mean response calculated for ppm·ℓ products from our laboratory (Adams et al, 1981) and the solid line the calculated relationship obtained by Folinsbee et al (1978a). Also shown are the values from the present study for FA and the O_3 exposures at 0.20 ppm and 0.35 ppm for both the continuous, training and competitive simulation protocols. There appears to be no systematic variation in this relationship observed in the present study from that represented by either line. Thus, the similar effect on $FEV_{1.0}$ as a function of O_3 effective dose in CE, obligatory mouthpiece inhalation method and the IE chamber procedure is extended to approximately 1500 ppm·ℓ.

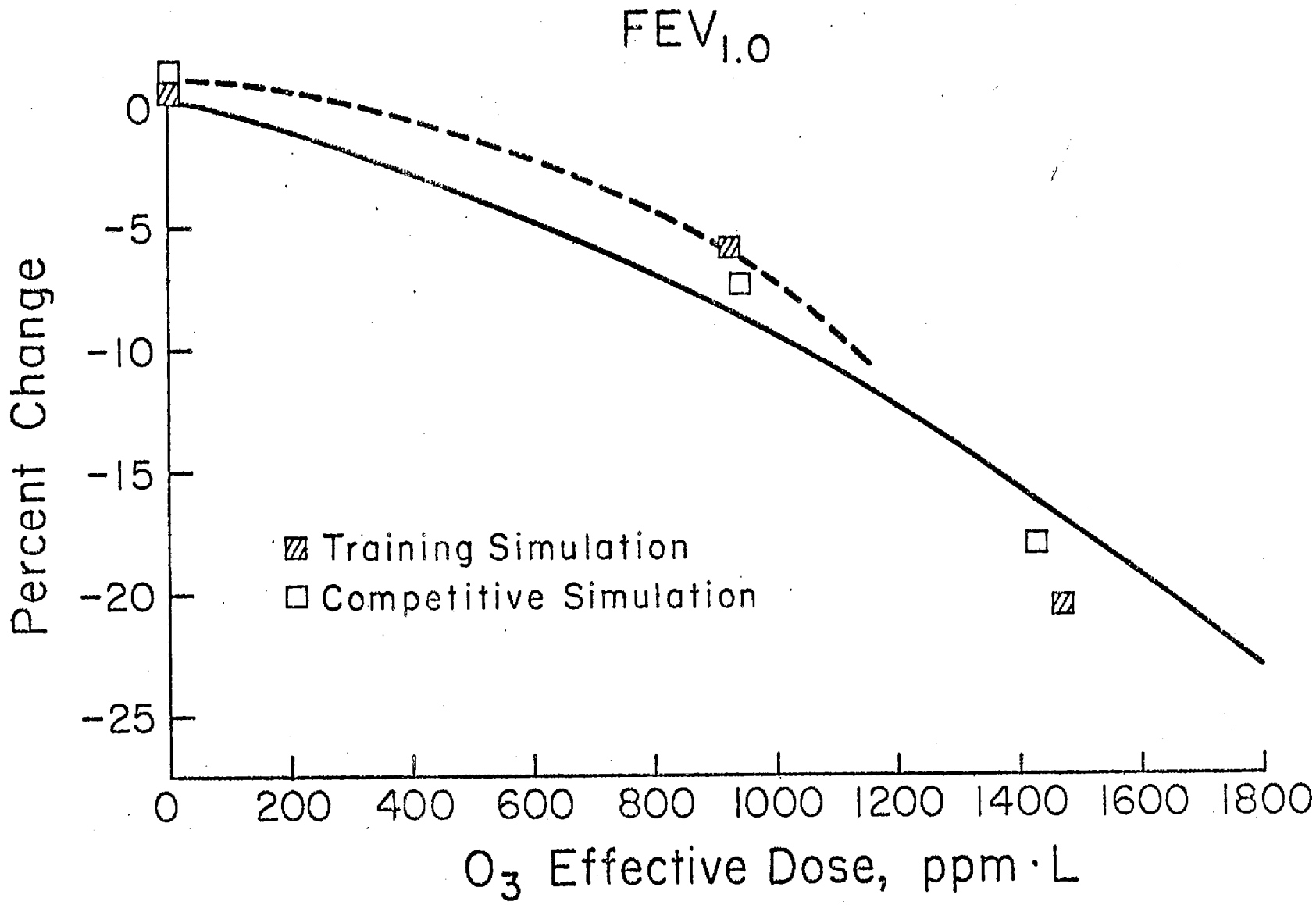

Fig. 8. Comparison of Percent Change in $FEV_{1.0}$ as a Function of O_3 Effective Dose.

Previous work with dogs (Yokoyama & Frank, 1972) indicates that O_3 uptake is greater when O_3 is administered orally rather than nasally. However, the comparison shown in Figure 8 also suggests that the spontaneous shift from nasal breathing at rest, in light IE, and recovery to primarily oral breathing at heavier workloads, noted by Folinsbee et al (1978a), does not substantially affect O_3 toxicity in humans within the range studied. Further, results from the present study imply that it is the total $\dot{V}_E$ and thus, the effective dose of O_3 inhaled, for a given concentration-time exposure, rather than significant differences in the rate and depth of breathing, which is paramount. That is, the uneven $\dot{V}_E$ incurred in the competitive simulation protocol (Figure 2), in which $\dot{V}_E$ varied from a high of 80 $\ell \cdot min^{-1}$ during warm-up to 15 $\ell \cdot min^{-1}$ in the last min of rest preceding the last 30 min of sustained exercise (in which $\dot{V}_E$ reached 97 $\ell \cdot min^{-1}$ within 6 min, and then increased steadily to 115 $\ell \cdot min^{-1}$), effected no significant difference in PF from that of the continuous, near steady-state $\dot{V}_E$ training simulation protocols.

