FINAL REPORT ON GRANT ARB-2098

PHYSIOLOGICAL EFFECTS OF AIR POLLUTANTS DURING LONG AND SHORT TERM WORK IN 25°C AND 35°C TEMPERATURE

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ABSTRACT

This study was designed to evaluate the interactions of carbon monoxide (50 ppm), peroxyacetylnitrate (0.27 ppm), and temperature stress on man's maximal working capacity and his ability to work at one-third capacity for four hours. Other factors evaluated were the effects of age and smoking habits. There were no consistent pollutant effects on attained maximal capacity, although carbon monoxide exposures were effective in reducing the work time of both younger nonsmokers and older subjects. Decrements of maximal aerobic power were related to age, heat, and length of time of smoking. With higher levels of ambient carbon monoxide (75 ppm and 100 ppm), reduction of maximal power occurred at 100 ppm - blood carboxyhemoglobin level of 5.0%. When initial levels of carboxyhemoglobin were elevated to the same degree, an ambient carbon monoxide concentration of 16-20 ppm was capable of maintaining the blood carboxyhemoglobin levels regardless of the level of pulmonary ventilation. Following four-hour exposures, reduction in forced vital capacity of the younger subjects occurred only when peroxyacetylnitrate was present. Generally, the pollutant exposures produced no significant changes in the cardiovascular, temperature regulatory, or metabolic responses to exercise. Older subjects working in carbon monoxide had slightly higher heart rates. This report was submitted in fulfillment of Grant ARB-2098, Institute of Environmental Stress, UCSB, under the sponsorship of the California Air Resources Board. Work was completed as of May 31, 1974.

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We also wish to acknowledge the opportunity of being able to purchase our supplies of peroxyacetylnitrate (PAN) from the Air Pollution Center, University of California at Riverside.

CONCLUSIONS

The conclusions drawn from the present investigation must be related to the context of the investigation, this being that the subjects investigated were healthy adult males who evidenced no cardiopulmonary abnormalities and were clinically described as being in good health.

It appears that significant reductions in man's maximal aerobic power occurs when the blood carboxyhemoblobin (COHb) content of nonsmokers is greater than 4.3% saturation. Whether an increased level of 4.3% saturation (COHb) for smokers would produce a significant decrement in maximal aerobic power remains unanswered. The results of the investigation into pollutant effects on maximal aerobic power indicate that the level of COHb in the blood is the determinant factor rather than the ambient level of carbon monoxide. In addition, the test level of peroxyacelylinitrate (0.27 ppm) does not reduce maximal aerobic power or maximal work time. However, the maximal work time of nonsmokers is reduced when the ambient level of carbon monoxide is 50 ppm.

It was shown that heat stress (35°C), age, and smoking habits significantly reduced maximal aerobic power. However, there were no interactions of these factors with the two pollutants singly or in combination to further reduce man's aerobic power nor did these interactions disturb man's thermoregulatory ability during maximal work. Subjective estimates (by both age groups investigated) suggested that smokers would be more adversely affected by the exercise regimens and always viewed themselves as being more irritable and depressed than nonsmokers regardless of ambient temperature. After heat exposure man is more likely to feel depressed. However, the presence of pollutants did not affect man's subjective impression while working maximally.

No significant change in man's thermoregulatory, metabolic, and cardiopulmonary ability to perform long term work (four hours at 35% of maximal aerobic power), when pulmonary ventilation is three times the resting ventilation, occurs when he is exposed to 50, 75, and 100 ppm carbon monoxide, 0.27 ppm PAN, or combinations of 50 ppm CO and 0.27 ppm PAN. However, significant decrement in pulmonary function of younger subjects following long term exposure occurs when PAN (0.27 ppm) is present as a pollutant. Also it was noted that levels of COHb following four-hour exposures to 50, 75, and 100 ppm CO reached or exceeded levels which previously were found to alter central nervous system functions. Subjectively all subjects reported greater physical distress whenever PAN was present as a pollutant regardless of ambient temperature. They also reported feeling physically and mentally lethargic when heat stressed.

The levels of carbon monoxide (50 ppm) and peroxyacetylnitrate (0.27 ppm) investigated in this study appear not to limit man's physiological ability to maximally or submaximally perform work, even when he is under a thermal stress. However, at ambient carbon monoxide levels of 100 ppm significant decrement in maximal aerobic power occurs. It is of some interest that if carboxyhemoglobin in nonsmokers, for some reason reaches greater than 4.3%, continued exposure to very low ambient carbon monoxide (16-25 ppm CO) can result in similar work performance decrements.

RECOMMENDATIONS

It is recommended that:

1. Carboxyhemoglobin be used as a determinant of critical exposures to carbon monoxide. (1a. A level of 5% COHb appears to be critical for both psychophysiological and physiological function).

2. Oxidant-type pollutants be evaluated both for their physiological effects and their behavioral effects.

3. New investigations be immediately implemented utilizing children, females, and older persons as subjects in order to clarify the expected differences due to increased effective doses of pollutants at the same ambient levels.

4. Smokers be evaluated separately from nonsmokers for both carbon monoxide and oxidant-type pollutants.

5. The investigators of pollutant effects using multifactorial designs be allowed a greater degree of working flexibility to enable them to change the design. This would offset the restrictive nature of the contract procedure and enable them to pinpoint critical levels without expending large amounts of energy in routine collection of data on fixed parameters of the environment.

BODY OF REPORT

Introduction

At the inception of this project there was no information regarding the effects of atmospheric pollutants and their interactions with heat stress on man's response to work. Previous studies did not consider prolonged work regimens, nor did they vary ambient conditions other than pollutants. Smith (1) reported an increased oxygen cost during short term moderate level work while breathing peroxyacetylnitrate (PAN), while Holland et al. (2) found no effect on performance during light work when exposed to ambient Los Angeles type pollutants. Undoubtedly the most ubiquitous pollutant is carbon monoxide. Furthermore, cardiorespiratory effects of moderately high levels of blood carboxyhemoglobin (COHb) while healthy men exercised have been demonstrated by a few investigators (3-7), while others have demonstrated detrimental effects of low levels of COHb on cardiovascular compromised patients (8,9) and central nervous system (CNS) function (10,11).

In a literature search assessing the influence of air pollutants on work capacity (12), we emphasized that (a) at no time during a "smog" episode is any one pollutant the only entity; (b) "smog" episodes always occur during a temperature inversion, whether a hot or cold inversion; (c) despite extensive epidemiological research demonstrating the need for the manipulation of both pollutants and weather variables, no studies of the interaction of these variables had been undertaken. In addition we noted that the Southern California Air Basin was more prone to have hot inversions, raising ambient temperatures to well above 32.2°C (90°F), and therefore, research into photochemical type "smog" should incorporate

an evalaution of heat stress. In view of the well documented adverse effects of heat stress on man's cardiorespiratory systems (13,14), it was suggested that future investigations of air quality standards (AQS) for the Southern California Basin should incorporate a multifactor approach, such that the air pollutant level was evaluated when man was stressed by heat, exercise, and a combination of pollutants. In an attempt to meet these aims, the following study was suggested and was accepted as a working framework for the investigation of the first alert level of carbon monoxide (CO) and a relatively newly identified pollutant, PAN.

General Objectives and Specific Aims

The study was designed to determine the effects of air pollutants (specifically PAN and CO) on man working at high intensity for brief periods and at moderate intensity for four hours under normal and high temperature conditions. By including two age groups, 18 to 30 and 40 to 55 years, equally divided between smokers and nonsmokers, it was anticipated that we would be able to evaluate the effects of age and smoking habits on the enviornmental conditions which were to be regarded as guidelines for government, state, and private agencies for determining the physiological effects of various ambient conditions.

Research Methods

Subjects

Thirty to 40 male volunteers divided into two age groups, 18 to 30 and 40 to 55 years old, with subgroups of smokers and nonsmokers in each age group, served as subjects in this study. The samples were drawn from occupation groups involved in outdoor work of moderate intensity in the

Santa Barbara area and the student population of the University of California, Santa Barbara campus. Each subject was given a complete medical examination, including pulmonary function tests, a resting 12-lead ECG, and an exercise ECG. Subjects with cardiac abnormalitites or pulmonary insufficiency were excluded from the experiments. Subjects were completely informed as to the purpose of the tests and were required to sign University consent forms to act as human subjects.

Experimental Design

Each subject was scheduled for eight experimental sessions at the Institute. On arrival at the Institute, following a light breakfast and eight or more hours of sleep, the subject was weighed nude. The subject then rested for 15 minutes while a resting blood pressure and blood sample were taken and ECG leads in a modified V_4 position were attached. Clothing worn during the experiments consisted of tennis shoes, socks, and shorts. The subject then entered the chamber within the environmental room at the prescribed conditions and sat quietly for 15 minutes while the following resting parameters were obtained: oxygen uptake, carbon dioxide production, heart rate, rectal and skin temperatures, and blood pressure. Following the rest, the maximum work capacity test (defined as the maximum oxygen uptake) was begun, a modified Balke treadmill walk (15) requiring a progressive increase in work load until exhaustion was reached. Minute by minute values of heart rate, oxygen uptake, and temperatures were recorded during the exercise and during a 15-minute sitting recovery. Following the maximum capacity test and the determination of oxygen debt during the recovery period, the subject filled out a 33-item questionnaire designed to evaluate his own assessment of his physical and mental condition.

The four-hour submaximal walks (35 to 40% maximum $\dot{V}_{O_2}$) were performed

on another day in the same environmental conditions. At 20 to 30, and 40 to 50 minutes of each hour, ventilatory volumes, oxygen uptake, carbon dioxide production, cardiac output, heart rate, blood pressure, and temperatures (skin, rectal, and environmental conditions) were measured. At 50 minutes of each hour, except in the last hour, the subject was allowed a 10-minute sitting rest. Routine checks of all on-line monitoring equipment was carried out during each exercise test. A post-exercise blood sample was taken to determine hemoglobin, hematocrit, plasma proteins, COHb, and lactate levels. A nude post-exercise weight was recorded to determine the evaporative weight loss due to sweating after correction for respiratory water and CO_2 production.

