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COMPARISON OF CHAMBER AND FACE-MASK 6.6-HOUR EXPOSURES TO OZONE ON PULMONARY FUNCTION AND SYMPTOMS RESPONSES

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Because of increased interest in an 8-h ozone (O_3) federal air quality standard, acute pulmonary function responses to prolonged square-wave O_3 exposure between 0.08 and 0.12 ppm have been examined in several U.S. Environmental Protection Agency (EPA) chamber studies. A low-cost face-mask O_3 exposure system was developed in this laboratory and found to produce closely similar pulmonary responses to those observed in prolonged exposures by U.S. EPA investigators. The primary purpose of the present study was to investigate the pulmonary function and subjective symptoms effects of 6.6-h square-wave exposure to 0.12 ppm O_3 by these two methods using the same group of subjects. In addition, further investigation of pulmonary function and symptoms responses upon 6.6-h exposures to lower levels of O_3 (0.04–0.08 ppm) were studied with the face-mask inhalation system. Thirty young adult subjects completed five 6.6-h exposures with six 50-min periods of exercise at an intensity requiring a minute ventilation rate (V_E) of ~20 L/min/m² of body surface area, each followed by 10 min of rest, except following 3 h when the rest period was lengthened for a lunch break. The total O_3 doses for the chamber and face-mask exposures to 0.12 ppm O_3 were not significantly different from each other, since the additional O_3 dose during the 35 min lunch break in the chamber exposure was offset by a slightly lower average exercise V_E (i.e., 19.1 L/min/m²). The data convincingly demonstrated that the two methods of exposing young adults to nearly identical total inhaled O_3 doses at 0.12 ppm produce very similar pulmonary function, symptoms, and exercise ventilatory pattern responses. On the other hand, results of the 6.6-h face-mask exposures to 0.08 ppm O_3 in the present study, compared to similar U.S. EPA exposure study results, revealed several incongruities that may be due primarily to high individual subject variability in responses to a relatively low O_3 exposure. Thus, a comparison of chamber exposure responses to those elicited via face-mask exposure to 0.08 ppm O_3 in the same subject group seems warranted.

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With the advent of interest in establishing an 8-h ozone (O_3) standard (Rombout et al., 1986), the U.S. Environmental Protection Agency (EPA) developed a prolonged exposure protocol (Folinsbee et al., 1988). These investigators studied O_3-induced pulmonary responses in humans at 0.12 ppm with a substantial amount of quasi-continuous exercise over a 6.6-h exposure. The basic protocol entailed a chamber square-wave O_3 exposure throughout, with 50 min of exercise at a mean minute ventilation rate (V_E) of ~40 L/min, that is, an equivalent ventilation rate (EVR) of 20 L/min/m^2 of body surface area (BSA), and 10 min rest during each hour for the first 3 h. A 35-min lunch break then occurred, followed by a second 3-h exposure as described for the first 3 h. Using the same 6.6-h protocol, other chamber exposure studies were conducted by U.S. EPA investigators (Horstman et al., 1990; McDonnell et al., 1991) with human subjects who were exposed to relatively low square-wave O_3 concentration profiles (0.08 to 0.12 ppm).

Due to the expense of building and operating an air pollution chamber, a Teflon-coated stainless-steel respiratory-valve obligatory mouthpiece inhalation method was developed in this laboratory (DeLucia & Adams, 1977). Because subjects felt that 2 h of continuous exposure via the obligatory mouthpiece inhalation system was near the maximum time they could tolerate this type of exposure system (McKittrick & Adams, 1995), a silicone rubber face mask (with Teflon coating overlay on the inner surface) exposure system was developed in this laboratory and first tested for periods up to 4 h (Adams, 1996). The face-mask inhalation system was well tolerated by all subjects, with each subject indicating upon questioning that 6.6-h exposures with this system would be feasible. Further, during the 4-h O_3 exposures, subjects were able to remove the face mask (whose inlet was stoppered to prevent O_3 delivery into the ambient air) at the end of each hour, complete two or three maximal forced expiratory maneuvers, remove the stopper from the face mask, and reposition it for continued O_3 exposure, all within 3 min.

In a study of 30 young adult subjects (15 of each gender) in this laboratory (Adams, 2000b) a face-mask exposure at the same square-wave O_3 concentration (i.e., 0.12 ppm) and mean exercise V_E (20 L/min/m^2 BSA) as the U.S. EPA 6.6-h exposure protocol was completed. Mean postexposure $FEV_{1.0}$ decrement was –13.6%, which was intermediate to the –13 to –15% group mean responses obtained in the U.S. EPA studies by Folinsbee et al. (1988) and Horstman et al. (1990). However, comparison of results across studies, even at equivalent O_3 concentration, V_E, and exposure time, is somewhat precarious as a large variation in individual pulmonary function response to a given O_3 exposure has been observed (Adams et al., 1981; Folinsbee et al., 1978; Kulle et al., 1985; McDonnell et al., 1983). These differences in response to a given O_3 exposure among individuals have been shown to be reproducible (Folinsbee, 1981; Gliner et al., 1983; McDonnell et al., 1985), indicating that some individuals are consistently more responsive to O_3 than others. McDonnell et al. (1985) concluded that this large intersubject vari-

ability in response is due to the difference in intrinsic responsiveness of individual subjects to O_3 exposure, although the factors that contribute to this variability remain poorly defined.

Horstman et al. (1990), utilizing the standard 6.6-h chamber protocol, observed a significantly reduced $FEV_{1.0}$ after 3 h of exposure to 0.12 ppm O_3, 4.6 h at 0.10 ppm, and 5.6 h at 0.08 ppm, indicating an interrelationship between duration of exposure and O_3 concentration. Utilizing the same 6.6-h protocol, McDonnell et al. (1991) also observed significant pulmonary function and symptoms responses following exposure to 0.08 ppm O_3. However, until recently (Adams, 1998), no 6.6-h exposures to O_3 concentrations less than 0.08 ppm (other than filtered air, FA) have been completed. In this study of a 6.6-h face-mask exposure to 0.06 ppm O_3, with exercise V_E of 23 L/min/m^2, no statistically significant differences in pulmonary function or symptoms responses from those observed for the FA exposure were observed. However, the group average $FEV_{1.0}$ and total symptoms score (TSS) responses, respectively, were numerically greater after 4 h for the 0.06 ppm exposure than for the FA exposure. Further, 6 of 30 subjects had $FEV_{1.0}$ decrements of >10%. Notable effects of exposure to 0.06 ppm O_3 observed in this study in some subjects, together with the observation of no significant effects of exposure to 0.08 ppm at a low exercise EVR (i.e., 10.9 L/min/m^2) in an earlier face-mask study (Adams & Ollison, 1997), suggest a need for 6.6-h exposures to O_3 concentrations between 0.04 and 0.08 ppm with an exercise EVR of 20 L/min/m^2.