Folinsbee et al (1977) state that the observed decrease in $FEV_{1.0}$ induced by O_3 inhalation is the result of a decrease in inspiratory capacity and an increase in airway resistance. However, the relative contribution of each factor has not been experimentally determined. While the comparison depicted in Figure 8 suggests that well trained endurance athletes PF impairment is affected in the same manner as healthy young adult male nonathletes studied by others (Adams et al, 1981; Folinsbee et al, 1978a), as shown in Figure 9, the ratio of FVC to $FEV_{1.0}$ impairment is greater for the athletes than for nonathletes working at lower absolute workloads (Adams, et al 1981; DeLucia & Adams, 1977; Folinsbee et al, 1978a). Thus, the athletes of the present study may have incurred a greater irritant effect at any given O_3 effective dose than that reflected by $FEV_{1.0}$ decrement, as it is likely airway resistance was counterbalanced in part by a bronchodilator effect in very heavy exercise (Lefcoe, 1969). The nonsignificant changes observed in the FA exposures for RV and FVC, combined with increases in $FEV_{1.0}$ and FEF_{25-75}, would be consistent with the hypothesis of increased sympathetic tone and widening of the bronchial tree with heavy exercise, advanced by Lefcoe (1969).

It has been proposed that the observed impairment in PF following O_3 inhalation is the result of a vagally mediated reflex bronchoconstriction via stimulation of irritant receptors (Silverman et al, 1976). Golden and colleagues (1978) have shown that O_3 exposure in humans produces bronchial hyperirritability via cholinergic postganglionic pathways, probably by damaging airway

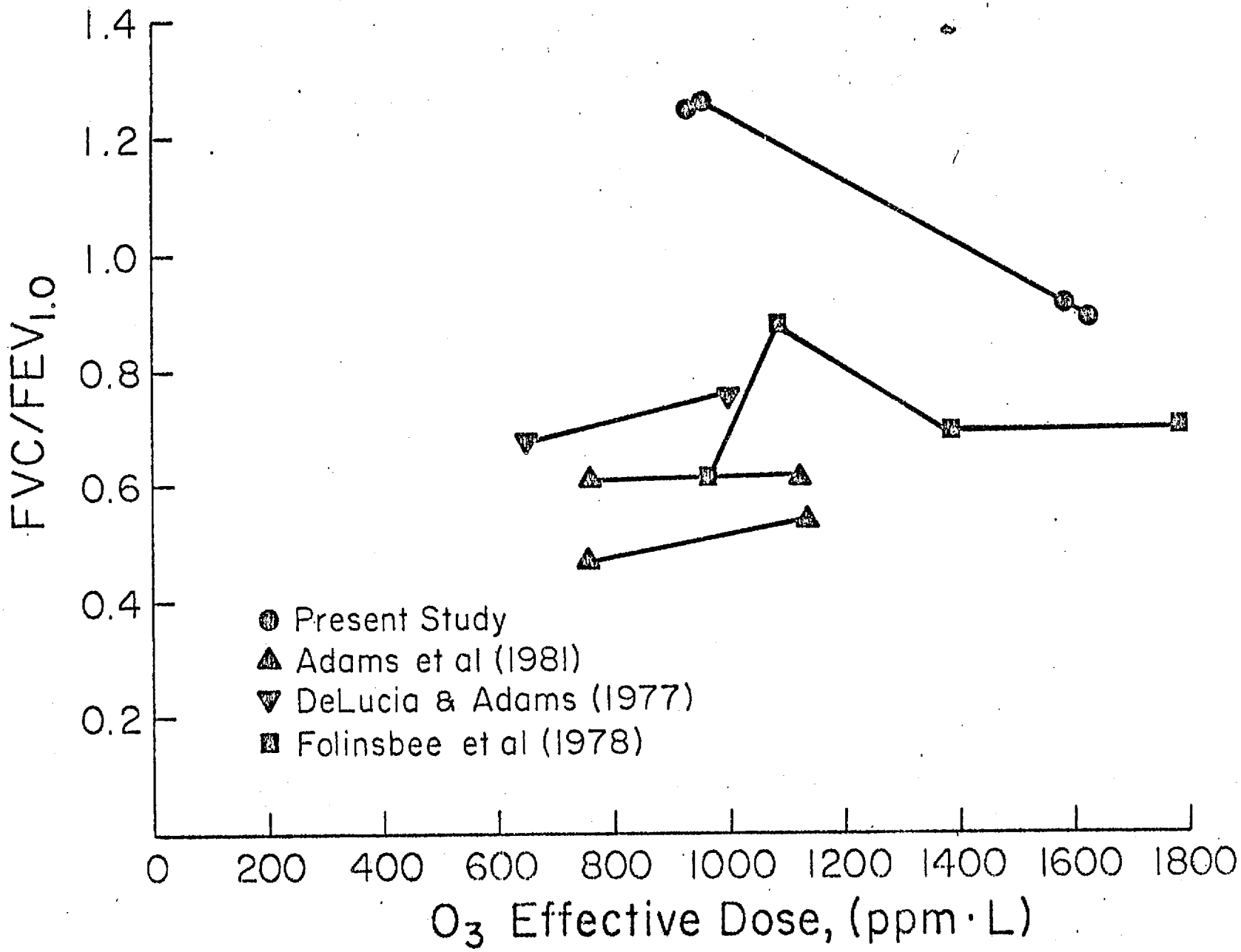

Fig. 9. Comparison of the Ratio of Percent Change in FVC to $FEV_{1.0}$ as a Function of O_3 Effective Dose.