Tne environmental rooms at the Institute maintained the temperature and humidity at the required levels "ad infinitum"; however, in order to study pollutants, considerable modification of the system was required. We essentially built a chamber within a chamber to accomplish the necessary controlled conditions. The environmental temperatures were 25 $\pm$ 1 and 35 $\pm$ 1°C at 20 $\pm$ 1% relative humidity. The levels of pollutants were 0.27 ppm peroxyacetylnitrate and 50 ppm carbon monoxide.

The design for the experimental sessions was a four-factor factorial analysis of variance with repeated measured across ambient air conditions (Factor A) and temperatures (Factor B). The order of experimental Factors A and B was randomized independently for each subject. A double-blind design was used in the acute work studies in order to assure that neither the subject nor the experimenter knew which air mixture was being used for any session. However, in the four-hour studies, a single-blind design was utilized, although it was doubtful when PAN was present that a blind was in effect, as the subjects had significant eye irritation.

Data were analyzed on the IBM 360 Model 75 computer on the Santa Barbara campus. In addition to the analysis of variance, relationships between variables were probed using correlation techniques.

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RESULTS AND DISCUSSION

I. Effect of Carbon Monoxide and Peroxyacetylnitrate on Man's Maximal Aerobic Capacity.

(a) Experiments involving subjects aged 18-30 years

The subjects were 20 healthy male volunteers, aged 21-30 years, equally divided into two groups, smokers and nonsmokers. A preliminary examination incorporating a resting 12-lead electrocardiogram, pulmonary function evaluation, and an exercise electrocardiogram was performed on each subject prior to the determination of his maximum aerobic capacity ($\dot{V}_{O_2\ max}$) under different contaminant conditions. A resting blood sample was taken during the physical examination for determination of carboxyhemoglobin levels and confirmation of the classification of the subject as a smoker or nonsmoker. Table 1 presents mean data on age, height, weight, and resting carboxyhemoglobin levels of the subjects as well as the clinical spirometric evaluation of the two groups. Exposures to the four ambient pollutant conditions were assigned randomly in a double-blind experimental design. All studies were conducted in a temperature-regulated room at 25 $\pm$ 0.5°C and 35 $\pm$ 0.5°C at 20 $\pm$ 2% relative humidity. The conditions of exposure were: a) filtered air (FA); b) 50 ppm carbon monoxide in filtered air (CO); c) 0.27 ppm peroxyacetylnitrate in filtered air (PAN); and d) 50 ppm carbon monoxide and 0.27 ppm peroxyacetylnitrate in filtered air (PANCO).

Maximal oxygen uptake was determined by a modified treadmill Balke test (1) which required a 1% per minute progressive increase in grade while walking at 93 m/min until the subject could no longer continue. The work was preceded by a five minute sitting rest and followed by a

15 minute sitting recovery for determination of oxygen debt. Pollutant gases were mixed with filtered air outside the environmental chamber by use of calibrated rotometers (Gilmont) and a "Pitot" tube calibrated against a dry gasmeter (Parkinson-Cowan). The mixtures were fed into the inspired side of a mouthpiece via thoroughly cleaned Pyrex glass tubing to prevent breakdown of PAN. Inspired concentrations of the pollutants were checked twice during each experimental session to insure that mixing was occurring as designed during the progressive increase in exercise ventilatory volume. A mixed expired syringe was also taken following the second of the inspired syringe tests. During PAN exposures inspired concentrations of PAN were 0.29 $\pm$ 0.03 and 0.30 $\pm$ 0.01 ppm, respectively, and during PANCO exposures inspired concentrations of PAN were 0.24 $\pm$ 0.03 and 0.26 $\pm$ 0.08 ppm, respectively. The resultant mixed expired concentrations of PAN were 0.06 $\pm$ 0.004 for both PAN and PANCO exposures.

During each test minute by minute resting, exercise, and recovery values were obtained for metabolic and temperature parameters. The ECG modified V_4 position, was monitored continuously and recorded for the last ten seconds of each minute. Ventilatory volumes were continuously recorded on a Heath recorder from a modified constant-flow gasmeter (Parkinson-Cowan). Oxygen content of the expired gas was determined on a Servomex oxygen analyzer (model O.A. 137) and the carbon dioxide content with a Beckman infrared analyzer (model LB1). Both gas analyzers were periodically checked by chromatographic and Haldane analysis. Room, skin, and rectal temperatures were measured with copper-constantan thermocouples and recorded on a 24-channel Honeywell multipoint recorder twice each mintue. Inspired carbon monoxide (50 $\pm$ 5 ppm) levels were monitored continuously by an infrared analyzer (Beckman IR215). PAN analysis was carried out on a Varian Aerograph

using an electron capture vapor phase chromatograph (Model 600 D). Source tanks of PAN[1] were checked periodically by infrared absorption (2) and stored at 8°C (3). Inspired filtered air conditions were routinely checked for impurities by gas chromatography of aliquot samples. A 5 ml blood sample was drawn from the antecubital vein prior to and four minutes following each maximal test. Pre and post test blood samples were analyzed for lactate by the modified Ström method (4), hemgolobin by the cyanmethemoglobin method, hematocrits by the microhematocrit method, total plasma protein by a Goldberg refractometer, and carbon monoxide content by a modified chromatographic technique (5).

Data were analyzed by factorial analysis of variance with repeated measures across the treatment factor. Significant interaction effects were probed by tests of simple main effects followed by a Neuman-Keuls (6) test of ordered means at the 0.05 and 0.10 levels of significance. The 0.10 level was included because of the exploratory nature of the study and the relatively equal importance of type 1 and type 2 decision errors (6). Included in the analysis were values obtained during the walk, at the minute maximal aerobic power was attained, and during rest and recovery periods. Submaximal periods selected for analysis were minutes 1 and 2 when oxygen uptake for the groups averaged approximately 25% and approximately 35% maximal aerobic power, with minutes 5 and 10 representing approximately 40% and approximately 60% maximal aerobic power, respectively.

Results at 25°C exposures

There were no differences between smokers and nonsmokers in body weight or surface area (Table 1), however, the nonsmokers were significantly

[1]Peroxyacetylnitrate 1,000 ppm balanced with nitrogen was purchased from the Air Pollution Research Center at the University of California, Riverside, California

TABLE I

DESCRIPTIVE DATA OF SUBJECTS

	Age, yr	Ht, cm	Wt, kg	Surface Area, m^2	Resting COHb, %	VC, Liters	$FEV_{1.0}$, Liters	MBC, L/min	RV/TLC, %
Nonsmokers (NS)									
$\overline{X}$	25.2	186.1	80.9	2.05	0.64	6.18	4.78	202.5	23.7
$SE_{\overline{X}}$	1.3	0.04	0.10	0.00	0.08	0.20	0.14	9.1	2.0
Smokers (S)									
$\overline{X}$	23.8	177.3	79.5	1.96	3.17	5.60	4.72	158.3	20.6
$SE_{\overline{X}}$	2.3	0.13	0.22	0.00	0.60	0.20	0.18	16.8	1.7
P		<0.05			<0.05	<0.05		<0.05	

Values are means $\pm$ SE

taller (3.5 cm) than the smokers ($P < 0.05$). The mean resting carboxyhemoglobin levels of the nonsmokers was 0.64% and that of the smokers was 3.17% (Table 1). The nonsmokers also had significantly greater vital capacities and maximum breathing capacities ($P < 0.05$), but these differences disappeared when body size was taken into account. Analysis of the data indicated that there were no apparent training or order effects on maximum oxygen uptakes for smokers ($\bar{X}\ \dot{V}O_{2\ max}$ of first session = 3.34 compared to 3.37 liter/min of last session) or nonsmokers ($\bar{X}\ \dot{V}O_{2\ max}$ of first session = 3.32 compared to 3.35 liter/min of last session).

Table 2 summarizes selected cardiorespiratory and temperature parameters obtained at $\dot{V}O_{2\ max}$ as well as post exercise blood parameters for both smokers and nonsmokers following their filtered air work. Generally there was no significant difference between smokers and nonsmokers nor were there any differences of these parameters due to the four ambient pollutant conditions. The average walking time was similar under all conditions for both smokers and nonsmokers alike (21-22 min). The post exercise carboxyhemoglobin levels of the nonsmokers reached 2.7 and 2.8% when exercising in CO and PANCO conditions respectively, whereas the smokers reached levels of 4.5 and 4.2% carboxyhemoglobin during CO and PANCO exposures.[2]

The responses of the subjects across time are shown in Figures 1-5. Where a group effect rather than a treatment effect was noted, the results for all treatment conditions were averaged for each group. Where the effects of pollutants were significant rather than smoking habits the data from the two groups were combined for each treatment. Differences between smokers and nonsmokers were most evident early in the walk and during the

[2]Unfortunately, due to technical problems, not all postexercise blood samples were analyzed for carbon monoxide content and the mean values represent samples from half the total number of subjects exposed, thereby negating a repeated measure analysis of the carboxyhemoglobin.

TABLE II

CARDIORESPIRATORY AND TEMPERATURE PARAMETERS AT $\dot{V}_{O_2\ max}$ AND POST EXERCISE BLOOD PARAMETERS FOR SMOKERS AND NONSMOKERS DURING FILTERED AIR CONDITIONS

	Oxygen Uptake ℓ/min	Oxygen Uptake ml O_2/kg·min^{-1}	Ventilatory Volumes, ℓ/min BTPS	Tidal Volumes Liters	Respiratory Exchange Ratio	Heart Rate Beats/min	Rectal Temperature °C	Mean Skin Temperature °C	Hemoglobin mmole
Nonsmokers (NS)									
$\overline{X}$	3.35	41.62	107.9	2.8	1.09	193	38.5	31.9	9.6
$SE_{\overline{X}}$	0.17	1.87	4.6	0.16	0.02	3	0.09	0.17	0.4
Smokers (S)									
$\overline{X}$	3.34	42.43	110.6	2.7	1.08	188	38.5	32.3	9.8
$SE_{\overline{X}}$	0.20	2.40	5.4	0.10	0.02	4	0.10	0.22	0.2

Values are means ± SE

recovery period. Smokers had higher respiratory exchange ratios ($\dot{R}$) than nonsmokers during the 5th and 10th minute of walk ($P < 0.05$), even though there were no differences in expired ventilatory volumes, tidal volumes, ventilatory equivalent ratio (VE), or respiratory rate (Figures 1-3). This group effect became more pronounced during recovery where during minutes 1 and 2 VE and respiratory rates were higher for smokers than nonsmokers ($P < 0.10$) (Figures 2 and 3). Respiratory rate differences between smokers and nonsmokers were observed during the entire recovery period ($P < 0.10$). Smokers consistently had lower rectal temperatures than nonsmokers (Figure 4) during submaximal exercise ($P < 0.05$). This difference was not evident at $\dot{V}_{O_2\ max}$ but became apparent again by minute 2 of recovery ($P < 0.10$).