Breathing through a face mask presents an "artificial burden" to the subject and might change the "natural" breathing pattern achieved with chamber exposure systems. Further, the additional dead space of the face mask (97 ml), though small, might reduce O_3 delivery to the respiratory tract (Gerrity et al., 1988). However, a face-mask system enables continuous monitoring of a subject's breathing rate, thus permitting continuous adjustments to be made to cycle ergometer resistance or treadmill speed/grade to maintain close control of a constant V_E. As a result, subject dose is known more precisely than in typical chamber studies where V_E is measured only a few minutes of each hour. Thus, direct validation of the face-mask exposure system against the generally accepted "gold standard" chamber exposure system seems warranted.

The primary purpose of the present study was to investigate pulmonary function and symptoms effects of 6.6-h exposure to 0.12 ppm O_3 by two methods: (1) nearly continuous breathing through a face mask and two-way breathing valve secured by Velcro straps attached to a cloth mesh head cap; and (2) unencumbered continuous breathing of controlled air mixtures inside a stainless-steel air pollution chamber. In addition, further investigation of pulmonary function and symptoms responses upon 6.6-h exposures to lower concentrations of O_3 (0.04 and 0.08 ppm) were studied with the face-mask inhalation system.

METHODS

Subjects

Thirty young adults, 15 of each gender, who were nonsmokers and had not lived in an area for 6 months where the State of California air quality standard for O_3 (0.09 ppm) was exceeded, served as subjects. Subjects were solicited volunteers from the University of California, Davis, or the surrounding community. They were screened for absence of asthma or significant allergies, and had normal baseline pulmonary function. Prospective participants read an Institutional Review Board-approved informed consent form, were shown the equipment used in the study, and had any questions answered before signing the consent form.

Subject Orientation

Each subject participated in a 1¼-h orientation session in which each first had his or her height and body weight measured. Following performance of at least three maximum forced expiratory maneuvers, each subject then pedaled an electronically braked cycle ergometer (Quinton, model 845) at 3 or 4 work rates for at least 3 min each until each reached a steady-state V_E of ~20 L/min/m^2 of BSA. Following ~5 min rest, each then walked on a motor driven treadmill (model 14-44A, Quinton Instruments, Seattle, WA) at 3.4 miles per hour (mph), at 2 to 3 grades between 1 and 8% for at least 3 min each until a steady-state V_E of ~20 L/min/m^2 was achieved. During exercise, V_E determinations were made via the subject wearing a Hans Rudolph translucent silicone rubber face mask (whose inside surface was lined with a Teflon overlay), to which a two-way non-rebreathing nylon plastic valve was attached (Adams, 2000a). Inspired FA was provided via the O_3 delivery system described later. Heart rate (HR) was monitored via an electrocardiograph R-wave detector. The subject then walked to another section of the laboratory and entered a stainless-steel environmental chamber (model 1328-M, Vista Scientific, Ivyland, PA). While breathing FA through a Teflon-coated respiratory valve (Hans Rudolph, Kansas City, MO) with mouthpiece and noseclip, the subject pedaled an electronic cycle ergometer (Monark model 829E, Varberg, Sweden) at 2 or 3 work rates for at least 3 min each until each reached a steady-state V_E of ~20 L/min/m^2. Following ~5 min rest, the subject then walked on a motor-driven treadmill (Odyssey LSD, Bodyguard Fitness, Hackensack, NJ) at 3.4 mph, at 1 or 2 grades between 3 and 8% for at least 3 min, each until a steady-state V_E of ~20 L/min/m^2 was achieved. Each orientation session was completed with the performance of at least two maximum forced expiratory maneuvers.

Experimental Design and Protocols

Five exposures were completed by each subject, including: (1) a repeat of the Folinsbee et al. (1988) 6.6-h protocol entailing a square-wave chamber exposure to 0.12 ppm O_3, with six 50-min exercise bouts at a mean

equivalent ventilation rate (EVR) of ~20 L/min/m^2; (2) the same 6.6-h chamber protocol while exposed to FA; (3) the same 6.6-h 0.12 ppm O_3 protocol, except that the face-mask exposure system utilized in earlier studies in this laboratory was used; (4) the same face-mask 6.6-h protocol while exposed to 0.08 ppm O_3; and (5) the same face-mask 6.6-h protocol while exposed to 0.04 ppm O_3. Because a 6.6-h FA face mask inhalation exposure had been done in a previous study utilizing a group of young adults with near identical body size and baseline pulmonary function (Adams, 2000b), an FA control exposure was done only in the chamber (protocol 2) in the present study. The 50-min exercise bouts for each exposure were done alternately each hour, first on the cycle ergometer and then on the treadmill. The exposures were conducted in single-blind fashion and completed by each subject in near-random order, with a minimum of 4 days intervening between each (Schonfeld et al., 1989).

During the face-mask protocols, subjects were exposed for 60 consecutive minutes, followed by 3 min without the face mask (and thus, without O_3 exposure) to obtain 2–3 maximal forced expiratory maneuvers. Further, after 3.1 h, the subject was not exposed for 24 min, during which pulmonary function measurements were first obtained, followed by rest-room use, fluid replenishment, and a brief lunch break. This was followed by a second 3.1-h exposure as described earlier. Thus, V_E was measured nearly continuously during the face-mask protocols, with only a 3-min break for measurement of pulmonary function each hour and 21 min for a lunch break. It is estimated that the 36 min when the subject was not exposed to O_3 (all while at rest) resulted in a V_E of less than 4% of the total ventilation (V_{tot}) during the 6 h of actual O_3 exposure.

