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THE EFFECT OF NITROGEN DIOXIDE ON LUNG FUNCTION IN NORMAL SUBJECTS

Health Effects Research Laboratory
Office of Research and Development
U.S. Environmental Protection Agency
Research Triangle Park, North Carolina 27711

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by

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FOREWORD

The many benefits of our modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the relative risk of existing and new man-made environmental hazards is necessary for the establishment of sound regulatory policy. These regulations serve to enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our Nation's population.

The Health Effects Research Laboratory, Research Triangle Park, conducts a coordinated environmental health research program in toxicology, epidemiology, and clinical studies using human volunteer subjects. These studies address problems in air pollution, non-ionizing radiation, environmental carcinogenesis and the toxicology of pesticides as well as other chemical pollutants. The Laboratory develops and revises air quality criteria documents on pollutants for which national ambient air quality standards exist or are proposed, provides the data for registration of new pesticides or proposed suspension of those already in use, conducts research on hazardous and toxic materials, and is preparing the health basis for non-ionizing radiation standards. Direct support to the regulatory function of the Agency is provided in the form of expert testimony and preparation of affidavits as well as expert advice to the Administrator to assure the adequacy of health care and surveillance of persons having suffered imminent and substantial endangerment of their health.

The investigation described in this report is part of the Laboratory's effort to provide a scientifically adequate health data base for refining existing criteria for regulated pollutants.

John H. Knelson, M.D.
Director,
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ABSTRACT

Cardiopulmonary and metabolic responses of three groups, each consisting of five adult males (age 19 - 29) were determined before, during, and after a 2-h exposure to 0.62 ± 0.12 ppm NO_2 at 25°C and 45% RH. The three groups exercised during exposure at 40% of $\dot{V}_{O_2\ max}$ for either 15, 30, or 60 min for groups C, A, and B, respectively. During the exercise periods the ventilation was about 33 liters/min, a four-fold increase over the resting level. There were no physiologically significant cardiovascular, metabolic, or pulmonary function changes which could be attributed to exposure to this level of NO_2 (0.62 ppm). There were no differences between the groups in their response despite the fact that groups A and B received more NO_2 as a result of 28% and 84% greater ventilations, respectively.

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SECTION I

CONCLUSIONS

No significant alterations in the multiple cardiovascular, pulmonary, or metabolic measures occurred as a result of a 2-h exposure to 0.62 ppm NO_2 at variable levels of activity.

SECTION II

RECOMMENDATIONS

1. The present air quality standards for NO_2 appear to be adequate to protect young healthy adult males from acute cardiovascular or pulmonary dysfunction. Long-term effects of ambient levels of NO_2 are uncertain especially if there remains a possibility of a future increase in ambient NO_2 concentration.

2. The synergistic action of other air contaminants with NO_2 in relation to the effect of various pollutant combinations on human health is still in need of evaluation. Specifically, the presence of sulfur dioxide and oxidants, notably ozone and peroxyacetylnitrate, may in combination with NO_2 exaggerate effects induced by those pollutants on the human respiratory system.

3. Individuals from other age groups, both male and female, and patients with pulmonary disorders should be evaluated under similar conditions to those employed in the present study.

SECTION III

INTRODUCTION

Nitrogen dioxide is a reddish-brown colored gas with a characteristic odor which is prevalent in areas where automobile use is heavy or where other high temperature combustion processes are used. NO_2 is important in the formation of photochemical smog and is also an important constituent of tobacco smoke. Concern over potential health effects from NO_2 exposure, either from the ambient atmosphere or from cigarettes, has produced a number of studies in animals and man. These studies have been primarily concerned with the role of NO_2 in acute and chronic pulmonary disease. Unfortunately, the majority of investigations have dealt with concentrations of NO_2 considerably in excess of those observed even on days of heavy community air pollution. Although a few experimental studies have been made on man, very little relevant data is available on the effects of atmospheric levels of NO_2 (< 1 ppm) on human subjects. Therefore, in this investigation we planned to study the effects of acute exposure to low levels of NO_2 (0.6 ppm) upon the pulmonary and circulatory function of young adult male subjects.

SECTION IV

REVIEW OF LITERATURE

In very high concentrations, NO_2 can produce edema (5) but manifestation of this response takes several hours. Following a brief exposure (10 min) to 4 - 5 ppm NO_2 Abe (1) found a lag time of 30 min before a maximum change in airway resistance had occurred. In contrast, exposure to SO_2 resulted in a rapid change in airway resistance which was reversed once the SO_2 was withdrawn. Whereas ozone causes a decrease in both vital capacity and forced expiratory flow (2,3), NO_2 apparently causes only a reduction in forced expiratory flow (1), an observation supported by epidemiological data reported for Tokyo school children (4). It is suggested that the acute response to NO_2 may be related to increased histamine release from the lung tissue although the evidence for this is not convincing (6).

In patients suffering from chronic non-specific lung disease, brief exposure (2 min) to NO_2 concentration of > 2 ppm caused a significant increase in airway resistance and the effects were correlated with the concentration inhaled (7). In normal subjects a 15-min period of exposure to a concentration of 2 - 5 ppm NO_2 caused a rise in airway resistance as well as a decrease in diffusion capacity; no effect was seen following a 15-min exposure to 0.5 - 1.5 ppm NO_2 (8,9).

Despite the epidemiologic data supporting a relationship between NO_2 and respiratory dysfunction (4,10), clearcut evidence of changes in pulmonary function due to reasonable ambient levels of NO_2 (0.20 - 1.0 ppm) is lacking. As Warner and Stevens (11) point out, it is difficult to assess the contribution of other environmental factors (particulates, high ambient temperatures, acid mists, SO_2) in such epidemiological studies.