PAN had no consistent effect on the physiological responses to exercise. However, there was an indication that CO may have an effect on both respiratory and thermoregulatory responses. During the first and second minutes of the walk VE was higher during CO exposure than any other condition ($P < 0.05$), and the respiratory rates for minutes 1 and 2 were higher during CO exposure than during filtered air exposures ($P < 0.05$). Pollutants did not affect thermoregulation consistently although tissue conductance (calculated by $M/T_{re}-\overline{T}_{sk}$) for minutes 1, 5, 10, and 13 was greater in PANCO exposures than during other conditions ($P < 0.05$), but during the CO exposure conductance was significtantly lower than during any other ambient conditions ($P < 0.05$) (Figure 5).

Results of 35°C exposures

Exposure to 50 ppm of CO resulted in a significant decrement in the length of time nonsmokers were able to continue the treadmill walk (Table 3). The minutes walked in the CO condition were significantly less than

FIGURE II

Ventilatory Efficiency Expressed as a Ventilatory Equivalent Ratio ($\dot{V}_E/\dot{V}_{O_2}$) During Exercise and Recovery, Smokers (X) and Nonsmokers (O).

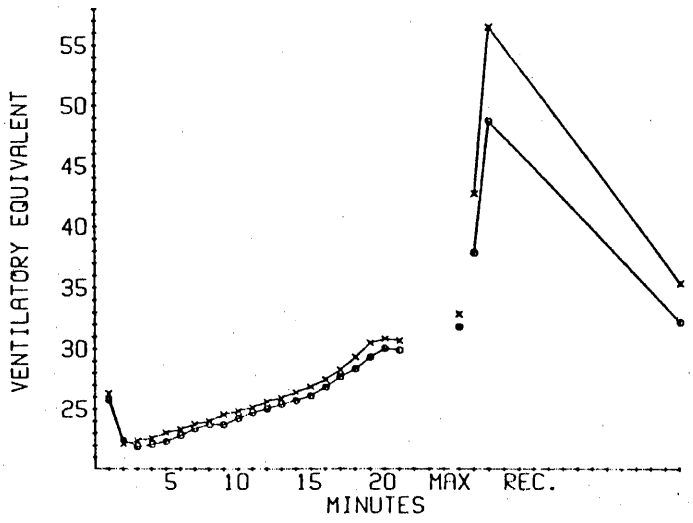


FIGURE III

Respiration Rate During Exercise and Recovery
Smokers (X) and Nonsmokers (O).

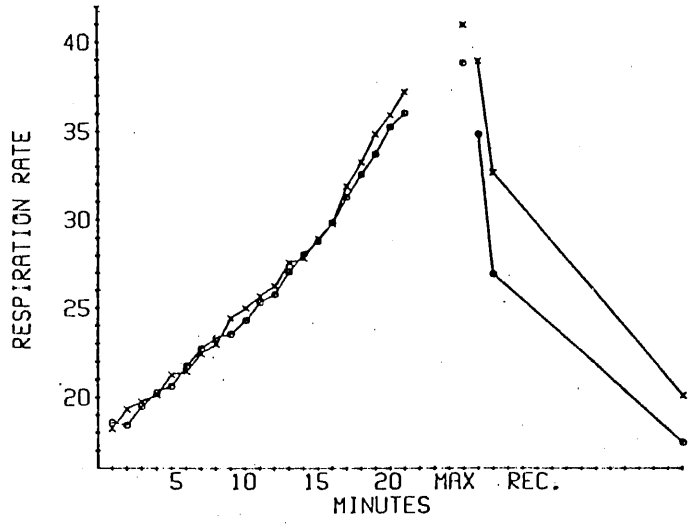
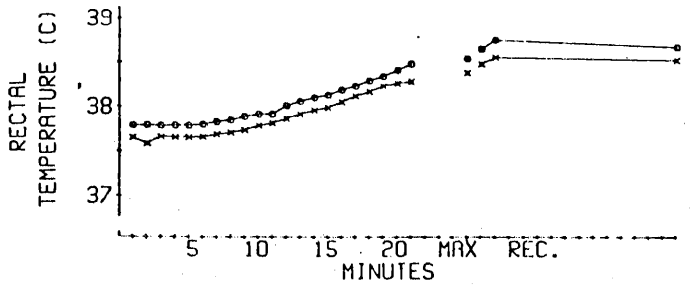


FIGURE IV

Rectal Temperature Response Over Time During Exercise and Recovery, Smokers (X) and Nonsmokers (O).



in either FA or PAN ($P < 0.05$) although there was no difference in the levels of maximal aerobic power attained (Table 3). The length of the smokers' walk was unaffected by the air mixture, although each time CO was present their respiration rates were higher than those of the nonsmokers ($P < 0.10$). Excess CO_2 and the respiratory exchange ratio were significantly higher during the CO exposure than for all other conditions for both smokers and nonsmokers ($P < 0.05$). In addition, smokers had a higher ventilatory equivalent ($P < 0.10$) and respiratory heat loss ($P < 0.05$) than nonsmokers at the time of maximal oxygen uptake, regardless of the air mixture.

The effect of CO on the respiratory system of the smokers persisted throughout the recovery period. During minutes 1 and 2 of recovery, the ventilatory volumes of the smokers were significantly higher under conditions of CO and PANCO ($P < 0.05$). Respiratory rates and the ventilatory equivalent were higher for smokers than for nonsmokers, regardless of conditions throughout the 15 minute recovery. There was no difference in oxygen debt due to smoking habits or air mixture nor did any hematological measurements other than carboxyhemoglobin (COHb) discriminate between groups or breathing conditions.

Pre exercise COHb levels for smokers and nonsmokers were 3.17% and 0.64% respectively. In the FA and PAN exposures, the COHb values for smokers decreased during exercise as a consequence of ventilatory exchange in the alveoli but were still three to four times higher than for nonsmokers (Table 3). However, CO (50 ppm), alone or in combination with PAN, raised the COHb levels of the nonsmokers to values approximating those found for smokers in the FA condition. At those levels of COHb, the respiratory exchange ratio (Figure 6) and excess CO_2 production of the two groups

TABLE III

CARDIORESPIRATORY VALUES OBTAINED AT MAXIMAL AEROBIC POWER FOR NONSMOKERS (NS) AND SMOKERS (S) DURING TREADMILL WALK AT 35°C (MEAN ± SE)

Cardiorespiratory Measures		*FA*	*CO*	*PAN*	*PANCO*
Oxygen uptake ml/kg·min	NS	40.05	39.28	41.33	39.92
		1.96	2.00	1.55	2.13
	S	40.64	40.90	41.14	40.76
		2.13	1.90	1.80	2.04
Ventilatory volume, liters/min body temperature, pressure, saturated	NS	95.9	97.2	98.7	93.9
		5.9	5.0	4.9	4.8
	S	102.5	112.2	102.1	104.5
		6.0	6.7	4.1	6.4
Respiratory exchange ratio	NS	1.00	1.07	1.02	1.02
		0.03	0.04	0.02	0.02
	S	1.05	1.09	1.03	1.06
		0.02	0.02	0.03	0.02
Ventilatory equivalent*	NS	29.96	30.84	30.18	29.52
		1.51	1.21	1.24	1.19
	S	32.70	35.00	31.88	33.20
		1.77	1.53	1.33	1.77
Heart rate, beats per minute	NS	187.7	189.7	192.2	188.3
		3.7	4.4	3.7	3.6
	S	189.1	189.5	187.8	191.9
		2.5	2.9	3.9	2.8
Oxygen pulse, milliliters per beat	NS	17.3	16.8	17.2	17.2
		1.1	1.2	1.1	1.2
	S	16.8	17.1	17.3	16.7
		1.1	1.2	0.9	1.2
Respiration rate	NS	37.5	35.6	35.8	35.2
		2.7	2.1	1.3	1.8
	S	38.0	42.2	40.2	41.4
		2.0	1.8	1.4	2.2
Time of walk, min	NS	20.9	19.9	21.6	20.6
		0.6	0.7	0.4	0.5
	S	20.3	20.5	20.2	20.5
		1.2	1.2	1.1	1.2

TABLE III

(continued)

CARDIORESPIRATORY VALUES OBTAINED AT MAXIMAL AEROBIC POWER FOR NONSMOKERS (NS) AND SMOKERS (S) DURING TREADMILL WALK AT 35°C (MEAN ± SE)