During the chamber protocols, subjects breathed the air mixture provided continuously according to the standard U.S. EPA prolonged exposure protocol (Folinsbee et al., 1988). During these exposures, V_E was measured between 8 and 12 min and between 45 and 49 min in the first and second hours, and only between 45 and 49 min of each hour thereafter. Ventilation minute volume was not measured during rest in the chamber protocols. Subjects were permitted to exit the chamber to use a nearby rest room anytime during rest periods (mean nonexposure time = 2.5 min; range = 0–6 min).

Face-mask exposures were conducted in a laboratory room in which dry bulb temperature and relative humidity were maintained at 21–25°C and 40–60%, respectively. In the chamber (2.45 m × 2.45 m × 2.39 m), temperature was controlled at 23 ± 1.0°C and relative humidity at 50 ± 10%. In both locations, ail-flow between 1 and 2 m/s was directed at the subject's frontal aspect during exercise by a small industrial-grade fan (model 9318. Air King Ltd., Brampton, Ontario, Canada) mounted on a wall.

Pulmonary Function Measurements

During the face-mask protocols, subjects performed two to four forced maximal expiratory maneuvers immediately before and after each experi-

mental exposure. In addition, following each hour during the 6.6-h exposures, subjects removed the face mask (which was then plugged at the inlet with a rubber stopper) for 3 min and performed 2 or 3 maximal forced expiratory maneuvers. The rubber stopper was then removed and the subject was assisted in reattaching the face mask to the cloth mesh head cap to continue the exposure. Online measurements of forced vital capacity (FVC), $FEV_{1.0}$ and forced expiratory flow rate in the middle half of FVC ($FEF_{25-75\%}$) were made with a data collection system consisting of a 10-L module spirometer (model 3000, Collins, Braintree, MA), which was interfaced to a modified Lab View software package (National Instruments. Austin, TX) supported by a Macintosh-compatible Power Center 120 computer (Power Computing Corp., Round Rock, TX). A printout of these data was obtained following each exposure. During the chamber protocols, subjects performed 2 to 4 forced expiratory maneuvers immediately before and after each experimental exposure, as well as during the last 3 min of each hour. Measurements of FVC and $FEV_{1.0}$ were made with a UCI-500 spirometry system (Vacumetrics, Ventura, CA). If the sums of the FVC and $FEV_{1.0}$ values for the first 2 maneuvers were within 200 ml of each other, the mean for each was used in statistical analyses. If not, then additional maneuvers were performed until this criterion was met for any two maneuvers.

Exercise and Resting Measurements

During face-mask exposures, minute-by-minute respiratory metabolism and V_E values were obtained with data acquisition instruments interfaced to the modified Lab View software package, supported by the Macintosh-compatible Power Center 120 computer. These instruments included an Alpha Technologies turbotachometer ventilation measurement module (VMM-2; Sensor Medics, Anaheim, CA), an LB-2 carbon dioxide (CO_2) analyzer (Beckman Instruments, Fullerton, CA), an S-3A oxygen (O_2) analyzer (Applied Electrochemistry, Pasadena, CA), an electrocardiograph R-wave detector, and a temperature thermistor located in the expired gas line. Minute-by-minute values for V_E, HR, tidal volume (V_T), respiratory frequency (f), percent O_2 and CO_2 in expired gas, expired gas temperature, and oxygen uptake (VO_2) were displayed each 15 s on an Apple Multiple Scan 15 monitor interfaced to the Power Center 120 computer. The prescribed EVR during exercise for each face mask protocol was maintained near constant by monitoring the minute-by-minute V_E values and adjusting the cycle ergometer resistance or treadmill grade as necessary.

In the chamber, data acquisition instruments interfaced to the same Lab View software package, supported by a second Macintosh-compatible Power Center 120 computer, included a VMM-400 ventilation measurement module (Interface Associates, Aliso Viejo, CA), a CD3A CO_2 analyzer (Applied Electrochemistry, Pasadena, CA), an OM-11 O_2 analyzer (Beckman Instruments, Fullerton, CA), an electrocardiograph R-wave detector, and a temperature thermistor located in the expired gas line. When the subject breathed

through a Teflon-coated respiratory valve with mouthpiece and noseclip, minute-by-minute values for V_E, V_T, f, percent O_2 and CO_2 in expired gas, expired gas temperature, and VO_2 were displayed each 15 s on an Apple Multiple Scan 15 monitor interfaced to the Power Center 120 computer. This occurred at 8–12 min and 45–49 min during the first and second hours. If V_E was more than 2 L/min above or below the subject's target value, the cycle ergometer work rate or treadmill grade was adjusted. Thereafter, exercise data acquisition occurred only at 45–49 min of each hour. If the total mean V_E at the end of each hour was more than 1 L/min above or below the target value, the cycle ergometer work rate or treadmill grade was adjusted at the beginning of exercise during the following hour. Minute-by-minute HR values were obtained every 15 s throughout the exposure.

In both locations, symptoms were monitored initially after 8 min; thereafter, they were evaluated during the next to the last minute of each exercise bout. In each case, subjects were asked to rate the severity of each of four symptoms—throat tickle, cough, shortness of breath, and pain on deep inspiration (PDI)—by pointing to a visual display. Each symptom was rated according to a severity scale (ranging from 0 [not present] to 40 [incapacitating] previously described (Adams et al., 1987). Total symptoms score was calculated as the sum of the ratings for the four individual symptoms.

O_3 Administration and Monitoring

All air mixtures inhaled by the subject during face-mask exposures were generated by mixing the appropriate amounts of air filtered via a Barneby–Cheney charcoal filter with ozonized dry purified cylinder O_2 generated by a Sander ozonizer (Type II). The air mixture was delivered to the subject via a Hans Rudolph (Kansas City, MO) two-way non-rebreathing nylon plastic valve attached to a translucent silicone rubber face mask. The inner surface of the face mask was covered with a Teflon overlay wrapping (Bytac; Norton Corp., Akron, OH). The subject's expired air was directed through a 5-L stainless-steel mixing and sampling chamber to the Alpha Technologies turbotachometer ventilation measurement module. It was then combined with the pollutant air mixture not inspired by the subject, passed through a Barneby–Cheney QDF multistage filter assembly, and then passed to the laboratory ventilation exhaust outlet.