epithelium and thereby sensitizing bronchial irritant receptors. However, these observations do not necessarily preclude a non-vagally mediated direct bronchoconstriction in the human as has been demonstrated in the cat (Watanbe et al, 1973). Whatever the mechanism, the present data suggest that decreases in inspiratory capacity and increase in airway resistance are not necessarily interdependent events.

Effect of Ozone Inhalation on Exercise Performance. The capacity for prolonged rhythmical muscular exercise is limited by an interrelated composite of cardiorespiratory, metabolic, environmental and psychological factors (Åstrand & Rodahl, 1977, p. 292). As such, it is not possible to define precisely the relative physiological and subjective impact of reduced maximum work performance. In the present study, our subjects undertook very heavy, prolonged exercise characteristic of aerobic endurance training and competition. All completed protocols in the FA and 0.2 ppm O_3 exposures, although four stated that, given their postexposure symptoms, they could not have achieved actual maximal performance in the latter condition. Further, upon exposure to 0.35 ppm O_3, 9 of 10 subjects stated they could not have performed maximally in actual competition, including four who failed to complete the competition simulation ride.

Reduced work performance consequent to O_3 inhalation has been observed by others (Folinsbee et al, 1977; Wayne et al, 1967), although causes of this decrement, including the role of individual sensitivity (DeLucia & Adams, 1977) are not well defined. Wayne and associates (1967) observed that the implicated role of O_3 in the failure of high school runners to improve their seasonal best performance time could not be differentiated between some physiological effect of the pollutant gas or an increased discomfort of performance in the polluted environment. While Folinsbee and colleagues (1977) observed a decreased $\dot{V}o_2$ max consequent to O_3 exposure, it was associated with a decrement in work performance and HR max. They concluded that these decrements were due to a ventilatory limitation of maximum effort, probably related to respiratory discomfort. Although DeLucia & Adams (1977) did not study the effects of O_3 inhalation on exercise performance, per se, 1 h of CE at 65% of $\dot{V}o_2$ max at 0.30 ppm became limiting to the two most sensitive subjects. That is, it was necessary to reduce their workload 20-30% during the final 15 min to enable them to complete the exposure.

In the present study, work performance capacity, per se, was not directly assessed, in that our subjects all completed the competitive simulation protocol

in FA while exercising at a mean $\dot{V}o_2$ of 83.6% of $\dot{V}o_2$ max. Pugh (1970) has observed that international caliber 10,000 meter runners sustain a $\dot{V}o_2$ of ~92% of $\dot{V}o_2$ max when running at competitive racing speed. Nonetheless, the competitive simulation protocol utilized in the present study clearly became limiting to four subjects when exposed to 0.35 ppm O_3, as they were unable to maintain the prescribed workload for the final 30 min. As such, these observations are deserving of analysis in some detail.

Although protocols were administered in random order and each preceded by generation of 1-2 min exposure to 0.30 ppm O_3 before placement of the noseclip and initiation of the protocol, subjects clearly became aware that they were receiving O_3 with the onset of subjective symptoms (Table 9). Hence, it is possible that the development of subjective respiratory discomfort, especially evidenced during the 0.35 ppm exposures, may have resulted in some subjects becoming unwilling to continue exercise at the prescribed workload. Alternately, the prolonged high rate of O_3 inhalation may well have produced physiological changes that could limit work performance. For example, the decreased FVC and the development of a more shallow exercise breathing pattern noted in the present study, might be expected to effect an increased V_D and to induce reduced $\dot{V}_A$ which, in turn, could result in a reduced $\dot{V}_A/\dot{Q}$ and SaO_2 (Bates, 1980). However, no significant alteration due to O_3 exposure in either V_D or $\dot{V}_A$ was observed. Further, there was no significant change in $\dot{V}o_2$ induced by O_3. This means that the inferred increase in airway resistance from significantly reduced $FEV_{1.0}$ and FEF_{25-75} at 0.35 ppm O_3 was not likely sufficient to incur an increased O_2 requirement due to enhanced respiratory muscular effort (Dressendorfer et al, 1977). It also implies that the exchange of O_2 at the lung was not impaired, and that there was no effect on the O_2 carrying and unloading functions of the RBC. The lack of a direct effect of O_3 on O_2 lung diffusion, transport and delivery is also substantiated by the lack of any indirect evidence of O_3 induced development of anaerobiosis. That is, neither HR or $\dot{V}_E$ were significantly altered by O_3 exposure, even at 0.35 ppm (Table 3).