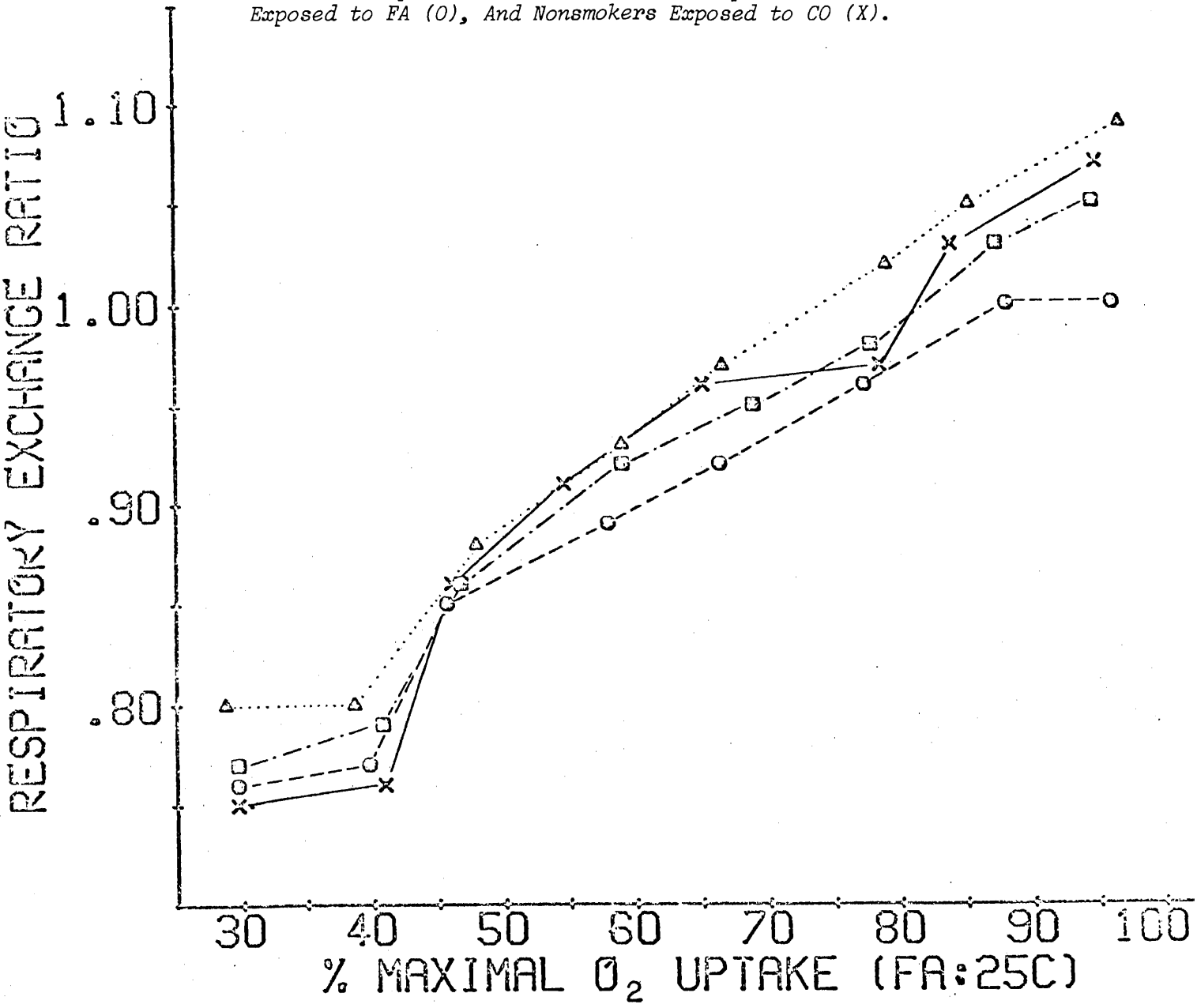
Cardiorespiratory Measures		*FA*	*CO*	*PAN*	*PANCO*
Carboxyhemoglobin, volume %	NS	0.9	2.5	0.7	2.5
		0.2	0.3	0.1	0.4
	S	2.6	4.1	2.2	4.4
		0.6	0.7	0.5	0.6
Excess CO_2** Liters/min	NS	0.80	1.03	0.90	0.87
		0.08	0.13	0.09	0.07
	S	0.95	1.09	0.89	0.96
		0.07	0.09	0.08	0.05
Respiratory heat loss, kilocalories/sq m·hr	NS	48.98	49.53	50.46	48.11
		2.73	2.60	2.24	2.40
	S	55.00	59.77	54.44	55.90
		3.09	3.05	1.69	2.96

* Ventilatory equivalent = ventilatory volume/oxygen uptake (liters per minute).

**Excess CO_2 = [ventilatory volume (standard pressure and temperature, dry) ($\%CO_2$ - 0.03) - (oxygen uptake [liters per minute] x 0.75)].

FIGURE VI

Effect of CO on Respiratory Exchange Ratio of Smokers and Nonsmokers During Work in 35°C Environment. Energy Requirements Expressed as Percent of Maximal Aerobic Power at 25°C. Smokers Exposed to FA (□), Smokers Exposed to CO (Δ), Nonsmokers Exposed to FA (O), And Nonsmokers Exposed to CO (X).



during the course of the walk were similar, although one group was breathing CO and the other FA. During the fifth and tenth minutes of exercise, the respiratory exchange ratio of the smokers was significantly higher than that of the nonsmokers, regardless of air mixture. At these same levels of exercise, ventilatory volumes for both groups were significantly higher ($P < 0.05$) in the CO exposure than under any other condition.

The effect of PAN as a single pollutant was significant only during the five minute period before the start of exercise. At that time, smokers had significantly ($P < 0.05$) higher respiratory exchange ratios and excess CO_2 values during inhalation of PAN than did the nonsmokers. Regardless of pollutant condition, smokers had higher ventilatory volumes and lower rectal temperatures prior to exercise than nonsmokers. At maximal aerobic power and during recovery there were no differences in temperature indices (Table 4) at 35°C that could not be accounted for by the length of the exercise or the elapsed time within the environmental chamber.

Heat stress was more effective in limiting the aerobic capacity of the men than either single pollutant or the combination of the two. As reported previously, in a 25°C environment inhalation of 50 ppm CO resulted in a 3% decrement in maximal aerobic power. Exposure to 35°C ambient temperature while breathing FA resulted in a 4% decrease from the level of maximal aerobic power attained in the 25°C FA condition. Regardless of breathing mixture or smoking habits, maximal aerobic power was significantly diminished ($P < 0.05$) by heat stress. This was also reflected in the length of the treadmill walk, which was less at 35°C ($P < 0.01$) for both groups under all pollutant conditions. There were no differences in oxygen uptake at submaximal grades across temperature or pollution conditions, nor were

TABLE IV

TEMPERATURE MEASUREMENTS OBTAINED AT MAXIMAL AEROBIC POWER FOR NONSMOKERS (NS) AND SMOKERS (S) DURING TREADMILL WALK AT 35°C (MEAN ± SE)

Temperature Measurements		*FA*	*CO*	*PAN*	*PANCO*
Rectal temperature (T_{re}), °C	NS	38.5 0.1	38.3 0.1	38.5 0.1	38.3 0.1
	S	38.2 0.1	38.4 0.1	38.3 0.2	38.4 0.1
Mean skin temperature ($\overline{T}_{sk}$), °C	NS	35.4 0.2	35.0 0.2	35.1 0.2	35.0 0.2
	S	34.9 0.2	35.1 0.3	35.2 0.2	35.2 0.2
Mean body temperature ($\overline{T}_{B}$), °C	NS	37.4 0.1	37.2 0.1	37.3 0.1	37.2 0.1
	S	37.0 0.1	37.3 0.1	37.2 0.1	37.3 0.1
Tissue conductance*, kilocalories/sq m·hr·°C	NS	157.0 11.1	149.2 13.9	153.3 13.3	149.6 12.7
	S	157.6 15.5	160.4 13.3	165.7 10.9	160.4 14.1

*Tissue conductance = metabolic heat production (kilocalories/sq m·hr)/ $(T_{re}-\overline{T}_{sk})$

there any differences in oxygen debt or post exercise blood lactates. Blood pressures (pre test average, 115/76/70 mm Hg; post test average, 176/69/0 mm Hg), hemoglobin, hematocrit, and plasma protein values were unaffected by smoking history, ambient air conditions, or temperature.

Nonsmokers' subjective estimates of their physical and mental condition (see Appendix A) after completion of the tests for aerobic capacity were more positive than those of the smokers ($P < 0.05$). Smokers tended to view themselves as more irritable and depressed and less satisfied and less refreshed after completing the walks. Even in the cooler environment (25°C), they had drier mouths and were thirstier than the nonsmokers. After exposure to 35°C, all subjects felt hotter, thirstier, and had drier mouths than at 25°C. They were also more depressed, less refreshed, felt lazier, and reported tired eyes in the hotter environments.

(b) Experiments involving subjects aged 40-57 years

Sixteen healthy male volunteers, 9 nonsmokers and 7 smokers, aged 40 to 57 years (mean ages 45.6 to 49.9, respectively), participated in these studies. A preliminary medical examination incorporating a resting 12-lead electrocardiogram, a pulmonary function evaluation, and an exercise electrocardiogram was performed on each subject prior to the determination of his maximum aerobic power under different contaminant conditions. Over 50% of the smokers who volunteered for the experiments were not selected for participation on the grounds of abnormal exercise electrocardiograms, even though they had apparently normal resting 12-lead electrocardiograms. A resting blood sample was taken during the physical examination for determination of COHb levels and confirmation of the classification of the subject as a smoker or nonsmoker. Those classified as smokers had been

smoking an average of more than 30 cigarettes each day for the last 30 years. Table 5 presents mean data on age, height, weight, resting COHb levels, and the clinical spirometric evaluation of the two groups.

Specific descriptions of techniques of measurement used to determine oxygen uptake, ventilatory volume, heart rates, thermoregulatory parameters, and pollutant administration[1] and analysis are described above in section (a).

Results

There were no differences between smokers and nonsmokers in age, height, or weight. Most pulmonary parameters showed no significant differences, possibly due to the small number of subjects (Table 5). However, inspiratory capacity (IC) and mid maximum flow (MMF) were significantly lower in smokers than in nonsmokers.

Tables 6 and 7 summarize selected cardiorespiratory responses at $\dot{V}_{O_2\ max}$, along with post exercise blood parameters. The average increase in COHb levels of the nonsmokers during CO and PANCO exposures was 1.49%, while for smokers the increase ranged from 0.1% to 0.7%, a reflection of their high intial COHb levels. Nonsmokers had a 27% greater $\dot{V}_{O_2\ max}$ than smokers ($P < 0.05$). The $\dot{V}_{O_2\ max}$ of both groups was not significantly affected by any of the pollutant exposures at either temperature, although at 25°C both groups walked significantly ($P < 0.05$) fewer minutes in CO than in FA or PAN. Smokers walked for significantly shorter times than nonsmokers under all conditions ($P < 0.05$). The ventilatory volumes of both groups at $\dot{V}_{O_2\ max}$ during 25°C exposures were similar and unaffected by pollutant conditions. However, during 35°C exposures, nonsmokers had

[1]During PAN and PANCO exposures, inspired concentrations of PAN were 0.260 ± 0.03 ppm and 0.275 ± 0.02 ppm, respectively, while expired concentrations of PAN for PAN and PANCO exposures were 0.065 ± 0.004 ppm.