The stainless-steel environmental chamber is a closed system with provision for damper-controlled fresh air intake. The damper controls the cross-sectional area of an 8-in-diameter duct. The damper is adjusted so that approximately 20% of the cross-sectional area of the duct is open to room air. After entering, the room air is mixed with air returning from the chamber. This air passes through two chemisorbant filters (Purafil Chemisorbent Media, Doraville, GA), a particle filter, through the blower, and over the humidifier, dehumidifier, cooling, and heating coils in succession. This FA is returned to the chamber through an 8-in × 12-in sheet metal duct. O_3 is introduced into this duct ~2 m prior to its outlet into the chamber. During

the O_3 chamber exposures, a known concentration of O_3 was generated by passing dry purified cylinder O_2 through an ozonizer (Sander model 200, Sander Aquarientechnik, Am Ostenberg, Germany). The O_3 was drawn through Teflon tubing into the chamber. During the FA chamber exposure, the O_2 tank and ozonizer were off. The filter system of the chamber ensured that even with low O_3 concentrations in the laboratory, measured O_3 in the chamber was <0.004 ppm throughout the FA exposure.

During face-mask exposures, appropriate levels of O_3 were maintained by continuous sampling from the inspiratory side of the Hans Rudolph valve and face mask assembly, through 0.64-cm inner diameter Teflon tubing, connected to an O_3 monitor (model 1003-AH; Dasibi, Glendale, CA). In the chamber, sampling occurred through 0.64-cm inner diameter Teflon tubing connected to another Dasibi O_3 monitor; the sample tubing outlet in the chamber was located on a wall at a height of ~1 m from the floor. Continuous measurement of O_3 was accomplished in both locations by an online data acquisition system with minute-by-minute averages obtained from the voltage output generated by the Dasibi monitor. The Dasibi monitors were calibrated before and after the study (change <0.003 ppm O_3 within the range used), using the ultraviolet (UV) absorption photometric method, at the Primate Research Center, University of California, Davis.

Subject Characterization

Upon completion of all experimental exposures, each subject was characterized in terms of body composition and maximal aerobic capacity (VO_{2max}). Body composition was determined by hydrostatic weighing as described elsewhere (Madsen et al., 1998). VO_{2max} was determined by a progressively incremented cycle ergometer (model 800S, Sensormedics, Yorba Linda, CA) test to volitional exhaustion (Adams & Schelegle, 1983). Pedal frequency was set at 70 full revolutions/min, with progressive increments in resistance of 20 to 30 W effected every 2 min, starting with 120–130 W for females and 150–170 W for males. A plateau in VO_2 (i.e., less than 0.10 L/min increase with the last work rate increment equivalent to between 0.25 and 0.30 L/min) was used to ensure that VO_{2max} was achieved (McArdle et al., 1996, pp. 198–200).

Statistical Procedures

Minute-by-minute V_E values were added separately for exercise and rest periods of each exposure, with separate averages for V_{tot} calculated for each subject, and then for the whole group. The latter, together with exposure duration and mean O_3 concentration, was used to determine the group mean total inhaled O_3 dose for each protocol. Duplicate (occasionally, triplicate) spirometric volumes and flows for pre- and postexposure, and at hourly intervals during the 6.6-h protocols, were obtained. The treatment effect was determined as percent change from the preexposure value. Similarly, values taken at the 8th to 10th minute of the first exercise bout

(i.e., "initial" value) and the final 3 min of each exercise bout for VO_2, V_E, f, V_T, and HR were utilized to calculate percent change from the initial value. The PDI and TSS ratings for all reported symptoms were analyzed as absolute changes from zero. The prolonged exposure data were analyzed for statistical significance ($p < .05$) using a two-way analysis of variance (ANOVA) with repeated measures, which tested for gas concentration effects and exposure protocol (time) effects. Upon obtaining a significant F value, the Scheffé post hoc test (Kleinbaum et al., 1988) was applied to determine which particular mean values were significantly different from each other.

RESULTS

A summary of the female and male subjects' anthropometry, VO_{2max}, and baseline pulmonary function is given in Table 1. The 30 subjects, with 5 exceptions (2 females), were not competitive athletes, although all of the nonathletes were regularly engaged in some form of personal recreational aerobic activity. Each subject's body size and composition was within 3 standard deviations of average for the person's gender, and all had normal pulmonary function, with the ratio of $FEV_{1.0}$/FVC ranging from 70.5 to 93.9%.

The group mean hour-by-hour V_E values for the five protocols, together with mean O_3 concentrations, V_{tot} and total inhaled O_3 dose, are given in Table 2. The V_{tot} values for the two chamber protocols (i.e., numbers 1 and 2), with exercise V_E of 19.1 L/min/m^2, were not significantly different from those for the face-mask inhalation protocols with exercise V_E of 20 L/min/m^2. This was due to the total 35-min lunch break estimated resting V_E of 367 L during the chamber exposures. The total inhaled O_3 doses for protocols 1 and 3 were not significantly different from each other but were significantly greater than those for the other three protocols. Also, as intended, the total inhaled O_3 doses for protocols 2, 4, and 5 were significantly different from each other.

Preexposure group mean pulmonary function and postexposure percent change values for the five protocols, together with the protocol postexposure statistically significant specific mean differences, are given in Table 3. None of the preexposure FVC values for the protocols differed significantly from

TABLE 1. Summary of subjects' anthropometric and functional characteristics

Gender	Age (yr)	Height (cm)	Weight (kg)	Body fat (%)	BSA (m^2)	$VO_{2_{max}}$ (L/min)	FVC (L)	$FEV_{1.0}$ (L/s)	$FEV_{1.0}$/ FVC (%)
Female	22.9	165.9	59.7	22.7	1.64	2.68	3.88	3.23	83.3
	(2.0)	(5.0)	(6.4)	(4.0)	(0.10)	(0.31)	(0.40)	(0.40)	(5.3)
Male	22.2	176.5	78.7	14.0	1.93	3.85	5.24	4.22	81.0
	(1.5)	(9.2)	(12.5)	(6.0)	(0.19)	(0.52)	(0.89)	(0.65)	(6.8)

Note. Numerical values are group means (standard deviations in parentheses).