It is interesting to note that 3 of the 4 subjects who could not complete the competitive protocol at 0.35 ppm O_3, were also unable to complete the training simulation protocol. Further, the mean O_3 effective dose effected at the time of training and competitive protocol cessation for the three subjects was 1066 and 1134 ppm·ℓ, respectively. This lends further support to the notion that the subjects discontinued the competitive protocols due to subjective

respiratory discomfort induced by O_3 irritant effects, since the discontinuation seems to be independent of metabolic demand but dependent upon a specific effective dose of O_3. Hence, our results imply that limitations in prolonged exercise performance consequent to O_3 exposure at ambient smog alert levels are not a result of physiological changes impairing O_2 pick-up, transport and delivery. Thus, performance is limited by an unwillingness and/or inability of the subject to tolerate the respiratory discomfort incurred with O_3 exposure, which is due to the physiological bronchoconstrictor response induced by vagal mediation (Golden et al, 1978) or possibly by direct irritant effect of the pollutant on the pulmonary epithelium (Watanabe et al, 1973).

Disparate Sensitivity to Ozone Inhalation. The broad range of sensitivity to O_3 inhalation was first noted by Hackney et al (1975) and subsequently by others (Adams et al, 1981; DeLucia & Adams, 1977). In the present study, an attempt was made to secure as near homeogeneous population as possible with respect to competitive endurance running history and absolute $\dot{V}o_2$ max. Further, individual workloads were set to elicit a mean $\dot{V}_E$ approximating 80 $\ell \cdot min^{-1}$, which resulted in a relatively homogeneous $\dot{V}_E$ in the training and competitive protocols (77.5 $\pm$ 7.2 and 77.4 $\pm$ 6.3, respectively). Nonetheless, a rather wide range of O_3 toxicity was observed in our subjects, which is accented by comparison of responses of the two most sensitive subjects to the two least sensitive subjects given in Table 10. Since no significant differences in response occurred across exercise protocols, the values for both training and competitive protocols were combined. Subjects 3 and 4 showed the greatest response to O_3 inhalation with large decreases occurring in FVC, $FEV_{1.0}$ FEF_{25-75} in the 0.20 ppm O_3 protocols. Exercise respiratory and metabolic parameters evidenced no trend which would be consistent with a greater O_3 toxicity as compared to the least sensitive subjects.

Consequent to the 0.35 ppm O_3 exposures, this difference in sensitivity was accentuated not only by greater decreases in FVC, $FEV_{1.0}$ and FEF_{25-75}, but also by a greater increase in F_R compared to the least sensitive subjects. Further, it should be noted that both sensitive subjects were forced to discontinue both protocols at the 0.35 ppm O_3 level. Upon comparison with the least sensitive subjects, it appears that the sensitive subjects evidenced no change in $\dot{V}_E$, $\dot{V}_A$, V_D, HR, and $\dot{V}o_2$ which would indicate a direct effect of O_3 on O_2 pick up, transport or delivery. Hence, it appears that the difference in responses between the least and most sensitive subjects can be explained simply by

TABLE 10. Comparison of the Responses of O_3 Sensitive and Insensitive Subjects

	O_3 Sensitive Subjects						O_3 Insensitive Subjects					
	Subj 3		Subj 4		Mean		Subj 2		Subj 8		Mean	
O_3 ppm	.20	.35	.20	.35	.20	.35	.20	.35	.20	.35	.20	.35
FVC	-20.3	-29.7	-10.7	-22.5	-15.5	-26.1	- 9.5	-11.8	- 4.3	- 6.3	- 6.9	- 9.1
$FEV_{1.0}$	-22.2	-36.2	-10.1	-14.8	-16.2	-25.5	1.3	- 8.3	2.4	- 3.4	1.9	- 5.9
FEF_{25-75}	-16.5	-43.0	- 5.9	-13.8	-11.2	-28.4	9.6	- 2.8	9.8	3.7	9.7	0.04
$\dot{V}_E$	17.0	14.2	7.9	12.7	12.5	13.5	10.7	8.6	17.9	9.6	14.3	9.1
F_R	29.1	22.0	25.3	42.2	27.2	32.1	21.4	22.0	25.4	25.2	23.4	23.6
V_T	- 9.1	- 6.0	-14.0	-19.9	-11.6	-13.0	- 7.5	-11.1	- 6.8	-12.0	- 7.2	-11.6

Values are percent change from preexposure.

the degree of response in FVC, $FEV_{1.0}$ and FEF_{25-75} and F_R, which is suggestive of a greater neurogenic sensitivity of bronchoconstrictor effect of the vagally mediated irritant receptors and/or direct pulmonary epithelium effect of O_3.

Subject 3, who showed the greatest O_3 toxicity effect in the present study (Table 10), has a prior history of asthma and current respiratory allergies. This is consistent with the observations of DeLucia and Adams (1977), in which their two most sensitive subjects had similar histories. This would suggest that individuals with normal PF measurements at rest and following exercise in FA, but who have a history of asthma and/or respiratory allergies may show a greater O_3 toxicity. This contention is supported, in part, by previous observations of heightened sensitivity to low levels of O_3 (<0.25 ppm), evidenced by some patients with significant history of asthma (Silverman, 1979). The latter observed extraordinary sensitivity in 8 of 17 asthmatic patients exposed to 0.25 ppm O_3 for 2 h while at rest. Linn et al (1978), however, found no significant PF impairment upon exposure of asthmatics to 0.20 ppm O_3 for 2 h of light IE. The observations of Linn et al (1978) and Silverman (1979) are not definitive regarding the possibility that asthmatics and/or individuals with a history of respiratory allergies might have a greater sensitivity to O_3, in that studies exposing such individuals to a wide range of O_3 effective doses near that found to result in toxic effects in clinically normal subjects, have not been reported.