TABLE V

DESCRIPTIVE DATA OF SUBJECTS

(Means and Standard Errors)

	Age (yr)	Height (cm)	Weight (kg)	Surface Area (m^2)	Resting COHb (%)	VC (ℓ)	$FEV_{1.0}$ (ℓ)	MBC (ℓ/min)	RV/TLC (%)	IC (ℓ)	MMF (ℓ)
Nonsmokers (N = 9)											
$\overline{X}$	45.6	180.4	77.9	1.97	0.82	5.43	4.15	173.3	31.6	3.82	4.93
$SE_{\overline{X}}$	4.56	2.13	2.40	0.031	0.13	0.28	0.24	13.9	0.94	0.18	0.32
Smokers (N = 7)											
$\overline{X}$	49.9	176.70	76.7	1.94	4.54	4.84	3.81	141.1	35.1	3.04	3.58
$SE_{\overline{X}}$	5.52	1.80	2.70	0.038	1.26	0.31	0.22	15.2	2.7	0.18	0.46
P	NS	NS	NS	NS	<0.01	NS	NS	NS	NS	<0.01	<0.05

TABLE VI

CARDIORESPIRATORY VALUES OBTAINED AT $\dot{V}_{O_2\ max}$ FOR NONSMOKERS (NS) AND SMOKERS (S) DURING A TREADMILL WALK AT 25°C AND 35°C. (MEANS AND STANDARD ERRORS)

			FA		CO		PAN		PANCO	
			25°C	35°C	25°C	35°C	25°C	35°C	25°C	35°C
Oxygen Uptake (ml O_2/kg·min^{-1})	NS	$\bar{X}$	39.06	40.05	37.74	37.74	38.42	37.44	39.07	38.71
		$SE_{\bar{X}}$	2.91	2.41	1.96	2.15	2.43	2.73	2.21	1.78
	S	$\bar{X}$	31.22	30.92	31.63	30.47	31.15	28.72	31.46	31.04
		$SE_{\bar{X}}$	1.21	0.85	1.34	1.42	0.94	0.93	2.06	2.11
Ventilatory Volume (ℓ/min BTPS)	NS	$\bar{X}$	99.7	98.8	93.3	93.1	95.7	92.2	100.0	95.4
		$SE_{\bar{X}}$	8.1	7.6	5.3	7.2	6.8	7.5	7.1	5.9
	S	$\bar{X}$	90.5	78.3	84.5	82.6	81.7	73.6	85.5	78.8
		$SE_{\bar{X}}$	4.2	3.9	4.9	5.0	4.5	5.0	6.1	5.0
Respiratory Exchange Ratio	NS	$\bar{X}$	1.07	1.02	1.05	1.04	1.04	1.00	1.07	0.99
		$SE_{\bar{X}}$	0.02	0.03	0.02	0.01	0.02	0.01	0.03	0.03
	S	$\bar{X}$	1.13	1.09	1.11	1.09	1.09	1.11	1.11	1.11
		$SE_{\bar{X}}$	0.02	0.02	0.01	0.03	0.04	0.04	0.02	0.03
Ventilatory Equivalent ($\dot{V}_E/\dot{V}_{O_2}$)	NS	$\bar{X}$	32.97	31.63	31.77	31.68	31.88	31.69	32.63	31.41
		$SE_{\bar{X}}$	1.64	1.51	1.24	1.60	1.00	1.62	1.65	1.33
	S	$\bar{X}$	38.37	32.92	35.08	35.35	33.88	33.51	35.73	33.42
		$SE_{\bar{X}}$	2.89	1.60	2.35	2.55	2.02	2.41	2.21	2.13
Heart Rate (beats/min)	NS	$\bar{X}$	175	177	173	176	175	175	176	176
		$SE_{\bar{X}}$	3	4	4	3	4	5	3	4
	S	$\bar{X}$	181	177	178	179	178	176	178	175
		$SE_{\bar{X}}$	4	4	3	6	4	5	4	6

TABLE VI

(continued)

CARDIORESPIRATORY VALUES OBTAINED AT $\dot{V}_{O_2\ max}$ FOR NONSMOKERS (NS) AND SMOKERS (S) DURING A TREADMILL WALK AT 25°C AND 35°C. (MEANS AND STANDARD ERRORS)

			FA		CO		PAN		PANCO	
			25°C	35°C	25°C	35°C	25°C	35°C	25°C	35°C
Respiration Rate (Breaths/min)	NS	$\bar{X}$	35	34	34	34	34	31	34	34
		$SE_{\bar{X}}$	2	1	2	2	1	1	2	1
	S	$\bar{X}$	34	31	33	31	32	30	34	30
		$SE_{\bar{X}}$	2	2	2	2	3	3	3	2
Time Walked (min)	NS	$\bar{X}$	19.6	18.9	19.1	17.9	19.8	18.4	19.2	18.6
		$SE_{\bar{X}}$	1.4	1.3	1.5	1.4	1.4	1.5	1.4	1.4
	S	$\bar{X}$	15.0	15.0	15.3	15.1	15.9	15.3	15.4	14.7
		$SE_{\bar{X}}$	0.8	1.0	0.6	0.8	0.8	0.7	0.7	0.7

TABLE VII

FOUR MINUTE POST EXERCISE BLOOD PARAMETERS AND OXYGEN DEBT. (MEANS AND STANDARD ERRORS).

			FA		CO		PAN		PANCO	
			25°C	35°C	25°C	35°C	25°C	35°C	25°C	35°C
Hemoglobin (mM)	NS	$\bar{X}$	9.7	9.7	9.8	9.5	9.7	9.5	9.6	9.5
		$SE_{\bar{X}}$	0.1	0.2	0.1	0.1	0.2	0.3	0.2	0.2
	S	$\bar{X}$	10.1	9.8	9.7	9.8	10.0	9.8	9.6	10.0
		$SE_{\bar{X}}$	0.3	0.3	0.4	0.4	0.5	0.3	0.5	0.4
Plasma Protein (g%)	NS	$\bar{X}$	7.4	7.3	7.5	7.3	7.4	7.5	7.3	7.5
		$SE_{\bar{X}}$	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.2
	S	$\bar{X}$	7.1	7.1	6.9	7.1	7.0	7.1	7.1	7.1
		$SE_{\bar{X}}$	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.2
Lactates (mEq/l)	NS	$\bar{X}$	7.1	7.1	7.2	6.5	8.1	7.2	8.5	7.8
		$SE_{\bar{X}}$	0.7	0.9	0.7	0.4	1.1	0.7	0.7	0.6
	S	$\bar{X}$	9.3	8.3	8.1	8.4	8.7	7.5	9.1	6.8
		$SE_{\bar{X}}$	1.4	1.0	0.6	0.7	1.2	0.9	0.9	0.9
Oxygen Debt (ml O_2/kg)	NS	$\bar{X}$	66.6	55.2	49.4	54.6	53.7	53.0	67.1	61.1
		$SE_{\bar{X}}$	8.6	3.6	6.7	4.9	5.8	4.1	4.2	3.2
	S	$\bar{X}$	54.6	48.9	54.1	51.3	49.5	51.5	49.9	55.7
		$SE_{\bar{X}}$	3.1	4.2	3.7	3.5	4.7	3.4	2.7	5.6

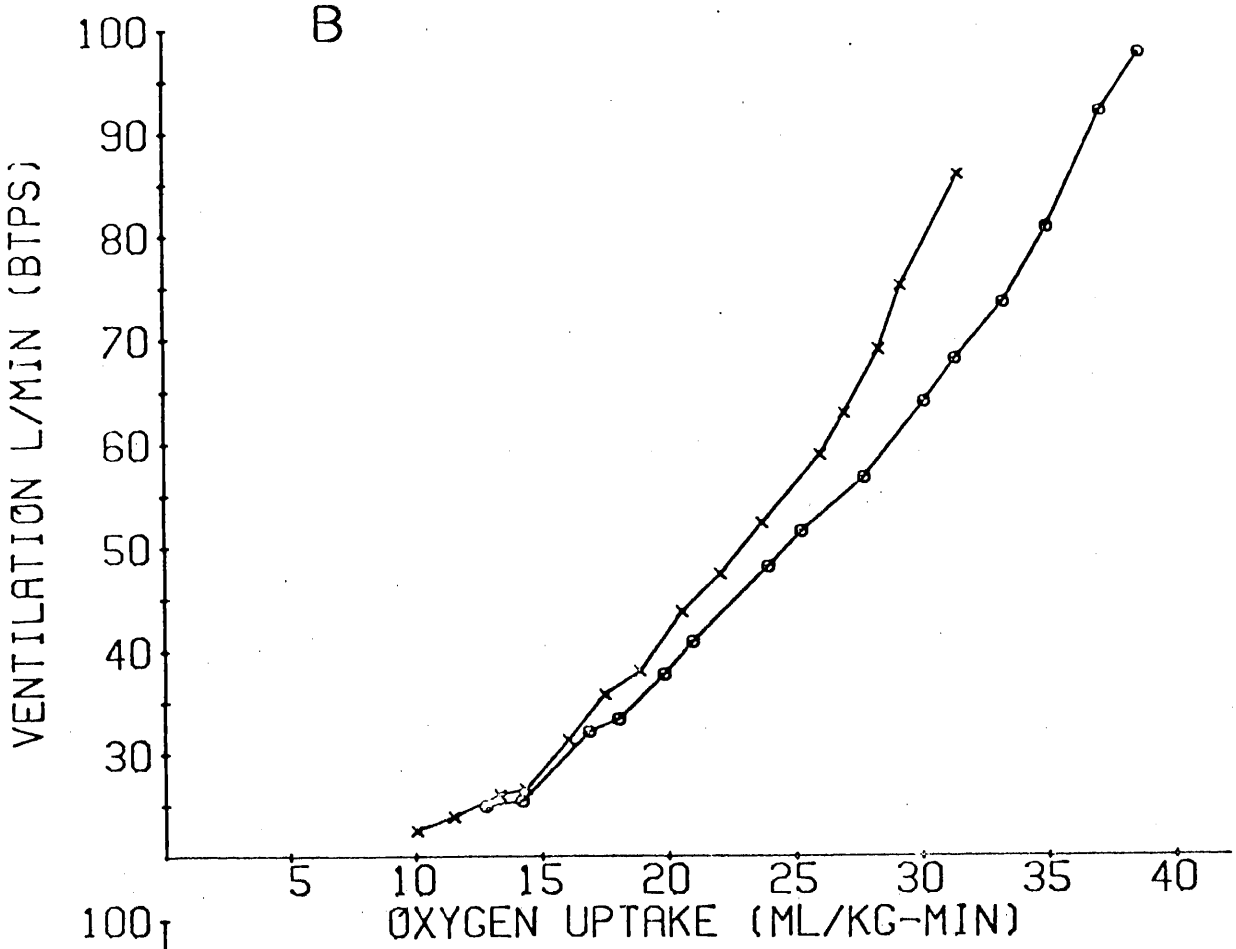
higher ventilatory volumes at $\dot{V}_{O_2\ max}$. Under all conditions, smokers had higher respiratory exchange ratios than nonsmokers ($P < 0.05$). There were no differences between smokers and nonsmokers or across pollutant conditions in post exercise lactates, oxygen debt, heart rate, tidal volume, or respiration rate obtained at $\dot{V}_{O_2\ max}$. Post exercise lactate values were significantly lower in the heat for both groups and all conditions ($P < 0.01$).