There is some suggestion that elevated NO_2 levels may be related to an increased frequency of respiratory illness (12) although these data are not conclusive. An increased incidence of asthmatic attacks has also been related to elevated pollutant levels (13) but weather changes may

be more significant factors than NO_2 concentration in this relationship. Makino (14), in Tokyo, demonstrated an increase in subjective symptoms among school children (eye irritation, headache, respiratory difficulty) when total oxidant levels exceeded 0.1 ppm, a relatively minor pollutant episode. Interestingly, girls reported more symptoms than boys.

Hackney et al. (15,16), in studying the response of normal and "sensitive" subjects to ozone (0.25 ppm) found no physiologically important effect of adding NO_2 (0.3 ppm) to their ozone atmosphere. Pengelly (17), reported that one of three subjects exposed to 0.9 - 1.4 ppm of NO_2 for two hours showed an increased pulmonary resistance for the duration of exposure. This same subject had previously shown a marked sensitivity to ozone. After 180 days of continuous exposure to 1 ppm NO_2, Kosmider and Miscewicz (18) found an increase in blood cholesterol, lipids, and lipoproteins in normal males and suggested that NO_2 may have arterio-sclerotic actions. Busey (19), found no physiological effects in monkeys after 87 weeks of continuous exposure to 0.51 ppm of NO_2. However, at 6.8 ppm NO_2, rapid shallow breathing occurred as well as bronchiolar thickening and focal emphysema.

The association of NO_2 exposure with increased respiratory tract infections and the emphysomogenic action of NO_2 have been studied more carefully in non-primates. Loss of cilia, damage to bronchiolar epithelial lining (20), reduced surfactant synthesis (21), increased evidence of infection and emphysema (22,23), depression of mucociliary transport (24,25), have all been observed in animals exposed to varying concentrations of NO_2 from 0.9 - 20.0 ppm for periods of from one week to more than a year. However, these and other rodent studies have a questionable relationship to responses which may be expected from environmental exposure to NO_2 because of the high concentrations of NO_2 used and the continuous rather than intermittent nature of the exposure. Furthermore, because of its relative insolubility, NO_2 tends to penetrate further towards the peripheral airways than either SO_2 or O_3 and thus in long term exposures appears to have a greater effect on small airways and alveolar septa (23,26). Prolonged exposure to lower NO_2 levels

(lifetime exposure to 0.8 ppm NO_2) did not increase the incidence of emphysema in rats. The only symptom observed was an increase (20%) in respiratory rate (27).

At present ambient levels (0.0 - 1.0 ppm) nitrogen dioxide is not associated with the marked effect on respiratory function that has been observed with exposure to ozone. Although some increase in respiratory infection may be expected with repeated NO_2 exposure, acute decrease in lung volume or forced expiratory flow would not be anticipated at the present ambient levels. The cumulative effect of several years of exposure to low levels of NO_2 on humans cannot be determined although some acceleration of the aging process of the lung is possible (28,29). Morrow (30) in a review of recent NO_2 literature concluded that "injurious effects and important predisposing actions of NO_2 are more likely to occur at levels between 1 and 3 ppm (2000 - 6000 $\mu g/m^3$)." He also stated that the current air quality standard (0.05 ppm NO_2) is not conservative and may represent a level where the probability of deleterious health effects is unacceptable. Goldstein (31), however, feels that the present NO_2 standard is adequate and furthermore suggests that a transient increase in airway resistance as a result of NO_2 exposure is inconsequential as a health hazard. This view is definitely open to question, since any detrimental physiological response, however small, represents a deterioration in the quality of life.

SECTION V

GENERAL OBJECTIVES AND SPECIFIC AIMS

This study was designed to determine the effects of acute exposure to 0.6 ppm nitrogen dioxide (NO_2) on the metabolic and cardiopulmonary systems of young men (18 - 30 years of age) under normal ambient temperature conditions (25°C, 45% RH).

Since studies on resting subjects do not adequately represent the normal state of man in his environment, the subjects of this study exercised for variable periods of time at levels equivalent to 35 - 45% of their maximal capability. The effect of exposure to NO_2 at different levels of intake could then be evaluated when man was either at rest or at work as well as the factor of differing absolute levels of inhaled NO_2. The findings obtained from this investigation may be used by regulatory agencies to evaluate a level of 0.5 ppm NO_2 as a possible guideline for the health protection of the general population.

SECTION VI

RESEARCH METHODS

SUBJECTS

Eighteen young healthy males (ages 18 - 30 years) were selected as subjects from some 20 volunteers (Table 1). All volunteers were non-smokers (confirmed by blood carboxyhemoglobin (HbCO) analysis) and were drawn from the student population of the University of California, Santa Barbara campus. Subjects were completely informed as to the purpose of the tests and signed University consent forms to act as human subjects. Each volunteer was medically screened. A medical history questionnaire, a resting 12-lead electrocardiogram, an exercise electrocardiogram (V_4) up to 160 beats each minute, determination of basal metabolic rate (BMR), and a battery of clinical spirometric tests were used in evaluating each subject. Following the screening the subjects performed a maximal aerobic capacity ($\dot{V}O_{2\ max}$) test on a treadmill. Each subject was then trained (1-hour sessions) in the procedures being utilized for the determination of cardiovascular and pulmonary functions.

EXPERIMENTAL DESIGN

The following basic approach was used with all exposure conditions presented in random order. Three groups of subjects (designated A, B, and C) were randomly exposed to two separate conditions. Exposure to each condition was separated by a minimum of one week for each individual subject. The exposure conditions for both the pollutant and ambient environment are outlined in Table 2.