Implications of Observations in the Present Study. It is virtually certain that highly trained endurance athletes are not in any way an immune sub-population to the acute toxicity effects of O_3. In fact, our subjects evidenced significant PF impairment and exercise ventilatory pattern alteration at 0.20 ppm, a level not previously shown to demonstrate effects within 1 h in most healthy male subjects exercising at similar relative intensity (~63% $\dot{V}O_2$ max), but at lower absolute workloads which entailed 20% lower $\dot{V}_E$ (Adams et al, 1981). Further, had the athletes been of international caliber, and capable of sustaining $\dot{V}_E$ of 100 $\ell \cdot min^{-1}$, or greater, for periods of 1 to 2¼ h (Adams, 1977; Costill et al, 1973; Maron et al, 1976), significant O_3 toxicity might be anticipated at O_3 levels lower than 0.20 ppm.

There appears to be no clear relationship between aerobic capacity and O_3 sensitivity. Thus, results of the present study indicate that O_3 sensitive endurance athletes will not be able to perform maximally at the lower end of the 1st stage smog alert level (i.e., 0.20 ppm) and, in fact, may experience trouble in maintaining their customary pace in prolonged training sessions. Further, at

the upper end of the 1st stage smog alert level (0.35 ppm O_3), most - if not all - endurance athletes will suffer decrements in maximal performance. It should be emphasized that it is the total O_3 inhaled, i.e., the effective dose, that appears to be the best indicator of O_3 toxicity. Thus, athletes engaged in competition not necessitating high $\dot{V}_E$ will not, in general, be adversely affected for a given exposure duration.

REFERENCES

1. Adams, W.C. Influence of exercise mode and selected ambient conditions on skin temperature. Ann. N.Y. Acad. Sci. 301:110-127, 1977.

2. Adams, W.C., W.M. Savin, and A.E. Christo. Detection of ozone toxicity during continuous exercise via the effective dose concept. J. Appl. Physiol: Respirat. Environ. Exercise Physiol. 51:415-422, 1981.

3. Air Quality and Meteorology. 25(9):16, September, 1979, South Coast Air Quality Management District, El Monte, Calif.

4. Åstrand, P.-O., and K. Rodahl. Textbook of Work Physiology. New York: McGraw-Hill, 1977 (2d edit.), p. 296.

5. Bates, D.V., G.M. Bell, C.D. Burham, M. Hazucha, J. Mantha, L.D. Pengelley, and F. Silverman. Short-term effects of ozone on the lung. J. Appl. Physiol. 32:176-181, 1972.

6. Bates, D.V. Effects of irritant gases on maximal exercise performance. In Exercise Bioenergetics and Gas Exchange. Elsevier North-Holland Biomedical Press, 1980, pp. 337-344.

7. Bedi, J.F., L.J. Folinsbee, S.M. Horvath, and R.S. Ebenstein. Human exposure to sulfur dioxide and ozone: Absence of a synergistic effect. Arch. Environ. Health 34:233-239, 1979.

8. Bell, K., Linn, W., Hazucha, M., Hackney, J., and Bates, D. Respiratory effects of exposure to ozone plus sulphur dioxide in Southern Californians vs. Eastern Canadians. Am. Ind. Hyg. Assoc. J. 38:696-706, 1977.

9. Bennett, G. Ozone contamination of high altitude aircraft cabins. Aerospace Med. 33:969-973, 1962.

10. Buckley, R.D., J.H. Hackney, K. Clark, and C. Posin. Ozone and human blood. Arch. Environ. Health 30:40-42, 1975.

11. Clamann, H., and R. Bancroft. Toxicity of ozone in high altitude flight. Advan. Chem. 21:352-359, 1959.

12. Committee on Medical and Biologic Effects of Environmental Pollutants: Ozone and Other Photochemical Oxidants. National Academy of Sciences, 1977, pp. 280-436.

13. Consolazio, C.F., R.E. Johnson, and L.J. Pecora. Physiological Measurements of Metabolic Functions in Man. New York:McGraw-Hill, 1963, pp. 5-9.

14. Costill, D.L., H. Thomason and E. Roberts. Fractional utilization of the aerobic capacity during distance running. Med. Sci. Sports. 5:248-252, 1973.

15. DeLucia, A.J., and W.C. Adams. Effects of O_3 inhalation during exercise on pulmonary function and blood biochemistry. J. Appl. Physiol: Respirat. Environ. Exercise Physiol. 43:75-81, 1977.

16. DeLucia, A.J., M.G. Mustafa, C.E. Cross, C.G. Plopper, D.L. Dungworth, and W.S. Tyler. Biochemical and morphological alterations in the lung following O_3 exposure. In: Air. I. Pollution Control and Clean Energy, edited by C. Rai and L.A. Spielman. A. I. Ch. E. Symp. Ser. 71:93-100, 1975.

17. DeMore, W.B., J.C. Romanovsky, M. Feldstein, W.J. Hamming, and P.K. Mueller. Interagency comparison of iodometric methods of ozone determination. In: Calibration in Air Monitoring. ASTM Technical Publication No. 598. Philadelphia: American Society for Testing and Materials, 1976, pp. 131-143.

18. Dressendorfer, R.H., C.E. Wade, and E.M. Bernauer. Combined effects of breathing resistance and hyperoxia on aerobic work tolerance. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 42:444-448, 1977.