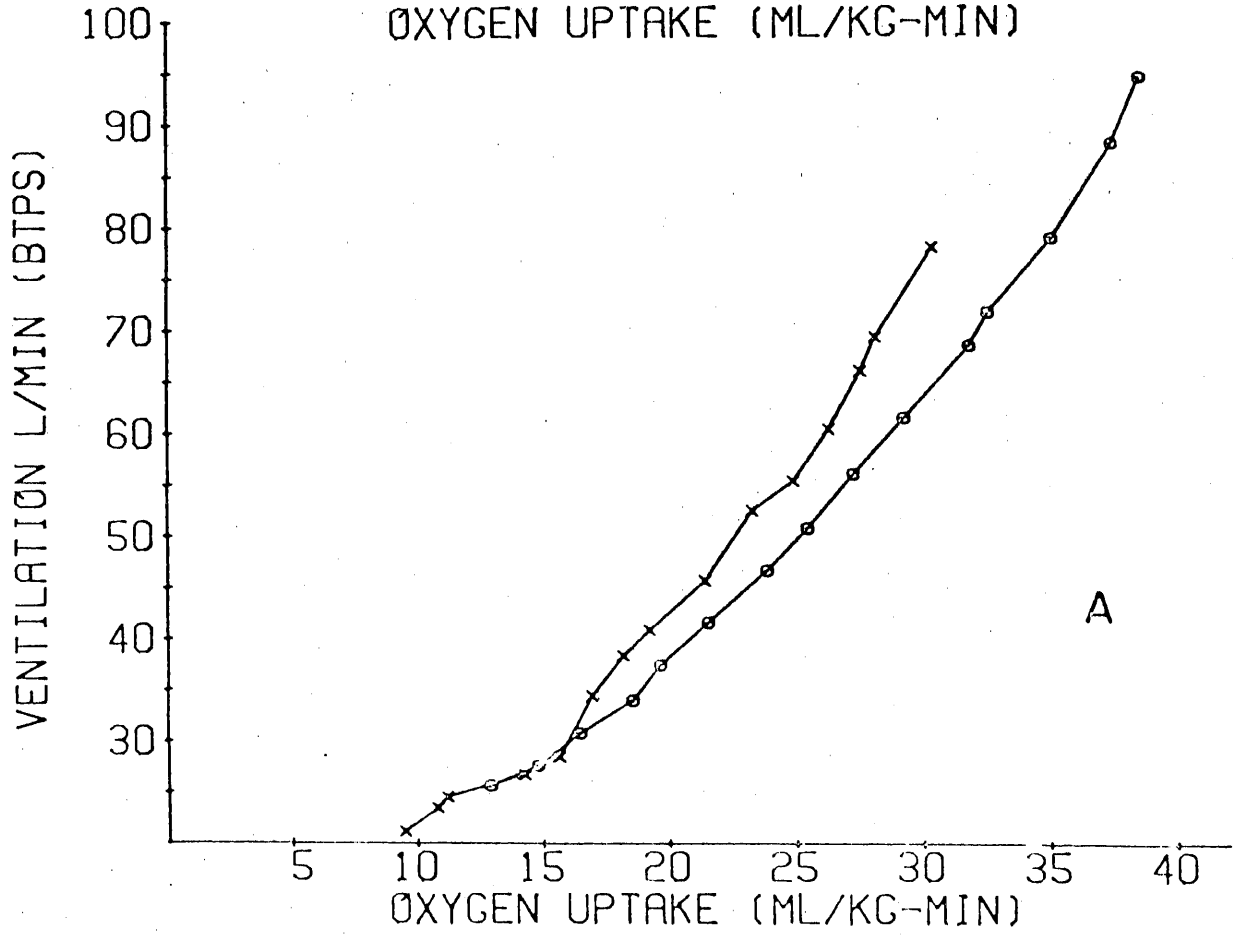
During recovery, there were no consistent effects related to the pollutants. In the first two minutes of recovery and in spite of the longer walk times by the nonsmokers, there were no differences between groups in heart rate, tidal volume, respiratory exchange ratio, or the ventilatory equivalence ratio. No differences in temperature parameters were observed at $\dot{V}_{O_2\ max}$ across pollutant conditions. However, during both 25 and 35°C exposures the calculated $\overline{T}_b$ (0.65 T_{re} and 0.35 $\overline{T}_{sk}$) was significantly higher for nonsmokers (36.08 at 25°C and 37.24 at 35°C) than for smokers (35.68 at 25°C and 36.88 at 35°C).

The results of a questionnaire indicated a significant subjective effect due to heat but did not demonstrate any pollutant effects. Both smokers and nonsmokers felt hotter, lazier, less confident, and had more tired eyes in the heat than in 25°C exposures. In both temperatures, smokers felt less active than nonsmokers.

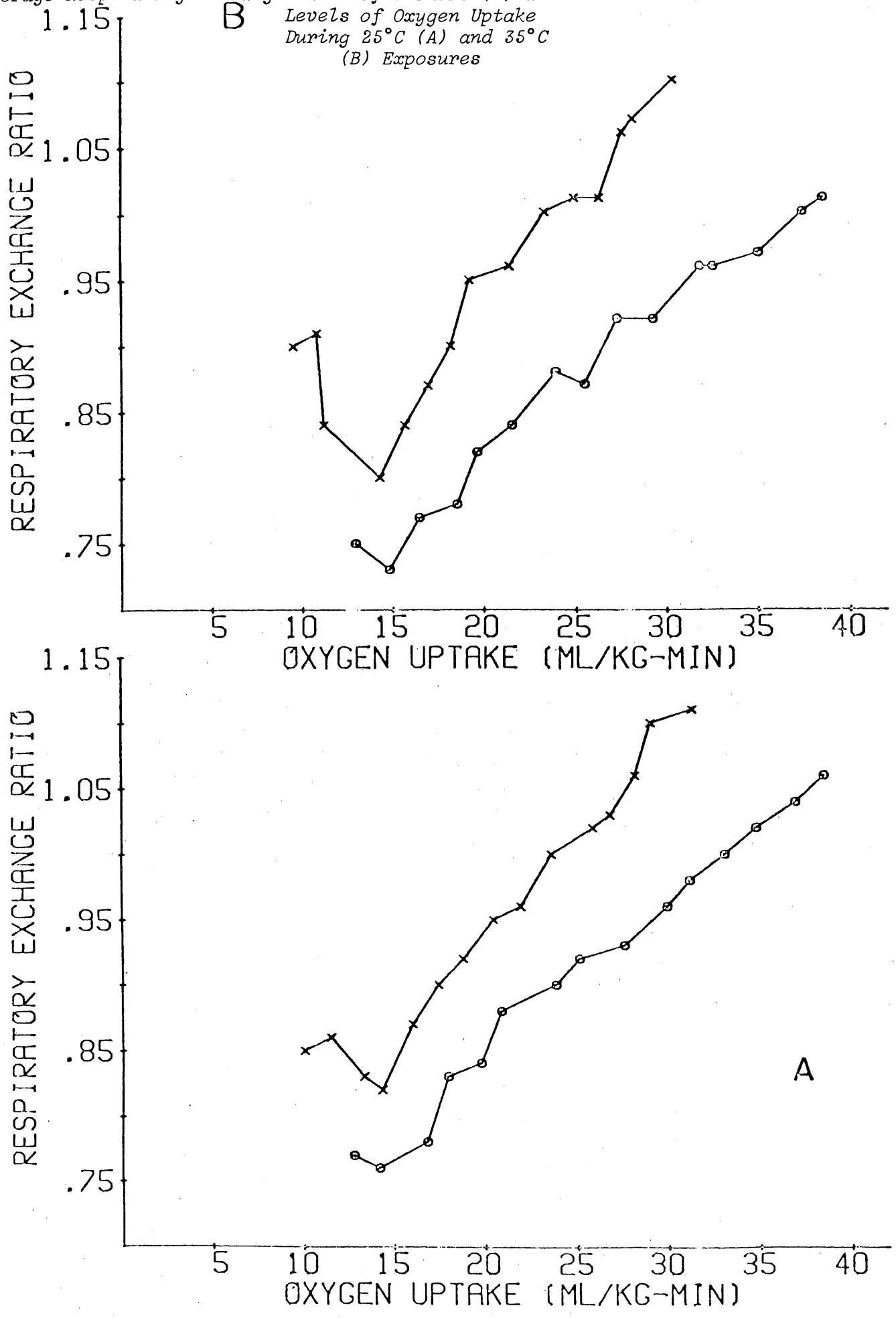
During the submaximal portion of the walking test, no significantly consistent pollutant effect on cardiorespiratory or temperature parameters was observed at either temperature. However, smokers were found to have higher ventilatory volumes at both temperatures when the oxygen uptake was greater than 15 ml $O_2/kg \cdot min^{-1}$ (Figures 7A and 7B), while the respiratory exchange ratio of the smokers was also consistently higher than that of