Table 1. SUBJECT INFORMATION

Subject No.	Age, yr	Ht, cm	Wt, kg	TLC, ml	FRC, ml	VC, ml	$FEV_{1.0}$, ml	$\dot{V}_{O_2\ max}$, liters/min	Workload, % $\dot{V}_{O_2\ max}$	
									FA	NO_2
7816	25	180	75.2	7778	3729	6129	4486	2.97	34	36
7834	21	178	79.0	7377	3743	5942	4921	4.39	23	25[a]
7970	22	181	78.0	8442	4734	6766	5012	3.32	41	40
7966	20	191	89.6	10,434	4974	8304	6615	4.22	37	34
7942	20	185	78.5	8074	3947	6420	5174	4.23	40	36
7915	20	191	83.0	8435	4758	6499	5028	4.38	40	42
7940	20	177	78.0	8002	3596	6604	5056	4.26	43	41
7986	23	165	52.2	6529	3751	4250	3846	2.68	44	36
7993	21	173	57.6	7333	4044	5729	5080	3.36	36	32
8088	20	172	65.0	6450	3423	4969	4247	3.33	40	39
8063	20	189	84.8	7906	3964	6302	4148	3.92	38	45
7996	20	173	77.0	7515	3833	5699	4360	3.70	46	30
8086	21	178	67.8	6636	3064	5343	4763	3.74	42	38
8080	21	185	73.0	8488	4785	6522	5860	3.98	44	43
8034	22	176	71.1	6944	2907	5626	4524	3.68	40	41
8071	23	188	64.6	7294	4263	5093	4860	3.39	44	30

[a] Workload was set too low in ozone study and was not changed in order to permit ozone-nitrogen dioxide comparison.

TABLE 2. EXPOSURE CONDITIONS

Exposure[a]	Temperature and relative humidity.
Ambient air (Control exposures)	25°C 45% RH (Code 1)
	WBGT = 64.4°F
NO_2 (Experimental exposure)	25°C 45% RH (Code 2)

[a]Exposure was for a 2-h period.

EXPERIMENTAL PROTOCOL

Groups A, B, and C underwent the routines outlined in Table 3.

TABLE 3. EXPERIMENTAL ROUTINE

	Control Period	Exposure Periods[a]								Recovery Period
	Code Number	1	2	3	4	5	6	7	8	
Group A	Pre-Exp. Tests	R	R	R	R	W	W	R	R	Post-Exp. Tests
Group B	Pre-Exp. Tests	W	R	W	R	W	R	W	R	Post-Exp. Tests
Group C	Pre-Exp. Tests	R	R	R	W	R	R	R	R	Post-Exp. Tests

[a]Each section = 15 min duration; R = sitting rest; W = work at 35 - 45% $\dot{V}_{O_2\ max}$.

Pre- and post-exposure tests lasted approximately 1 h each. During exposure, the group A subjects rested in the sitting position for 1 h then exercised for 30 min on a motor-driven treadmill at approximately 35 - 45% $\dot{V}_{O_2\ max}$ followed by a 30 min seated rest. Group B underwent a

similar 2-h exposure except that the exercise sessions occurred intermittently during the exposure each 15-min period of exercise being followed by a 15-min rest period. Group C exercised in the fourth period only.

Exposures occurred throughout the day although each individual was always scheduled at the same time of day. On arrival at the Institute, the subject was weighed nude and then connected to the appropriate monitoring leads for electrocardiogram and rectal temperature for Group B. Clothing worn during the experiments consisted of tennis shoes, socks, and shorts. Each subject was given a clinical chest examination. The subject performed a battery of pulmonary tests on a 13.5-liter chain-compensated spirometer (W. E. Collins) and in a body plethysmograph (W. E. Collins). The subject then entered the exposure chamber, set at the required ambient conditions, and was connected to appropriate monitoring cables. The 2-h exposure was divided for convenience of analysis into eight 15-min segments (numbered 1-8) (Table 3). Each period for either group A, B, or C was utilized as outlined in the following protocol.

PROTOCOL DURING EXPOSURES

PERIOD 1

GROUP A	Minutes 2-4	-- Ventilatory volume ($\dot{V}_E$), O_2 and CO_2 percentages, heart rate (HR), tidal volume (V_T), and respiratory frequency (f_R). Temperatures: Room (T_{rm}), radiant (R_r).
	Minutes 4-6	-- Cardiac output ($\dot{Q}$), blood pressure (BP), and HR.
	Minutes 6-10	-- Steady-state diffusion capacity to carbon monoxide (DL_{CO}).
	Minutes 10-15	-- Pulmonary function tests: forced vital capacity (FVC), forced expired volume at 1.0, 2.0, and 3.0 secs ($FEV_{1.0,\ 2.0,\ 3.0}$); forced expiratory flow at 50% and 75% of vital capacity exhaled (FEF 50%, FEF 75%),

mean forced expiratory flow (FEF 25 - 75%) in duplicate. Closing volume (CV), with slow vital capacity (VC) in duplicate. T_{rm}, T_r.

PERIOD 2

GROUP A

Minutes 5-6 -- HR, BP, T_{rm}, T_r.

Minutes 10-11 -- HR, BP, T_{rm}, T_r.

Minutes 11-14 -- FVC, $FEV_{1.0, 2.0, 3.0}$, FEF 50%, FEF 75%, and FEF 25 - 75%, in duplicate. CV with slow VC in duplicate.

PERIOD 3

GROUP A -- BP, HR, T_{rm}, T_r (each at 5, 10, and 15 min).

PERIOD 4

GROUP A

Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, HR, V_T, f_R, T_{rm}, T_r.