19. Drinkwater, B.L., P.B. Raven, S.M. Horvath, J.A. Gliner, R.O. Ruhling, N.W. Bolduan, and S. Taguchi. Air pollution, exercise and heat stress. Arch. Environ. Health 28:177-181, 1974.

20. Edwards, A.L. Statistical Methods for the Behavioral Sciences. Holt, Rinehart, and Winston, New York, 1960, pp. 136-140.

21. Fairchild, E.J. Neurohumoral factors in injury from inhaled irritants. Arch. Environ. Health 6:79-86, 1963.

22. Folinsbee, L.J., B.L. Drinkwater, J.F. Bedi, and S.M. Horvath. The influence of exercise on the pulmonary function changes due to low concentrations of ozone. In: Environmental Stress. (L.J. Folinsbee et al, editors). New York: Academic Press, 1978a, pp. 125-145.

23. Folinsbee, L.J., S.M. Horvath, J.F. Bedi, and J.D. Delehunt. Effect of 0.62 ppm NO_2 on cardiopulmonary function in young male nonsmokers. Environ. Res. 15:199-205, 1978b.

24. Folinsbee, L.J., F. Silverman, and R.J. Shephard. Exercise responses following ozone exposure. J. Appl. Physiol. 38:996-1001, 1975.

25. Folinsbee, L.J., F. Silverman, and R.J. Shephard. Decrease of maximum work performance following O_3 exposure. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 42:531-536, 1977.

26. Golden, J.A., J.A. Nadel, and H.A. Boushey. Bronchial hyperirritability in healthy subjects after exposure to ozone. Am. Rev. Respir. Dis. 118:287-294, 1978.

27. Goldsmith, J.R., and J.A. Nadel. Experimental exposure of human subjects to ozone. J. Air Pollut. Control Assoc. 19:329-330, 1969.

28. Hackney, J.D., W.S. Linn, D.C. Law, S.K. Karuza, H. Greenberg, R.D. Buckley, and E.E. Pederson. Experimental studies on human health effects of air pollutants. III. Two-hour exposure to ozone alone and in combination with other pollutant gases. Arch. Environ. Health 30:385-390, 1975.

29. Hazucha, M., and D.V. Bates. Combined effects of ozone and sulphur dioxide on human pulmonary function. Nature 257:50-51, 1975.

30. Hazucha, M., F. Silverman, C. Parent, S. Field, and D.V. Bates. Pulmonary function in man after short-term exposure to ozone. Arch. Environ. Health 27:183-188, 1973.

31. Holub, R., M.S. Morgan, R. Frank, and P. Meyer. Ozone induced changes in arterial O_2 saturation, pulmonary mechanics and distribution of ventilation in healthy man. Am. Rev. Respir. Dis. 117:242, 1979.

32. Horvath, S.M., J.A. Gliner, and J.A. Matsen-Twisdale. Pulmonary function and maximum exercise responses following acute ozone exposure. Aviat. Space Environ. Med. 50:901-905, 1979.

33. Jaffe, L.S. Photochemical air pollutants and their effects on men and animals. II. Adverse effects. Arch. Environ. Health 16:241-255, 1968.

34. Jones, N.L., E.J.M. Campbell, R.H.T. Edwards, and D.G. Robertson. Clinical Exercise Testing. Philadelphia: W.B. Saunders Co., 1975.

35. Kindya, R.J., and P.C. Chan. Effect of ozone on erythrocyte membrane adenosine triphosphate. Biochim Biophys Acta 429:608-615, 1976.

36. Lefcoe, N.M. The time course of maximum ventilatory performance during and after moderately severe heavy exercise. Clin. Sci. 36:47-52, 1969.

37. Linn, W.S., R.D. Buckley, C.E. Spier, R.L. Blessey, M.P. Jones, D.A. Fischer, and J.D. Hackney. Health effects of ozone exposure in asthmatics. Am. Rev. Respir. Dis. 117:835-843, 1978.

38. Man In t Veld, A., and H. Zeedijk. The effect of ozone on the physical working capacity of athletes. Tijdschr. Soc. Geneesk. 50:441-445, 1972.

39. Maron, M.B., S.M. Horvath, J.E. Wilkerson, and J.A. Gliner. Oxygen uptake measurement during competitive marathon running. J. Appl. Physiol. 40:836-838, 1976.

40. Menzel, D.B. Toxicity of ozone, oxygen, and radiation. Ann. Rev. Pharmacol. 10:379-394, 1970.

41. Menzel, D.B., R.J. Slaughter, A.M. Bryant, and H.Q. Jaurequi. Heinz bodies formed in erythrocytes by fatty acid ozonides and ozone. Arch. Environ. Health 30:296-301, 1975.

42. Mosher, J.C., W.G. MacBeth, M.J. Leonard, T.P. Mullins, and M.F. Brunelle. The distribution of contaminants in the Los Angeles Basin resulting from atmospheric reactions and transport. J. Air Pollut. Control Assoc. 20:35-42, 1970.

43. Paproski, D.M., and J.R. Walker. Air Quality in Canadian Urban Areas. Discussion Paper 18. Ottawa: Economic Council of Canada, 1974.

44. Pugh, L.G.C.E. Oxygen intake in track and treadmill running with observations on the effect of air resistance. J. Physiol. 207:823-835, 1970.