TABLE 2. Group mean O_3 concentration, V_E for each hour, V_{tot}, and total inhaled O_3 dose for the five protocols

Protocol number	Mean $[O_3]$ (ppm)	V_E						V_{tot}[a] (L)	Total inhaled dose (ppm·L)[b]
		Hour 1	Hour 2	Hour 3	Hour 4	Hour 5	Hour 6		
1	0.1194	30.8 ± 4.6	29.6 ± 3.9	30.3 ± 4.1	30.6 ± 3.6	30.4 ± 3.5	29.8 ± 4.5	11236 ± 1349	1342
2	0.0017	30.7 ± 4.3	30.4 ± 3.7	30.0 ± 4.6	30.1 ± 3.5	30.7 ± 4.1	29.0 ± 3.7	11191 ± 1292	19
3	0.1196	31.8 ± 3.6	31.8 ± 3.8	31.8 ± 3.8	31.6 ± 3.9	31.8 ± 3.8	31.2 ± 4.1	11403 ± 1356	1364
4	0.0798	31.8 ± 3.7	31.6 ± 3.8	32.0 ± 3.5	31.7 ± 3.8	31.8 ± 3.6	31.5 ± 3.7	11426 ± 1307	912
5	0.0402	31.9 ± 3.6	31.7 ± 3.9	32.0 ± 3.6	31.5 ± 3.8	31.9 ± 3.7	31.2 ± 3.7	11408 ± 1318	459

[a] V_{tot} equals exercise plus resting values (in liters) for all 6 h of exposure; for protocols 1 and 2, it also includes resting V_E during the lunch break.
[b] Total inhaled dose equals the product of V_{tot} (liters) and mean O_3 concentration (ppm).

each other, which was also true for $FEV_{1.0}$ and percent $FEV_{1.0}$/FVC. Postexposure percent change in $FEV_{1.0}$ for the chamber protocol with O_3 concentration of 0.12 ppm (i.e., number 1) was not significantly different from that for the same face-mask exposure (protocol 3). Postexposure percent change in $FEV_{1.0}$ for these two protocols were significantly greater than those observed for the other three protocols. Postexposure percent change in $FEV_{1.0}$ for protocol 4 (0.08 ppm O_3) was significantly different from those observed for protocol 2 (FA) and protocol 5 (0.04 ppm O_3), which did not differ significantly from each other. Postexposure percent change for FVC for all protocols closely paralleled those for $FEV_{1.0}$. Changes in $FEV_{1.0}$/FVC were somewhat more variable than those observed for $FEV_{1.0}$ and FVC.

Hourly percent changes in $FEV_{1.0}$ for the five protocols are shown in Figure 1. The $FEV_{1.0}$ percent change from preexposure was significantly greater for protocols 1 (chamber, 0.12 ppm O_3; exercise V_E = 19.1 L/min/m^2) and 3 (face mask, 0.12 ppm O_3; exercise V_E = ~20 L/min/m^2) than that for FA (protocol 2) by 3 h. That for protocol 4 (face mask, 0.08 ppm O_3) was significantly greater than FA by 5 h. Percent change values for $FEV_{1.0}$ observed during protocol 5 (face mask, 0.04 ppm O_3) did not differ significantly from those observed for the FA protocol.

Group mean final symptoms responses to the five exposures are given in Table 4. Pain on deep inspiration (PDI) and TSS values at 6.6 h of exposure to 0.12 ppm O_3 for protocol 1 (chamber) and protocol 3 (face mask) were significantly greater than for all other protocols. Total symptoms score, but not PDI, was significantly greater for protocol 4 (0.08 ppm O_3) than for FA, but not significantly different from protocol 5 (0.04 ppm O_3). Neither PDI or TSS values observed at the end of protocol 5 (0.04 ppm O_3) differed significantly from those observed for FA. Hour-by-hour TSS for the five protocols are depicted in Figure 2. Total symptoms score did not change significantly during the FA exposure (protocol 2) nor during the exposure to 0.04 ppm O_3 (protocol 5). Total symptoms score for the two 0.12 ppm O_3 exposures, that is, protocol 1 (chamber) and protocol 3 (face mask), became significant at 3

TABLE 3. Group mean pulmonary function responses to the five protocols

Protocol number	FVC (L)[a]		$FEV_{1.0}$ (L)[b]		%$FEV_{1.0}$/FVC[c]	
	Pre	Change (%)	Pre	Change (%)	Pre	Change (%)
1	4.615 ± 1.004	−10.74 ± 8.24	3.725 ± 0.741	−13.25 ± 11.19	81.2 ± 6.9	−3.09 ± 5.7
2	4.657 ± 1.045	+0.27 ± 2.95	3.754 ± 0.774	+2.39 ± 4.01	81.2 ± 6.8	+2.12 ± 5.0
3	4.563 ± 0.992	−10.95 ± 7.88	3.713 ± 0.734	−13.02 ± 9.21	82.0 ± 6.7	−2.39 ± 5.7
4	4.551 ± 0.980	−4.34 ± 5.25	3.722 ± 0.708	−3.96 ± 7.50	82.3 ± 6.7	+0.44 ± 5.2
5	4.550 ± 1.024	−1.24 ± 4.23	3.718 ± 0.734	+1.15 ± 4.20	82.3 ± 6.3	+2.46 ± 3.9

[a]Specific significant mean differences between protocols 1–2, 1–4, 1–5, 2–3, 2–4, 3–4, and 3–5.
[b]Specific significant mean differences between protocols 1–2, 1–4, 1–5, 2–3, 2–4, 3–4, 3–5, and 4–5.
[c]Specific significant mean differences between protocols 1–2, 1–4, 1–5, 2–3, and 3–5.