Minutes 4-6 -- Q, BP, HR.

Minutes 6-10 -- Steady-state $D_{L_{CO}}$.

Minutes 10-15 -- FVC, $FEV_{1.0, 2.0, 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, HR.

PERIOD 5

GROUP A -- BP, HR, T_{rm}, T_r (each at 5, 10, and 15 min).

PERIOD 6

GROUP A

Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, T_{rm}, T_r, HR.

Minutes 4-6 -- $\dot{Q}$, BP, HR.

Minutes 6-10 -- Steady-state $D_{L_{CO}}$.

Minutes 10-15 -- T_{rm}, T_r, HR.

PERIOD 7

GROUP A -- BP, HR, T_{rm}, T_r (each at 10 and 15 min).

Minutes 3-10 -- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate.

PERIOD 8

GROUP A Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, HR, T_{rm}, T_r.

Minutes 4-6 -- $\dot{Q}$, BP, HR.

Minutes 6-10 -- Steady-state $D_{L_{CO}}$.

Minutes 10-15 -- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. HR, BP, T_r, T_{rm}.

PROTOCOL DURING EXPOSURES

PERIOD 1

GROUP B Exercise

Minutes 6-8 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, T_{rm}, T_r, T_{re}, HR.

Minutes 8-10 -- $\dot{Q}$, BP, HR.

Minutes 10-14 -- Steady-state $D_{L_{CO}}$.

Minutes 14-15 -- T_{rm}, T_{rad}, T_{re}, HR.

PERIOD 2

GROUP B Minutes 5-6 -- BP and HR, T_{rm}, T_r, T_{re}.

Minutes 6-14 -- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%,

FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, T_{re}.

Minutes 14-15 -- BP and HR.

PERIOD 3

GROUP B Exercise

Minutes 6-8 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, T_{rm}, T_r, T_{re}, HR.

Minutes 8-10 -- Q, BP, HR.

Minutes 10-14 -- Steady-state $D_{L_{CO}}$.

Minutes 14-15 -- T_{rm}, T_{rad}, T_{re}, HR.

PERIOD 4

GROUP B Minutes 5-6 -- BP and HR, T_{rm}, T_r, T_{re}.

Minutes 6-14 -- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, T_{re}.

PERIOD 5

GROUP B Exercise

Minutes 6-8 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, T_{re}, HR.

Minutes 8-10 -- Q, BP, HR.

Minutes 10-14 -- Steady-state $D_{L_{CO}}$.

Minutes 14-15 -- T_{rm}, T_{rad}, T_{re}, HR.

PERIOD 6

GROUP B Minutes 5-6 -- BP and HR, T_{rm}, T_r, T_{re}.

Minutes 6-14 -- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, T_{re}.

Minutes 14-15 -- BP and HR.

PERIOD 7

GROUP B — Exercise

Minutes 6-8 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, T_{rm}, T_r, T_{re}, HR.

Minutes 8-10 -- Q, BP, HR.

Minutes 10-14 -- Steady-state $D_{L_{CO}}$.

Minutes 14-15 -- T_{rm}, T_{rad}, T_{re}, HR.

PERIOD 8

GROUP B

Minutes 5-6 -- BP and HR, T_{rm}, T_r, T_{re}.

Minutes 6-14 -- FVC, $FEV_{1.0, 2.0, 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, T_{re}.

Minutes 14-15 -- BP and HR.

PROTOCOL DURING EXPOSURES

PERIOD 1

GROUP C

Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, HR, V_T, f_R, T_{rm}, T_r.

Minutes 4-6 -- Q, BP, HR.

Minutes 6-10 -- Steady-state $D_{L_{CO}}$.

Minutes 10-15 -- FVC, $FEV_{1.0, 2.0, 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, and HR.

PERIOD 2

GROUP C -- BP, HR, T_{rm}, T_r (each at 5, 10, and 15 min).

PERIOD 3

GROUP C

Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, HR, V_T, f_R, T_{rm}, T_r.

Minutes 4-6 -- $\dot{Q}$, BP, HR.

Minutes 8-15 -- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, HR.

PERIOD 4

GROUP C Exercise

Minutes 6-8 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, T_{rm}, T_r.

Minutes 8-10 -- $\dot{Q}$, BP, HR.

Minutes 10-14 -- Steady-state DL_{CO}.

Minutes 14-15 -- T_{rm}, T_r, HR.

PERIOD 5

GROUP C Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, HR, V_T, f_R, T_{rm}, T_r.

Minutes 4-6 -- $\dot{Q}$, BP, HR.

Minutes 8-15 -- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, HR.

PERIOD 6

GROUP C Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, HR, V_T, f_R, T_{rm}, T_r.

Minutes 4-6 -- $\dot{Q}$, BP, HR.

Minutes 8-15 -- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, HR.

PERIOD 7

GROUP C	Minutes 2-4	-- $\dot{V}_E$, O_2 and CO_2 percentages, HR, V_T, f_R, T_{rm}, T_r.
	Minutes 4-6	-- Q, BP, HR.
	Minutes 8-15	-- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. T_{rm}, T_r, HR.

PERIOD 8

GROUP C	Minutes 2-4	-- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, HR, T_{rm}, T_r.
	Minutes 4-6	-- Q, BP, HR.
	Minutes 6-10	-- Steady-state $D_{L_{CO}}$.
	Minutes 10-15	-- FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, FEF 50%, FEF 75%, FEF 25 - 75% in duplicate. CV with slow VC in duplicate. HR, BP, T_{rm}, T_r.