45. Raven, P.B., B.L. Drinkwater, R.O. Ruhling, N. Bolduan, S. Taguchi, J. Gliner, and S.M. Horvath. Effect of carbon monoxide and peroxyacetyl nitrate on man's maximal aerobic capacity. J. Appl. Physiol. 36:288-293, 1974.

46. Savin, W.M., and W.C. Adams. Effect of ozone inhalation on work performance and Vo_2 max. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 46:309-314, 1979.

47. Silverman, F. Asthma and respiratory irritants (ozone). Environ. Health Perspect. 29:131-136, 1979.

48. Silverman, F., L.J. Folinsbee, J. Barnard, and R.J. Shephard. Pulmonary function changes in ozone-interaction of concentration and ventilation. J. Appl. Physiol. 41:859-864, 1976.

49. Stokinger, H.E., and D.L. Coffin. Biological effects of air pollutants. In: Air Pollution, edited by A.C. Stern. New York: Academic, 3rd edition, 1968, Vol. 1, pp. 401-456.

50. Stokinger, H.E., W. Wagner, and P. Wright. Studies of ozone toxicity. 1. Potentiating effects of exercise and tolerance development. AMA Arch. Ind. Health 14:158-162, 1956.

51. Watanabe, S., R. Frank, and E. Yokoyama. Acute effects of ozone on lungs of cats. 1. Functional. Am. Rev. Respir. Dis. 108:1141-1151, 1973.

52. Wayne, W., P. Wehrle, and R. Carroll. Oxidant air pollution and athletic performance. J. Am. Med. Assoc. 199:901-904, 1967.

53. Wilmore, J.H. A simplified method for determination of residual lung volumes. J. Appl. Physiol. 27:96-100, 1969.

54. Wilmore, J.H., and D.L. Costill. Semiautomated systems approach to the assessment of oxygen uptake during exercise. J. Appl. Physiol. 36:618-620, 1974.

55. Yokoyama, E., and R. Frank. Respiratory uptake of ozone in dogs. Arch. Environ. Health 25:132-138, 1972.

56. Young, W.A., D.B. Shaw, and D.V. Bates. Effects of low concentrations of ozone on pulmonary function in man. J. Appl. Physiol. 19:765-768, 1964.

GLOSSARY OF TERMS, ABBREVIATIONS AND SYMBOLS

ANOVA	Analysis of Variance
CARB	California Air Resources Board
CE	Continuous Exercise
CO	Carbon Monoxide
DL_{CO}	Lung Diffusion for Carbon Monoxide
ED	Effective Dose
FA	Filtered Air
FEF_{25-75}	Forced Expiratory Flow Between 25-75 Percent of FVC
$FEV_{1.0}$	Forced Expiratory Volume at 1 sec
F_R	Respiratory Frequency
FVC	Forced Vital Capacity
HR	Heart Rate
IE	Intermittent Exercise
NO_2	Nitrogen Dioxide
O_3	Ozone
PAN	Peroxyacetyl Nitrate
PC	Parkinson-Cowan
PF	Pulmonary Function
ppm	Parts per Million
ppm·L	Parts per Million x Liters
RV	Residual Volume
SaO_2	Arterial Saturation with Oxygen
SD	Standard Deviation
SO_2	Sulfur Dioxide
TLC	Total Lung Capacity
$\dot{V}_A$	Alveolar Ventilation
$\dot{V}_A/\dot{Q}$	Ventilation to Perfusion Ratio
VC	Vital Capacity
V_D	Dead Space Volume
V_D/V_T	Dead Space Volume to Tidal Volume Ratio
$\dot{V}_E$	Expiratory Ventilation Volume
$\dot{V}o_2$	Oxygen Uptake
$\dot{V}o_{2max}$	Maximal Oxygen Uptake Volume
V_T	Tidal Volume

APPENDIX

Subjective Symptoms Report

Human Subjects Informed Consent Form

Subjective Symptoms Report

Exposure Date: Time:

Subject:

We would like you to assist in our evaluation of the effects of O_3 inhalation on human subjects performing exercise. This you can provide by noting below: (1) Which symptoms you noticed during your exercise today, (2) Designating your own subjective feeling of the severity of these disturbances, and (3) Logging (to your recollection) an approximate time of onset. In addition, you are requested to rate the difficulty of today's testing compared to the others (if any) of this experiment which you have participated in.

Symptom	No	Yes (+, mild to ++++, severe)	Time of Onset (min. into ride)
Shortness of breath			
Cough			
Excessive sputum			
Throat tickle			
Raspy throat			
Wheezing			
Congestion			
Headache			
Nausea			
Other (describe completely)			

In your opinion, did today's experiment involve O_3 inhalation?

Competitive simulation only: In your opinion, given your present subjective symptoms, do you feel that in an actual competitive situation you could perform maximally?

Title of Study: Effects of Sustained Near-Maximal Exercise on Ozone Toxicity in Highly Trained Endurance Athletes.

Principal Investigator: William C. Adams
Department of Physical Education

Telephone No.: 752-0511

INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

You are being invited to participate in a physiological study to determine the effects of sustained near-maximal exercise on ozone (O_3) toxicity as measured by standard pulmonary function tests. The purposes of this study as well as the procedures used, will be explained, in general, before your first visit to the laboratory.

During your first visit to the laboratory we will discuss each aspect of the experiment as you view the equipment. The principal investigator, or his trained assistant, will answer your questions, and give you an opportunity to practice performing several standard pulmonary function measurements while at rest.