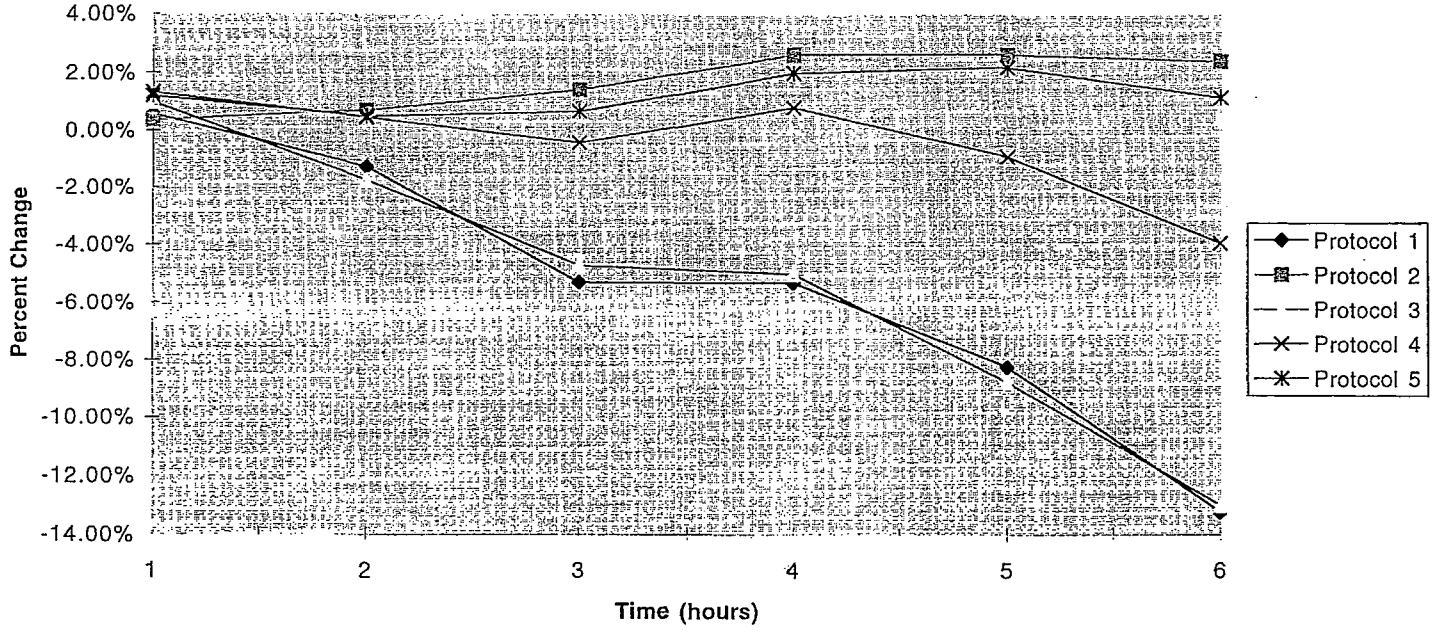

FIGURE 1. Hour-by-hour percent change in $FEV_{1.0}$.

TABLE 4. Group mean symptoms response for the five protocols

Protocol number	Pain on deep inspiration[a] (PDI)	Total symptoms score[b] (TSS)
1	9.9 ± 9.3	26.4 ± 25.4
2	0.3 ± 1.5	0.8 ± 3.4
3	9.8 ± 9.4	26.9 ± 27.1
4	3.5 ± 6.4	8.4 ± 20.5
5	1.5 ± 2.7	3.1 ± 6.0

[a]Specific significant mean differences between protocols 1–2, 1–4, 1–5, 2–3, 3–4, and 3–5.

[b]Specific significant mean differences between protocols 1–2, 1–4, 1–5, 2–3, 2–4, 3–4, and 3–5.

h. Hour-by-hour TSS for protocol 4 (0.08 ppm O_3) did not reach statistical significance until 6 h. Hour-by-hour PDI scores followed a pattern closely similar to those for TSS.

Group mean values for cardiorespiratory and ventilatory responses for the "initial" exercise period (between 8 and 10 min) and the last 3 min of exercise (i.e. ~6.6-h) are given in Table 5. Reflecting the ~5% lower exercise V_E in the chamber protocols (i.e., numbers 1 and 2), "initial" HR and VO_2 values were significantly lower (~4% and ~8%, respectively) than those observed for the face mask protocols with exercise V_E = ~20 L/min/m^2. However, the initial values observed for f and V_T in the chamber protocols were not significantly different from those observed for the face mask protocols with exercise V_E = ~20 L/min/m^2.

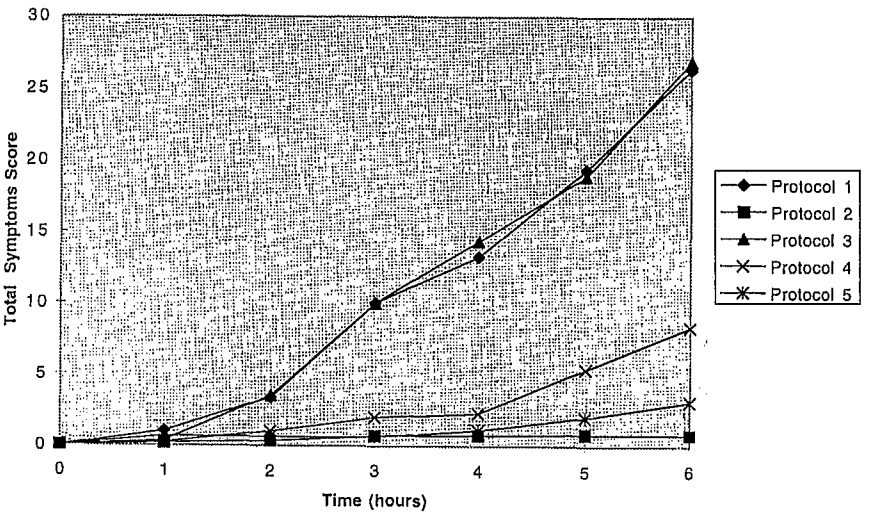

FIGURE 2. Hour-by-hour change in total symptoms score (TSS).

TABLE 5. Group mean exercise cardiorespiratory and ventilatory responses to the five protocols

	HR (beats/min)		VO_2 (L/min)		V_E (L/min)		f (breaths/min)		V_T (L)	
Protocol number	Exer. 1 (8–10:00)	Change (%) (last 3:00)	Exer. 1 (8–10:00)	Change (%) (last 3:00)	Exer. 1 (8–10:00)	Change (%) (last 3:00)	Exer. 1 (8–10:00)	Change (%) (last 3:00)	Exer. 1 (8–10:00)	Change (%) (last 3:00)
1	121.6 ± 11.4	+1.6 ± 7.3	1.35 ± 0.25	−2.1 ± 9.1	33.8 ± 4.0	+0.6 ± 6.3	28.5 ± 4.1	31.9 ± 15.9	1.21 ± 0.25	−23.0 ± 7.7
2	121.9 ± 12.0	+1.5 ± 5.1	1.37 ± 0.27	−1.4 ± 8.0	34.1 ± 4.7	−1.4 ± 4.8	28.5 ± 4.5	10.8 ± 6.0	1.22 ± 0.30	−10.8 ± 6.1
3	126.0 ± 12.0	+3.6 ± 6.7	1.48 ± 0.25	−5.8 ± 6.2	35.6 ± 4.1	+0.4 ± 4.0	29.2 ± 3.6	36.6 ± 15.8	1.25 ± 0.23	−25.7 ± 8.0
4	126.6 ± 12.9	+4.5 ± 7.4	1.50 ± 0.26	−4.2 ± 9.8	36.0 ± 4.0	−0.3 ± 1.5	29.2 ± 4.1	28.8 ± 12.5	1.28 ± 0.26	−22.9 ± 7.9
5	125.4 ± 13.7	+5.2 ± 5.5	1.46 ± 0.32	−2.6 ± 7.2	35.8 ± 4.2	−0.5 ± 2.1	29.1 ± 3.9	18.7 ± 9.1	1.26 ± 0.26	−15.7 ± 5.6

Note. Values are group means ± standard deviation.