At the end of the 2-h exposure, the subject was disconnected from the monitoring wires, returned to the filtered air atmosphere of the laboratory, and seated on a chair. The attending physician immediately undertook a clinical chest examination. The subject then repeated the battery of spirometric tests. Following these post-exposure tests, the subject completed a 33-item questionnaire, was weighed nude, and then allowed to leave the laboratory on permission of the examining physician.

MEASUREMENT TECHNIQUES

Metabolic measurements were made using open-circuit indirect calorimetric techniques (32). Ventilatory volumes were monitored by collecting timed volumes in a 120-liter chain-compensated spirometer. Gas samples were analyzed for O_2% and CO_2% in a Quintron gas chromatograph, calibrated against standard Haldane analyzed gases. Accuracy of analysis was ±0.02% for CO_2 and ±0.05% for O_2. All metabolic parameters (see Glossary) were calculated.

Copper-constantan thermocouples were used to monitor rectal temperature (T_{re}) at the depth of 12 cm into the rectum. Globe temperature and chamber air temperature as well as a continuous monitor of relative humidity provided a description of environmental conditions in terms of WBGT (approximately 64 for groups A, B, and C). The thermocouple temperatures were recorded by a Honeywell multichannel digital recorder and simultaneously recorded by a laboratory computer (PDP-12). All temperatures were measured with an accuracy of ±0.1°C.

Cardiac output was determined using the carbon dioxide rebreathing technique of Defares (33) as modified by Jenous et al. (34). Calculation of mixed venous CO_2 ($P\bar{v}CO_2$) was performed by the extrapolation method (35) utilizing the laboratory computer display. This enabled the operator to discard those points which obviously were not fitted to the general rebreathing pattern and thereby obtain a better estimate of the point of equilibrium. The coefficient of variation for repeated measurements on one subject within a period of one hour was 10%. Tidal volume and respiration rate were determined during the measurement of end tidal carbon dioxide. Blood pressure was obtained by the indirect Riva Rocci method and heart rate from V_4 lead recorded on a Sanborn 500 Viso-Cardiette electrocardiograph. All electrocardiogram tracing were read by the Institute's cardiologist. An oscilloscope display of the electrocardiogram was continuously monitored. The $D_{L_{CO}}$ was determined using the steady-state technique of Filley et al. (36) as modified by Bates et al. (37). The coefficient of variation of $D_{L_{CO}}$ determination for repeat measurements of one subject at rest was 12% and at moderate exercise (40% $\dot{V}_{O_2\ max}$) was

6%. Combinations of the cardiovascular and metabolic data enabled the calculations of various cardiorespiratory parameters, i.e. diffusion/perfusion ratio and ventilation/perfusion ratio (see Appendix for a sample printout of measured and calculated data).

The procedures outlined by Kory et al. (38) were used for pulmonary function tests. A 13.5-liter chain-compensated spirometer (W. E. Collins Co.) was used for pre- and post-exposure pulmonary measures and a wedge spirometer (Med. Science Electric Co.) connected via appropriate pre-amplifiers to a multichannel pen recorder was used during the exposure period for the determination of FVC, $FEV_{1.0,\ 2.0,\ 3.0}$, IC, ERV, FEF 50%, FEF 75%, and FEF 25 - 75%. The helium dilution technique was used for the measurement of functional residual capacity. Before and after exposure the total lung capacity (TLC) was calculated using this value. MVV was determined prior to and following exposure. All volumes and flow rates measured in these tests were corrected to BTPS. During exposure duplicate determinations of closing volume (CV) and slow vital capacity (SVC) using a helium bolus technique (39,40) were made. Thoracic gas volume (TGV) and airway resistance were measured in a body plethysmograph (Collins) using the method of DuBois (41,42). Calculation of other pulmonary function parameters were performed by computer (see Appendix). Comparison of volumes measured on numerous subjects at the same time of day on the chain-compensated spirometer and the wedge spirometer indicated that at volumes between 3 and 6 liters the wedge spirometer was consistently higher by 200 ml -- a difference ranging from 3 - 7%. However, as comparisons between values obtained by the two methods were not made, corrected values were not utilized. The coefficients of variation of repeat measurements of vital capacity on one subject made at hourly intervals during one day ranged from 0.9% to 5.0%, whereas the coefficient of variation of repeated measurements of closing volume would range from 10% to 30%, which is consistent with recently reported results (43,44).

CHAMBER DESIGN AND CONTROL

A 1.8 m wide by 2.4 m long by 2.6 m high double-walled flow-through acrylic environmental chamber was utilized for chamber exposures. Inlet air was filtered through activated charcoal, Baralyme, soda lime, Drierite, and gauze before entering the chamber. Air was forced into the chamber at flow rates ranging from 200 liters/min to 500 liters/min resulting in exchange turnover in the chamber ranging from once every 56 min to once every 22 min. Minimal air movement across the subject occurred due to the dispersive design of the inflow air. A regulated heating dehumidifier and air conditioner allowed for appropriate temperature control. When needed for humidification steam was piped directly into the air inflow. Nitrogen dioxide was added directly to chamber air inlet via a proportional system from a gas cylinder containing 1% NO_2 in nitrogen. The chamber was equipped with a small motor-driven treadmill, chair, and appropriate equipment for the subject to perform the tests without experimenter assistance. All rubber components were protected from possible effects of air pollutants by a weekly coating of anti-oxidant (Armor-all).

NO_2 concentration was continuously monitored by the chemiluminescence technique. An aliquot sample was drawn through fritted glass bubblers, once each exposure for the determination of NO_2 concentration by the Saltzman (45) method. The mean 2-h exposure NO_2 concentration measured by the chemiluminescence technique and that checked by aliquot samples chemically analyzed was 0.62 ± 0.12 ppm. The NO_2 sampling inlet was placed near to an average position of the subject's head during exposure (always within 24 inches).