The Average Ventilatory Volumes of Smokers (X) and Nonsmokers (O) at Various Levels of Oxygen Uptake During 25°C (A) and 35°C (B) Exposures





The Average Respiratory Exchange Ratio of Smokers (X) and Nonsmokers (O) at Various Levels of Oxygen Uptake During 25°C (A) and 35°C (B) Exposures



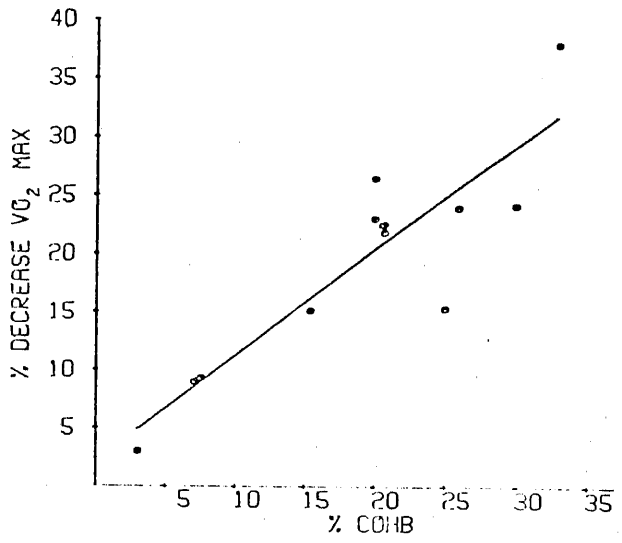
nonsmokers at both temperatures and across all pollutant conditions (Figures 8A and 8B).

Discussion

It has been appreciated for some time that individuals having a large burden of carbon monoxide were unable to perform effectively (7-9). Subjects studied by Chiodi et al. (9) were unable to carry on tasks requiring low levels of physical exertion when their blood carboxyhemoglobin levels had exceeded 45%. In fact, several collapsed while attempting to conduct routine laboratory tasks. Recently, further evidence of the deterioration in aerobic power capacity has been reported by a number of investigators (10-15). Most attention has been directed to the study of the influence of intermediate levels of carboxyhemoglobin on the maximum aerobic work capacity. It should be noted that these levels of carboxyhemoglobin were higher than those found in urban populations. These subjects were given CO to breathe for a period of time so as to attain desired levels of carboxyhemoglobin prior to beginning the maximum exercise test. The aerobic capacity tests were made on either a bicycle ergometer (10-12, 15) or a treadmill (10, 13) with a time duration of 2-6 minutes. In the present studies the subjects also breathed CO for a period of 5 minutes prior to beginning the aerobic capacity test which required approximately 22 minutes to complete. Figure 9 presents the decrement in maximum oxygen uptake related to percent carboxyhemoglobin levels as reported in a number of studies (10, 12-15). It was quite evident that there was considerable deviation but in general a linear decline in $\dot{V}_{O_2\ max}$ occurred with a progressive increase in carboxyhemoglobin levels. The decrement in $\dot{V}_{O_2\ max}$ found in the present studies falls within one standard error of the estimate of the regression line, although the observed decrease was statistically insignificant. It would appear that if levels of ambient CO were around 50 ppm no significant

FIGURE IX

A Regression Line for the Decrease in $\dot{V}_{O_2\ max}$ With Increasing Levels of Carboxyhemoglobin ($r = 0.89$), $Y = 0.91X + 2.2$. These Data were Plotted From Values Reported in This Study and Ref. 10, 22, 30 and 31.



decrement in performance capacity ensued. Those studies showing considerable decreases in $\dot{V}_{O_2\ max}$ were seen at higher carboxyhemoglobin levels which were induced rather quickly by a bolus plus maintenance technique and this may be a factor responsible for the magnitude of the decrement. Additional studies by which higher than the present 2.8-4.5% carboxyhemoglobin are attained by having subjects breathe from the beginning of exercise higher levels of CO than 50 ppm would be needed in order to determine the importance of methods of elevating blood carboxyhemoglobin levels. The important data for levels of carboxyhemoglobin between 3 and 7% have not been obtained. Studies where men breathe 100 and 150 ppm for time intervals similar to present experiments needed to be carried out in order to determine the precise levels of carboxyhemoglobin at which a significant reduction in aerobic work capacity will occur. These additional studies were carried out and the results are described below. Chevalier and coworkers (16-18) have reported no difference in $\dot{V}_{O_2\ max}$ in their smoking and nonsmoking subjects. Unfortunately the levels of carboxyhemoglobin in his subjects were not measured. However, the present data also failed to detect differences in $\dot{V}_{O_2\ max}$ between smokers and nonsmokers.

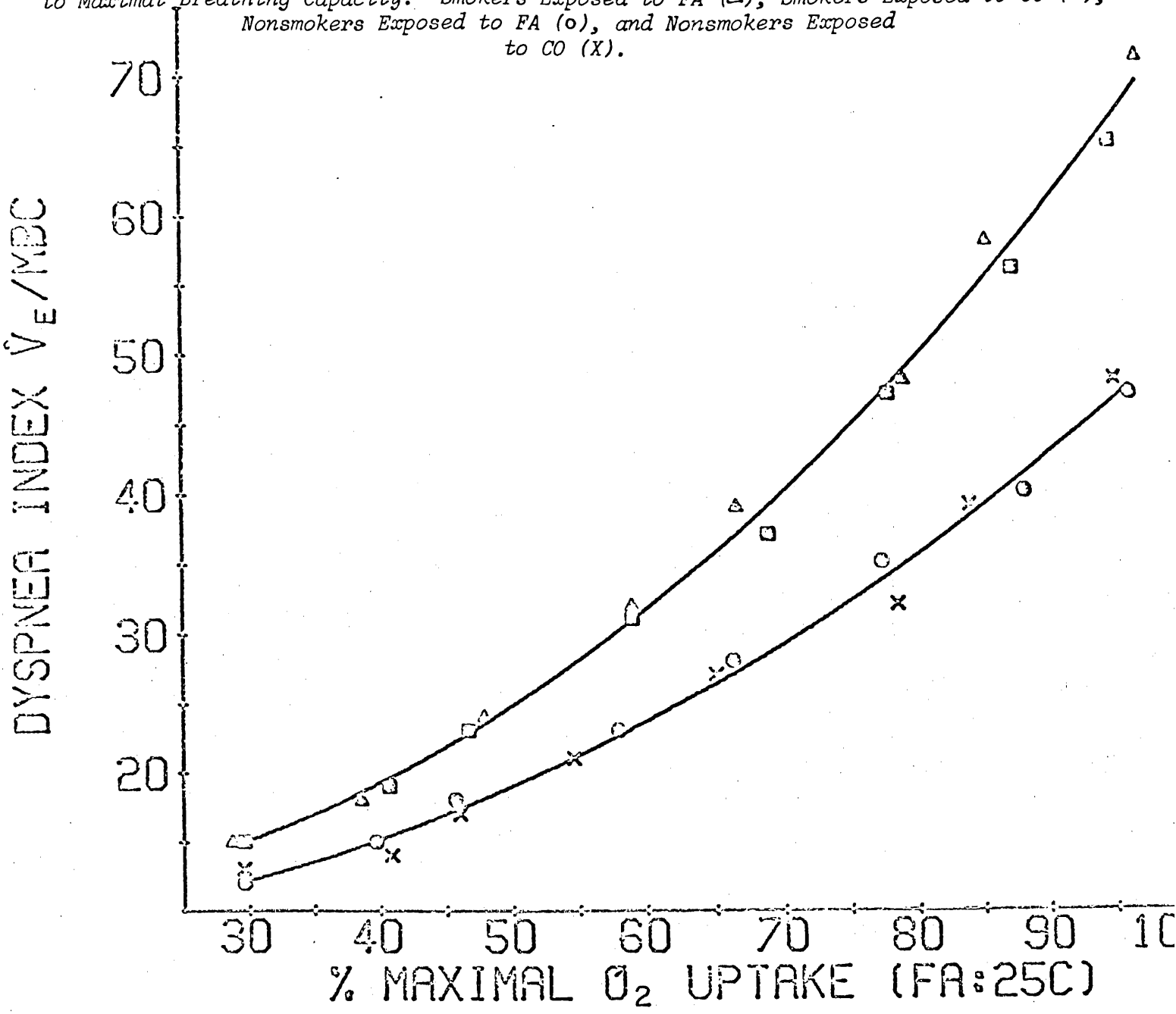
The maximal aerobic power of young men at an ambient temperature of 35°C was unaffected by exposure to CO, PAN, or PANCO. However, there was a significant decrement in work time for nonsmokers while breathing CO at 35°C. Although not significant, the decrease in maximal aerobic power from FA to the CO condition did represent a difference larger than that found between the last two minutes of walk in the FA condition.

Taken in that perspective, the decrease in work time for nonsmokers breathing CO was matched by the expected drop in oxygen uptake for the lower work load. However, the practical significance of such small decrements in performance is minimal. In terms of air pollution standards, the importance of this observation is whether it marks a critical level of COHb for nonsmokers, a point beyond which their performance would continue to deteriorate. Such a question can be answered only by additional studies at 75 or 100 ppm CO. Since smokers' maximal aerobic power and walk time were unaffected by exposure to 50 ppm CO, even though their resultant COHb levels were 64% higher than those of nonsmokers, the question arises as to whether smokers have adapted to high levels of COHb and, if so, in what way. It has been suggested that adaptation to CO might involve an increase in hemoglobin concentration, cardiac output, plasma volume, or alveolar ventilation (19). While the design of this study does not permit a definitive answer to this question, it is of interest to note that there were no differences in resting (nonsmokers: 14.8 mg/100 ml; smokers: 14.7 mg/100 ml) or post exercise (nonsmokers: 15.6 mg/100 ml; smokers: 15.5 mg/100 ml) hemoglobin values between these smokers and nonsmokers.