At ~6.6 h, HR was significantly greater than the "initial" value for the face-mask protocols with exercise V_E = ~20 L/min/m^2, but not for the chamber protocols. The ~6.6-h VO_2 values were also significantly lower than their respective "initial" values for the face mask protocols, but not for the chamber protocols. The final (~6.6 h) V_E values were not significantly different from their respective "initial" values for any protocol. While the prolonged exercise induced a significant rapid shallow breathing (i.e., increased *f* and decreased V_T) for the FA chamber exposure (protocol 2), that observed for the chamber O_3 protocol (number 1) was of significantly greater magnitude. Further, the increased *f* and decreased V_T observed for the face mask 0.12 ppm O_3 exposure (i.e., protocol 3), as well as that for the 0.08 ppm O_3 exposure (protocol 4), were significantly greater than those for the FA and 0.04 ppm O_3 protocols (numbers 2 and 5, respectively).

DISCUSSION

To compare O_3-induced pulmonary responses effected by the chamber exposure (protocol 1) and face-mask exposure (protocol 3) to 0.12 ppm, with exercise V_E = ~20 L/min/m^2, it must be remembered that V_E was measured both during exercise and rest for 6 h of the 6.6 h protocol with face mask. However, during the chamber exposure, V_E was not measured during rest; thus, it was necessary to develop an estimate of V_E during chamber rest periods in order to compare the total inhaled O_3 dose between the chamber and face mask exposures. Use of a mouthpiece and/or face mask with respiratory valve results in an increased V_E, due to both a greater depth of breathing (V_T) and an increased *f*, although VO_2 remains unaffected. These breathing change effects have been attributed primarily to increased breathing dead space (Barlett et al., 1972; Sackner et al., 1980). The effects of using a mouthpiece and noseclip averaged 19% increased V_E in 3 studies of subjects at rest (Askanazi et al., 1980; Sackner et al., 1980; Weissman et al., 1984), but Gilbert et al. (1972), using a mouthpiece with only 44 ml dead space, found no significant effect on V_E. Further, Barlett et al. (1972) observed no significant difference in V_E at rest using a mouthpiece with 2 small respiratory valves (36 and 48 ml, respectively), but an increase of 27% using a valve with 215 ml dead space. The face-mask, nylon plastic, non-rebreathing respiratory valve inhalation system used in the present study had a dead space volume of 97 ml (Adams, 2000a). Hence, a 10% increase in face-mask V_E during rest periods between exercise bouts was assumed in arriving at an estimate of the between exercise resting V_E for the chamber protocols (i.e., 7.45 L/min/m^2 × .90 = 6.7 L/min/m^2). The mean V_E during the lunch break was reduced by another 5% to account for the longer duration of rest following exercise.

During the chamber exposure (protocol 1), V_E was measured between 8 and 12 min and between 45 and 49 min during the first and second hours of exercise and then only between 45 and 49 min of each hour thereafter.

This procedure implies that measured V_E during 4 min of exercise each hour accurately reflects the mean exercise V_E during the chamber exposures. This appears very likely, in that mean V_E for the last 3 min of exercise was less than 1% different from that measured during the initial 8- to 10-min period of exercise for both the chamber and face mask exposures (Table 5). Further, for the face mask exposure, these V_E values were less than 0.5 L/min different from the mean exercise V_E for all six 50-min exercise periods. Using these procedures resulted in V_{tot} values for protocol 1 (11,236 L) and protocol 3 (11,403 L) that were not significantly different (Table 2). This was because the chamber lunch break resting V_E (estimated to average 367 L) largely offset the slightly lower exercise V_E for the chamber protocol (~19 L/min/m^2) compared to that for the face-mask protocol (~20 L/min/m^2). The group mean total O_3 inhaled dose for protocol 1 (1342 ppm•L) was not significantly different from that for Protocol 3 (1364 ppm•L).

Does Prolonged Exposure to the Same Total Inhaled O_3 Dose at an O_3 Concentration of 0.12 ppm via Face Mask and Chamber Methods Produce Equivalent Pulmonary Responses?

Folinsbee et al. (1988) and Horstman et al. (1990) reported pulmonary responses of young adult males to 6.6-h exposures to a continuous, square-wave O_3 concentration of 0.12 ppm in which subjects performed 50 min of exercise each hour at a mean V_E of ~20 L/min/m^2 of BSA. Mean $FEV_{1.0}$ decrements in these studies were –12.9% and –14.4%, respectively, which bracketed the –13.7% value recently observed in a 6.6-h face mask exposure to 0.12 ppm O_3 with exercise V_E = 20 L/min/m^2 (Adams, 2000b). While these results are strongly suggestive that, with similar exercise V_E and O_3 concentration, ad libitum oronasal breathing of O_3 via face mask (with Teflon overlay coating on the inner surface) yields $FEV_{1.0}$ responses very similar to those effected in chamber studies, difference in subject population sensitivity remains an unknown effect (McDonnell et al., 1985, 1997). Thus, the primary purpose of the present study was to conduct a more definitive comparison of these two methods of O_3 inhalation by using subjects as their own controls.