STATISTICAL EVALUATION OF DATA

Data were analyzed by a series of analyses of variance. For pre- and post-test measurements, a two-factor factorial analysis of variance with repeated measures across time and ambient air was used; for the pre-exercise and post-exercise periods, a one-factor analysis of variance with repeated measures across ambient air. In all cases where a significant

interaction was observed, a test was made of the simple main effects followed by a Newman-Keuls test of ordered means where appropriate. All hypotheses were tested for significance at an alpha level of 0.05.

SECTION VII

RESULTS AND DISCUSSION

RESULTS

Group A

The protocol for this group was identical to that in a previously completed study of the effects of ozone on cardiorespiratory performance (46). All subjects in this group had participated in our earlier ozone experiments.

There were no demonstrable cardiovascular or pulmonary effects due to the pollutant, nitrogen dioxide. The pulmonary function measurements taken before and after NO_2 exposure are presented in Table 4. The MVV was lower ($P < 0.05$) after NO_2 exposure than in the pre-exposure period. However, this was not accompanied by any other significant changes in pulmonary function which would suggest that this change was produced by NO_2. The pulmonary function measurements made during the exposure period are summarized in Table 5. When the pre-exercise pulmonary function measurements were compared with the post-exercise measurements, there was a tendency for the measures of maximum expiratory flow ($FEV_{1.0}$, $FEV_{2.0}$, FEF 50% - $P < 0.10$, FEF 25 - 75% - $P < 0.05$) to decrease slightly. However, these changes were small and within the variability of similar measurements made throughout the exposure and therefore we believe they are of minimal importance. Cardiorespiratory data collected during the exposure is presented in Table 6. There were no significant changes attributable to nitrogen dioxide exposure. During the exercise period, as expected, there was an increased metabolic rate and the consequent increase in ventilation, cardiac output, blood pressure, and associated variables.

The pulmonary function changes occurring with ozone were compared to the values obtained during NO_2 exposure (Table 7). Significant decreases in VC, $FEV_{1.0}$, FEF 25 - 75%, FEF 50%, and FEF 75% had occurred

Table 4. PULMONARY FUNCTION CHANGES BEFORE AND AFTER EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP A)

(NOTE: Values are mean ± SD; n = 5.)

	Filtered Air (Code 1)		Nitrogen Dioxide (Code 2)	
	Pre	Post	Pre	Post
FVC, ml	6686±478	6698±446	6738±465	6720±490
$FEV_{1.0}$, ml	5215±322	5294±424	5268±499	5227±367
FEF25-75%, liters/sec	5.57±0.72	5.07±0.71	4.84±0.93	4.60±0.58
FEF50%, liters/sec	5.12±0.47	5.23±0.61	4.85±0.31	4.91±0.41
FEF75%, liters/sec	1.95±0.16	2.35±0.56	2.23±0.48	2.25±0.28
IC, ml	4237±363	4201±397	4154±376	4164±406
ERV, ml	2449±205	2497±127	2584±212	2556±151
FRC, ml	4292±375	4493±456	4158±224	4274±229
RV, ml	1843±202	1996±379	1574±123	1718±182
TLC, ml	8529±675	8694±824	8312±527	8438±616
R_{aw}, cm H_2O/liters·sec	1.82±0.10	1.90±0.24	1.86±0.22	1.87±0.19
MVV, liters/min	225.34±16.3	219.2±20.2	231±19	210±26[a]

[a] $P < 0.05$.

Table 5. PULMONARY FUNCTION CHANGES DURING 2-HOUR EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP A)

(NOTE: Exercise at 45% $\dot{V}_{O_2\ max}$ during minutes 60-90.)

	Time, min	FVC, ml	$FEV_{1.0}$, ml	$FEV_{2.0}$, ml	$FEV_{3.0}$, ml	FEF25-75%, liters/sec	FEF50%, liters/sec	FEF75%, liters/sec
Code 1 (Filtered Air)	12	6941±475	5438±563	6492±580	6714±539	5.57±0.90	6.54±1.26	2.72±0.55
	27	6812±407	5312±345	6343±470	6585±442	5.31±0.69	6.20±0.88	2.49±0.32
	57	6727±452	5272±533	6230±572	6552±514	4.69±0.67	5.67±1.00	2.54±0.75
	100	6718±379	5222±481	6247±493	6486±445	4.73±0.77	5.71±0.80	2.50±0.68
	117	6936±546	5344±607	6255±715	6785±588	5.38±0.91	5.66±1.12	2.48±0.57
Code 2 (Nitrogen Dioxide)	12	6952±462	4875±740	6230±355	6652±475	4.29±0.26	4.87±0.28	2.15±0.20
	27	7152±579	5060±338	6479±580	6927±668	4.32±0.36	4.92±0.16	2.03±0.29
	57	6977±437	5305±435	6392±515	6697±514	4.96±0.48	5.70±0.61	2.22±0.26
	100	6811±421	5070±354[b]	6251±511[b]	6533±494	4.54±0.49[a]	5.24±0.51[b]	2.24±0.37
	117	6888±449	5208±394	6397±557	6677±518	4.75±0.54	5.74±0.65	2.21±0.23

[a] $P < 0.05$.
[b] $P < 0.10$.
} 100 min < 57 min.