If you decide to participate, you will go through a series of preliminary tests to determine baseline characteristics. This will involve height and weight determinations, as well as body composition determination via hydrostatic weighing, where you will briefly (10-15 sec) immerse completely in water, exhaling all the air from your lungs, while your weight is taken. The immersion test also requires that your residual lung volume be determined, which is done by having you breathe forcefully two-three times through a respirometer for 15-30 seconds. A second preliminary test you will undergo is a bicycle ergometer test to determine your aerobic capacity, or maximal oxygen uptake. During this test (lasting from 12-20 min) you will ride the electric resistance ergometer at gradually intensified workloads every 2 minutes until you reach a point of volitional fatigue. You will be breathing through a mouthpiece so that expired gas volumes can be collected and analyzed. Your heart rate will also be monitored throughout this test, through chest leads to an electrocardiograph. After a brief rest, you will then practice riding at lower workloads for 20-30 minutes while breathing filtered air supplied to you by a special air mixing apparatus to be used in the subsequent experimental protocols. This orientation and baseline characteristics testing session will require about two hours.

There are six experimental protocols in which you will be asked to ride the bicycle ergometer for one hour while inhaling filtered air or one of two O_3 concentrations. Three of these will be "race" protocols with sequence of workloads at which you will ride designed to mimic a cross country warm up and race. The initial light workload, equivalent to a 7:00-8:00/mile jog will last for 10 minutes. It is immediately followed by a series of seven "pick-ups" (i.e., heavy workloads of one minute duration with at least one minute of rest between them). You will be allowed seven minutes rest, and then the "race" begins. This consists of one half hour of riding at approximately 90% of your maximal level. In addition, you will be asked to ride the bike for three continuous, one hour bouts at a single workload comparable to your running training pace.

You may experience some temporary dryness of the throat and muscular soreness during exercise. During some of the protocols you will be supplied filtered air only (no O_3), while during the others, you will receive filtered air containing O_3 concentrations of 0.25 or 0.35 parts per million (ppm). You will perform the protocols in random order without being told which of the above air mixtures you are receiving.

00002915
ASSET

Human Subjects Protocol # _____

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Principal Investigator: William C. Adams
Department of Physical Education

Telephone No.: 752-0511

A special mixing apparatus with constant monitoring of O_3 concentration, insures that you will not inhale concentrations other than those specified. Ozone may cause you to feel some substernal soreness, chest tightness, or other ill effects such as dizziness, wheezing, and coughing. Other researchers have found that individuals vary in their sensitivity to O_3. The levels of O_3 you will receive are equal to and above the level at which smog alerts are called and exercise is discouraged. However, you will not be verbally encouraged to continue any exposure beyond your volitional endpoint. Furthermore, at the low levels used in this study, any symptoms would be expected to disappear within 2-24 hours. At least three days will intervene between tests.

During exercise your heart rate and ventilatory parameters will be measured periodically. Immediately before and after each experimental protocol, you will be asked to perform several standard pulmonary function tests on a spirometer. After each experimental protocol, you will be asked to complete a brief O_3 inhalation subjective symptoms report form. There are no attendant risks in these pulmonary function procedures. The total time involved for each experimental protocol will be 1½ hours.

Although you have been selected for this study because you are an endurance trained athlete with a high work capacity, you should be aware that cycling makes its principal demands on some muscles not receiving prime stress during running. Thus we are asking that you modify your present training program to include several vigorous cycling workouts during the two weeks before your first ride. You are welcome to use the bicycle ergometers available in our laboratory for your training, or you may train out of doors on your own bike.

Possible benefits you may receive as a result of participation in this study will include identification of your fitness state, as reflected by the graded exercise test and the body composition determination. Your tolerance to O_3, as measured by ventilatory function during exercise and pulmonary function differences pre- and post-exposure, should provide helpful information to guide your actions when exposed to significant ambient smog conditions. At the conclusion of the study, you will be given a written summary of the results and a statement regarding their meaning. It is understood that you will not receive any financial renumeration for participating in this investigation.

The information obtained on you during the course of this study will be privileged and confidential to the full extent of the law and will be disclosed only with your permission. The information obtained may be used for a statistical or scientific purpose with your right of privacy retained.

The University has a specific policy on medical treatment for injuries resulting from participation in research. The University does not provide any other form of compensation in the event of injury.

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Department of Physical Education

Telephone No.: 752-0511

Your decision whether or not to participate will not prejudice your future relations with the investigator, the Physical Education Department, or the Human Performance Laboratory. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without prejudice.

If you have any questions, please ask. If you have additional questions later, you may contact W.C. Adams at 752-0511.

This research project has been reviewed by the Human Subjects Review Committee of the University of California, Davis, which was established for the protection of research participants. You may request information from this committee in regard to any research which involves volunteer participants. You may also seek assistance, should the need arise, by calling (916) 752-2075, or writing to the Human Subjects Review Committee, 275 Mrak Hall, University of California, Davis, 95616. You need not identify yourself if you prefer.

You will be given a signed and dated copy of this form to keep.

YOU ARE MAKING A DECISION WHETHER OR NOT TO PARTICIPATE. YOUR SIGNATURE INDICATES THAT YOU HAVE DECIDED TO PARTICIPATE, HAVING READ THE INFORMATION PROVIDED ABOVE.

_____ Date

_____ Signature of Participant

_____ Signature of witness to consent process

_____ Signature of investigator providing information for consent process