Group mean percent change in final $FEV_{1.0}$ from preexposure for the chamber 0.12 ppm exposure (protocol 1; –13.25%) was nearly identical to that for the face mask exposure (protocol 3; –13.02%). This was also true for FVC (–10.74% and –10.95%, respectively) and for $FEV_{1.0}$/FVC (–3.09% and –2.39%, respectively). Further, the hour-by-hour percent change from preexposure $FEV_{1.0}$ (Figure 1) varied by less than 1% throughout the 6.6 h period for protocol 1 (chamber) and protocol 3 (face mask). None of these very small differences approached statistical significance. When final $FEV_{1.0}$ percent change from preexposure for the face mask exposure was regressed as a function of the chamber exposure percent change in $FEV_{1.0}$, the R^2 was .742 ($y = -3.57 + 0.712$). The proportion of subjects experiencing an $FEV_{1.0}$ response greater than –15% was closely similar for the chamber exposure (protocol 1, 33%) and the face-mask exposure (protocol 3, 30%), both some-

what lower than the predicted 38% value obtained by McDonnell et al. (1995) from the two early U.S. EPA studies of 6.6-h O_3 exposures to 0.12 ppm (Folinsbee et al., 1988; Horstman et al., 1990).

Final group mean TSS (Table 4) were also near identical for protocol 1 (26.4) and protocol 3 (26.9), as were those for group mean final PDI (9.9 and 9.8, respectively). The hour-by-hour group mean TSS values (Figure 2) did not vary systematically throughout the 6.6-h period between protocol 1 (chamber) and protocol 3 (face mask). None of these very small differences approached statistical significance. The hour-by-hour mean PDI values for these two exposures were also closely similar ($p > .05$). The final group mean percent changes for f and V_T (Table 5) also did not differ significantly between protocol 1 (chamber) and protocol 3 (face mask). Taken together, these data demonstrate convincingly that the two methods of exposing young adult subjects to near identical total inhaled O_3 doses at 0.12 ppm—by face mask and in a chamber—produce very similar pulmonary function, symptoms, and exercise ventilatory pattern responses.

Does Prolonged Exposure to O_3 Concentrations at and Below the Federal Air Quality Standard Elicit Significant Pulmonary Function and Symptoms Responses?

Other than FA control exposures, only one study of prolonged exposure to an O_3 concentration less than 0.08 ppm has been reported (Adams, 1998). In the present study, subjects completed a face-mask inhalation exposure to 0.04 ppm O_3, with exercise V_E of 20 L/min/m^2 (protocol 5). They experienced no significant pulmonary function or symptoms responses. In fact, as shown in Figure 1, their mean $FEV_{1.0}$ response varied between +0.50% (at 2 h) and +2.2% (at 5 h), with +1.2% at end exposure. Individual postexposure $FEV_{1.0}$ response varied between +7.8% and –8.2%, with only 8 of 30 subjects showing a decrement. Although no statistically significant differences in pulmonary function or symptoms responses from those observed for the FA exposure were observed in an earlier study of a 6.6-h face mask exposure to 0.06 ppm O_3, with exercise V_E of 23 L/min/m^2, (Adams, 1998), 6 of 30 subjects had an $FEV_{1.0}$ decrement >10%. Collectively, these results demonstrate no significant pulmonary response to 6.6 h exposure to O_3 concentrations <0.06 ppm, although some sensitive subjects experience notable effects at 0.06 ppm.

The net postexposure $FEV_{1.0}$ response to 0.08 O_3 via face mask in the present study (protocol 4) was –6.4% (including the +2.4% response to FA), which was statistically significant. This response was somewhat less than the –7.4% (including + 0.8% response to FA) observed in a chamber exposure to 0.08 O_3 with exercise V_E of ~20 L/min/m^2 by Horstman et al. (1990) and the –7.7% (including – 0.66% response to FA) observed by McDonnell et al. (1991). Using data from three U.S. EPA 6.6-h studies, with exercise V_E ~20 L/min/m^2 (Folinsbee et al., 1988; Horstman et al., 1990; McDonnell et al., 1991), McDonnell and Smith (1994) developed a model to estimate the

mean $FEV_{1.0}$ decrement at 4.6, 5.6, and 6.6 h. For the 0.08-ppm O_3 exposure, they found values of –3.0, –5.7, and –7.9%, respectively. In the present study, the mean $FEV_{1.0}$ responses to the 0.08 ppm O_3 exposure (protocol 4) tended to be somewhat lower in the last 2 h, namely, –3.5, –3.5, and –6.4%, respectively (when expressed as net change, including +2.4% for the FA exposure; protocol 2).

McDonnell et al. (1995) developed a model to estimate, as a function of O_3 concentration (range, 0.08 to 0.12 ppm) and exposure time (range, 1 to 6.6 h), the proportion of individuals in the population who experience a given $FEV_{1.0}$ decrement (–5%, –10%, and –15%). They found that even at 0.08 ppm O_3, a notable proportion of subjects experienced >10% $FEV_{1.0}$ decrements during exposure for 4.6 h (7%), 5.6 h (17%), and 6.6 h (3O%). In the present study, the proportion of subjects experiencing >10% $FEV_{1.0}$ decrements were 6.7%, 6.7%, and 20% at 4.6, 5.6, and 6.6 h, respectively.

Horstman et al. (1990) observed a response plateau during the last hour of their 6.6-h exposures to 0.08 and 0.12 ppm O_3, but not for the 0.10 ppm exposure. On the other hand, McDonnell et al. (1991) did not observe a plateau in $FEV_{1.0}$ response during the last 2 h of exposure to 0.08 ppm O_3. In the present study, as revealed in Figure 1, no plateau in $FEV_{1.0}$ response was observed during the last 2 h in any exposure to 0.08 (face-mask protocol, number 4) or 0.12 ppm O_3 (either in the chamber protocol or the face mask protocol).

In their study of 6.6-h exposure of young adult male subjects to FA and to 0.08 ppm O_3, McDonnell et al. (1991) observed significant postexposure decrements in pulmonary function and symptoms of cough and inspiratory difficulty, but not in shortness of breath or exercise ventilatory pattern. In the present study, in addition to significant postexposure FVC and $FEV_{1.0}$ responses, a significant alteration in exercise ventilatory pattern (i.e., $>f$ and $<V_T$) was observed, but the mean responses for PDI was not statistically significant.

The results of the 6.6-h face mask exposure to 0.08 ppm O_3 in the present study, compared to U.S. EPA chamber exposure study results, reveal several incongruities that may be due primarily to relatively high individual subject differences in sensitivity of response to a relatively low O_3 exposure (McDonnell et al., 1985). Thus, a direct comparison of chamber exposure responses to those elicited via face-mask exposure to 0.08 ppm O_3, in the same subject pool, with subjects serving as their own controls, seems warranted.

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