Table 6. METABOLIC AND CARDIOVASCULAR CHANGES DURING EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP A)

	Time, min	$\dot{V}_{BTPS}$, liters/min	$\dot{V}_A$, liters/min	RR, breaths/min	$\dot{V}_{O_2}$, liters/min	% $\dot{V}_{O_2}$ max	R	O_2 Pulse, ml/beat	CI, liters/min·m^2
Code 1 (Filtered Air)	5	8.53±1.23	5.53±0.99	13.6±1.8	0.29±0.04	7±1	0.82±0.03	3.93±0.49	3.03±0.24
	50	8.61±1.15	5.65±1.18	12.8±1.7	0.29±0.05	8±1	0.80±0.03	3.95±0.50	2.39±0.23
	80	33.13±4.14	26.8±3.58	23.2±2.7	1.33±0.16	35±4	0.89±0.02	11.83±1.58	7.8±0.73
	110	9.2±0.77	6.13±0.49	13.8±1.3	0.31±0.02	8±1	0.80±0.04	3.97±0.27	3.18±0.36
Code 2 (Nitrogen Dioxide)	5	10.33±1.17	6.96±1.24	13.8±1.4	0.34±0.03	9±1	0.81±0.01	4.65±0.40	2.92±0.40
	50	8.60±0.48	5.61±0.51	13.4±2.0	0.27±0.02	7±1	0.83±0.02	3.72±0.41	2.37±0.35
	80	32.89±3.01	27.03±2.85	21.4±3.5	1.28±0.10	34±3	0.90±0.02	10.61±1.03	7.84±0.63
	110	9.21±0.91	6.14±0.70	14.4±1.4	0.31±0.04	8±1	0.78±0.03	3.80±0.44	3.64±0.44

[a] FA < NO_2.

Continued on next page

Table 5. (Continued)

	Time, min	HR, beats/min	BP, torr		TPR, dyn·sec cm^{-5}	CW, kg·m/min	D_{LCO}, ml/min·torr	$\dot{V}_A/\dot{Q}$	Diff. Perf.
			SP	DP					
Code 1 (Filtered Air)	5	72.4±5.0	117±2	82±2	1262±120	9.79±1.07	24.9±5.1	0.89±0.11	4.28±1.17
	50	76.2±2.7	118±3	83±5	1614±160	7.72±0.75	20.4±3.6	1.17±0.16	4.22±0.63
	80	111.8±3.2	130±4	71±3	473±69	27.83±3.37	52.6±7.8	1.74±0.25	3.39±0.50
	110	78.6±2.0	122±2	79±6	1235±190	10.63±1.23	26.2±5.2	1.01±0.15	4.26±0.88
Code 2 (Nitrogen Dioxide)	5	72.6±2.2	120±3	83±3	1404±222	9.53±1.33	25.2±4.3	1.30±0.38	4.57±1.14
	50	71.4±2.7	121±4	79±3	1665±230	7.75±0.96	25.4±2.9	1.25±0.21	5.59±0.81
	80	122.4±3.2*	131±3	77±1	494±47	28.09±2.65	56.4±6.3	1.74±0.19	3.43±0.41
	110	80.4±2.8	118±3	82±3	1081±146	11.86±1.78	26.9±2.6	0.86±0.07	4.01±0.90

* FA < NO_2.

Table 7. COMPARISON OF PULMONARY FUNCTION CHANGES BEFORE, DURING, AND AFTER EXPOSURE TO 0.5 ppm OZONE OR 0.6 ppm NITROGEN DIOXIDE (GROUP A)

		FVC, ml	$FEV_{1.0}$, ml	FEF25-75%, liters/sec	FEF50%, liters/sec	FEF75%, liters/sec
Code 1	Pre-exposure	6081±410	4782±165	5.09±0.29	5.11±0.54	2.59±0.32
(Filtered Air)	Post-exercise	6127±391	4613±195	4.39±0.46	5.09±0.65	2.29±0.26
n=8	Post-exposure	6096±415	4714±329	4.80±0.40	5.37±0.55	2.39±0.33
Code 5	Pre-exposure	6123±395	5052±329	5.29±0.56	5.86±0.66	2.67±0.34
(0.5 ppm Ozone)	Post-exercise	5991±392[b]	4541±215[b]	4.30±0.32	4.93±0.32	2.36±0.42
n=8	Post-exposure	5938±407[a]	4649±282[a]	4.57±0.44[a]	5.38±0.36[a]	2.18±0.15[a]
Code 1	Pre-exposure	6686±478	5215±322	4.99±0.72	5.12±0.47	1.95±0.16
(Filtered Air)	Post-exercise	6718±379	5222±481	4.73±0.77	5.71±0.80	2.50±0.68
n=5	Post-exposure	6698±446	5294±424	5.07±0.71	5.23±0.61	2.35±0.56
Code 2	Pre-exposure	6738±465	5268±499	4.84±0.93	4.85±0.31	2.23±0.48
(0.6 ppm NO_2)	Post-exercise	6811±421	5070±354	4.54±0.49	5.24±0.51	2.24±0.37
n=5	Post-exposure	6720±490	5227±367	4.60±0.58	4.91±0.41	2.25±0.28

[a] Significantly reduced after O_3 exposure.

[b] Significantly less than other measurements made during exposure at other times.

in all eight subjects following ozone exposure (46). No such changes were observed during or consequent to NO_2 exposure in the subsample of five subjects.

Group B

The subjects in Group B exercised during the first, third, fifth, and seventh 15-min periods of the exposure, a total of 60 min of increased ventilation. The pulmonary function measurements made before and after exposure in filtered air (Code 1) and nitrogen dioxide - 0.60 ppm (Code 2) are presented in Table 8. No striking alterations in pulmonary function occurred as a result of nitrogen dioxide exposure. The vital capacity decreased slightly following exposure in both the filtered air and nitrogen dioxide experiments. This change in VC was accompanied by a slight decrease in expiratory reserve volume. None of the measures of forced expiratory flow showed significant changes or trends indicative of a decrement in pulmonary performance. The pulmonary function measures made during the exposure in the rest period after each exercise period are summarized in Table 9. No significant changes were observed either with time of exposure or with NO_2 exposure.