However, some differences in the respiratory responses of smokers and nonsmokers were consistent across all air mixtures and for both temperatures and were apparent during rest and recovery, as well as during exercise. Although smokers had lower vital capacities and maximum breathing capacities than nonsmokers, there were no differences in the maximum expired ventilatory volumes of the two groups. As a result, smokers had a higher dyspnea index (minute expired ventilatory volume/maximal breathing capacity) throughout the test (Figure 10). However, hyperventilation cannot entirely explain the higher values for CO_2 production found for smokers during rest

FIGURE X

Ventilatory Response of Smokers and Nonsmokers to CO and FA Exposures at 35°C Expressed as Ratio of Ventilatory Volume to Maximal Breathing Capacity. Smokers Exposed to FA (□), Smokers Exposed to CO (△), Nonsmokers Exposed to FA (o), and Nonsmokers Exposed to CO (X).



and submaximal work or for both groups in CO exposures. The significant increase in the respiratory exchange ratio and excess CO_2 for nonsmokers in the CO condition was not matched by a comparable rise in expired ventilatory volume or ventilatory equivalent. It is known that endogenous CO is metabolized to CO_2 in man (20) but to what extent at specific levels of COHb cannot be determined until the mechanisms of CO catabolism are better understood.

Despite the inroads of increasing age and smoking habits on man's ability to perform work (20, 21), the findings of the present studies demonstrated that no additional significant decrease in maximal aerobic power occurred when men aged 40-55 years were exposed to CO, PAN, or PANCO. The 3.4% decrement in $\dot{V}_{O_2\ max}$ of nonsmokers in 25°C and 5.8% in 35°C on exposure to CO was similar to that reported above for young nonsmokers. However, the smokers' $\dot{V}_{O_2\ max}$ was not influenced by exposure to CO or PANCO at either ambient temperature. It was noted that the older smokers had a pre exercise body burden of CO (4.5% COHb) greater than that found in older nonsmokers (2.3% COHb) following their walks in 50 ppm CO. During their walks, smokers' COHb increased very slightly (by 0.6% to 5.1% COHb) so that in effect their control walks breathing purified air were essentially similar to their walks breathing 50 ppm CO. Initially, the pre exercise level of COHb of the older smokers was probably sufficiently elevated to cause a significant back pressure of CO from the blood to the alveolar air such that the diffusion gradient favored a net efflux of CO from the body. However, at some point in time, dependent primarily on the initial body burden of CO and the alveolar ventilation, the diffusion gradient was reversed, so that CO was added to the body. The empirical CO uptake equations of Forbes et al. (22) and Stewart et al. (23) are probably not applicable to smokers at these levels of CO in ambient

air for this short period of exposure.

The large inter-individual variability observed in clinical spirometric tests and the small number of subjects precluded the demonstration of significant pulmonary dysfunction at rest in most parameters measured. However, it was observed that the older smokers had significantly less inspiratory capacities and mid maximal flows than the older nonsmokers. Furthermore, consistent differences were found between these smokers and nonsmokers (in the older subjects) while exercising. Older nonsmokers had a greater $\dot{V}_{O_2\ max}$ (39.06 ml $O_2/kg \cdot min^{-1}$) than smokers (31.22 ml $O_2/kg \cdot min^{-1}$). This difference was even more striking considering that the smokers were a more select group of subjects than were the nonsmokers, since only one of every two candidates for the smoking group successfully passed the screening examination. Comparison with the younger subjects in which it was found that there was no difference in $\dot{V}_{O_2\ max}$ between smokers (42.43 ml $O_2/kg \cdot min^{-1}$) and nonsmokers (41.62 ml $O_2/kg \cdot min^{-1}$) emphasizes the detrimental effect of long term smoking. Hence, if the cross-sectional groups of this study were representative of their respective populations, the detrimental aging effect on $\dot{V}_{O_2\ max}$ (6% for the nonsmokers and 26% for the smokers) was significantly enhanced by smoking.

At 25°C thermoregulatory parameters of the younger subjects evidenced no consistent pollutant effect, although during CO exposures tissue conductance was lower. Explanation of this effect is difficult as the reverse was found during PANCO exposures, suggesting antagonistic effects of the pollutants of which the PAN effect is greater than the CO effect. Also if carbon monoxide was the prime cause for the conductance differences, presumably by means of carboxyhemoglobin formation, a similar difference between smokers and nonsmokers should have been noted for all conditions.

Interestingly, there was a significantly lower rectal temperature of the smokers compared to the nonsmokers during submaximal work and recovery. The T_{re} during the initial stages of work may be reflecting the lower T_{re} of the smokers at the start of exercise. However, as the T_{re} during recovery from work becomes lower by the second minute the smokers must be dissipating heat more efficiently than the nonsmokers. Possible differences in thermoregulatory "set point" due to carbon monoxide poisoning has been recently suggested (12); however, it is not clear what effect a 2-3% difference in carboxyhemoglobin would have on the "set point" or the peripheral vasculature.

For this group of young men, heat stress was more effective in reducing work capacity than any pollutant condition. The 4.3% decrease in maximal aerobic power from the 25 to 35°C environment was greater than the differences in aerobic power found between FA and any of the pollutant conditions. It also appears that the interaction of CO and heat stress is important in eliciting some of the respiratory effects found in the CO exposure at 35°C, since thay were not as pronounced in the 25°C environment as in FA at 35°C. For normal healthy young men, the air pollution standards for CO in the Los Angeles area appear to be set at a realistic level. Whether this same standard is appropriate for individuals with cardiovascular or respiratory problems, or women and children requires further investigation. It should also be noted that these exposures were of relatively short duration and may not reflect the responses of men working within the same environment for longer periods of time.

Although $\dot{V}_{O_2\ max}$ expressed per unit of body weight for the older subjects evidenced no statistically significant change, a 7.1% decrease in aerobic capacity of smokers was noted during PAN exposures at 35°C (Table 6).

The decrease appeared to be linked with total ventilatory volume at $\dot{V}_{O_2\ max}$, and when expressed in absolute terms (FA at 35°C, $\dot{V}_{O_2\ max}$ = 2.39 liters O_2/min; PAN at 35°C, $\dot{V}_{O_2\ max}$ = 2.21 liters O_2/min) the $\dot{V}_{O_2\ max}$ was decreased significantly ($P < 0.10$). It was possible, therefore, that the level of PAN used in this study was at a threshold level sufficient to interact with temperature, age, and long-term smoking to lower the ventilatory performance so that maximal work tended to be compromised. Further studies on higher levels of PAN would be required to provide definitive data on the potential decrement in performance capacity. Other differences between older smokers and nonsmokers found at $\dot{V}_{O_2\ max}$, such as increased body temperature, were primarily related to the longer walk times of the nonsmokers.

No physiological effects could be demonstrated for PAN. Since PAN was delivered to the subjects through a mouthpiece, these subjects experienced no irritation of the eyes and nose. It is possible that in the normal environment, discomfort caused by the irritative properties of PAN might be sufficient to introduce a psychological factor that could influence work performance.

The combination of CO and PAN produced no noticeable effects on the subjects' responses to maximal exercise. The slight tendency for PANCO to minimize differences noted in the CO condition was probably a result of measurement variability or an interactive effect of PAN or its components with CO on the subject.

However, Wayne et al. (22) have reported that Los Angeles high school cross-country runners performed at lower levels during races when photochemical smog was present. The highest correlation to performance was that of the oxidant level in the hour immediately before the races. Even

relatively low levels of oxidant had a definite adverse effect. The one component of photochemical smog investigated here, PAN, had no significant influence of maximal oxygen uptake. Neither was there any difference found in maximum aerobic capacity when PAN and CO were given simultaneously. Earlier reports by Smith (23) on PAN and Holland et al. (24) on photochemical smog regarding the suspected influence of photochemical smog to modify the energy requirements for light levels of work conducted for short periods of time were contradictory. The present studies showed that during the early stages of the maximum capacity tests where subjects were performing light work for approximately the same intervals of time as the above investigations (23, 24), no appreciable effect on oxygen uptake or respiratory and cardiovascular parameters were observed. Obviously some other component(s) in Los Angeles air must be responsible for the effects noted by Wayne et al. (22) or probably they may be explained on psychological factors due to decreased motivation related to discomfort.

For the older subjects the major functional differences observed in this study were related to smoking and were not affected by CO or PAN. For a given unit of oxygen uptake, the ventilatory volume required was greater in smokers than in nonsmokers (Figures 7A and 7B). The need of the smoker to increase alveolar ventilation can be explained by the findings of Krumholz et al. (18), who demonstrated that smokers had a decreased diffusion capacity when compared to nonsmokers and therefore increased their ventilation to overcome their diminished diffusion capability. This hyperventilation of the smokers was apparently reflected by an increase in their respiratory exchange ratio per unit of oxygen uptake (Figures 8A and 8B). Unfortunately, the physiological meaning of the differences in respiratory exchange ratios cannot be ascertained from the observed data.

Having accounted for order effects and psychological effects, this study indicates that exposure to two common air pollutants singly or in combination for a mean time of 42 minutes, while healthy men were undertaking a test to determine their maximum aerobic capacity and recovery from this effort, resulted in only minor alterations in metabolic, cardiovascular, and temperature regulatory parameters. These findings would suggest that other constituents of photochemical smog such as nitrogen oxides, ozone, and high temperatures need to be evaluated regarding their interactive effect on work capacity before one can determine if a causal relationship exists between high oxidant levels and decreased performance.

However, it would be premature on the basis of the results of these studies to conclude that neither CO nor PAN had an adverse effect on the ability of men to perform strenuous work under these ambient conditions. All of these subjects had been screened for cardiac and pulmonary abnormalities and therefore represented a select segment of the population. Nor was there any attempt in this study to ascertain the cumulative effects of daily exposures or longer periods of exercise under these conditions on man's ability to work. Taking into account the relatively small number of subjects with the fact that in one instance (PAN, 35°C, older smokers) the difference in $\dot{V}_{O_2\ max}$ was statistically significant when expressed in absolute terms suggests that a further increase in levels of the pollutants or time of exposure may produce changes which would become physiologically meaningful. Also, it was possible that this level of PAN may be a threshold level for a specific group of people; that is, older smokers or subjects with pulmonary impairment similar to that observed in long-term smokers.