Cardiovascular and metabolic measurements made during the four exercise periods are summarized in Table 10. Several changes were noted with repetition of the exercise period. Respiratory exchange ratio diminished ($P < 0.01$) as did end tidal P_{CO_2} ($P < 0.05$), and rectal temperature was increased ($P < 0.01$) with each subsequent exercise period. In addition, steady state exercise heart rate increased ($P < 0.05$), as did pulse pressure ($P < 0.01$), systolic pressure ($P < 0.05$), and cardiac work ($P < 0.05$). The total peripheral resistance was lower ($P < 0.01$) during NO_2 exposure than during filtered air exposure although neither cardiac output nor mean blood pressure (the data used to calculate TPR) were significantly different during NO_2 exposure. Other cardiovascular and metabolic measurements showed no variation with NO_2 exposure.

Table 8. PULMONARY FUNCTION CHANGES BEFORE AND AFTER EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP B)

	Filtered Air (Code 1)		Nitrogen Dioxide (Code 2)	
	Pre	Post	Pre	Post
FVC, ml	5649±399	5555±428[a]	5718±414	5541±415[a]
$FEV_{1.0}$, ml	4512±232	4616±258	4622±266	4746±307
FEF25-75%, liters/sec	4.64±0.58	4.69±0.47	4.56±0.55	4.29±0.63
FEF50%, liters/sec	4.75±0.59	5.22±0.73	4.9±0.61	4.88±0.68
FEF75%, liters/sec	2.38±0.33	2.48±0.33	2.45±0.25	2.54±0.41
IC, ml	3456±294	3625±288	3584±255	3470±248
ERV, ml	2194±161	1930±204[a]	2134±218	2070±198[a]
FRC, ml	3963±283	3844±340	3882±218	3832±301
RV, ml	1769±285	1913±328	1748±131	1762±194
TLC, ml	7418±388	7468±396	7466±391	7302±484
R_{aw}, cm H_2O/liters·sec	1.8±0.21	1.93±0.22	1.45±0.21	1.65±0.27
MVV, liters/min	175±8	165±9	167±11	166±9

[a] $P < 0.05$.

Table 9. PULMONARY FUNCTION CHANGES DURING 2-HOUR EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP B)

(NOTE: Exercise at 45% $\dot{V}_{O_2\ max}$ during minutes 0-15, 30-45, 60-75, and 90-105.)

	Time, min	FVC, ml	$FEV_{1.0}$, ml	$FEV_{2.0}$, ml	$FEV_{3.0}$, ml	FEF25-75%, liters/sec	FEF50%, liters/sec	FEF75%, liters/sec
Code 1 (Filtered Air)	27	5606±381	4185±263	5020±290	5242±351	4.88±0.48	4.67±0.65	2.33±0.34
	57	5591±465	4199±356	4949±416	5181±456	4.51±0.96	4.45±0.88	2.47±0.73
	87	5506±479	4104±322	4850±418	5123±486	4.29±0.88	4.41±0.67	2.15±0.34
	110	5579±435	4142±324	4998±399	5241±451	4.01±0.85	4.56±0.78	2.36±0.31
Code 2 (Nitrogen Dioxide)	27	5708±457	4472±315	5329±393	5571±461	4.22±0.68	4.76±0.72	2.38±0.44
	57	5575±470	4304±364	5072±379	5469±523	4.27±0.61	4.49±0.81	2.33±0.42
	87	5600±459	4334±447	5103±434	5366±418	4.07±0.63	4.69±0.73	2.35±0.52
	110	5498±437	4322±362	5100±368	5340±389	4.01±0.57	4.25±0.71	2.43±0.37

Table 10. METABOLIC AND CARDIOVASCULAR CHANGES DURING EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP B)

	Time, min	$\dot{V}_{BTPS}$, liters/min	$\dot{V}_A$, liters/min	RR, breaths/min	$\dot{V}_{O_2}$, liters/min	% $\dot{V}_{O2}$ max	R	O_2 Pulse, ml/beat	CI, liters/min·m^2
Code 1 (Filtered Air)	5	33.35±3.45	27.15±3.02	18.2±2.0	1.42±0.14	39±2	0.9±0.03	13.01±1.40	8.34±0.37
	35	32.33±3.10	26.87±2.56	19.2±1.9	1.43±0.12	39±2	0.87±0.01	12.44±1.42	8.16±0.47
	65	33.77±3.51	28.22±3.03	21.2±1.8	1.47±0.12	40±2	0.85±0.02	12.76±1.29	8.37±0.53
	95	33.73±3.65	27.39±2.78	19.7±1.7	1.48±0.14	40±1	0.83±0.01	12.87±1.60	8.21±0.29
Code 2 (Nitrogen Dioxide)	5	32.47±3.94	27.83±2.98	17.8±1.7	1.45±0.17	39±2	0.90±0.01	13.23±1.70	8.99±0.94
	35	32.24±3.45	27.31±2.92	19.2±1.2	1.45±0.17	39±2	0.87±0.02	13.04±1.51	9.28±1.10
	65	31.50±3.55	26.43±2.95	18.5±1.6	1.39±0.17	38±2	0.86±0.02	12.12±1.36	8.51±0.55
	95	32.55±3.34	27.59±3.04	18.2±1.7	1.49±0.18	40±2	0.84±0.02	12.70±1.44	9.09±0.74

[a] $P < 0.01$ (NO_2 < FA).

Continued on next page

Table 10. (Continued)

	Time, min	HR, beats/min	BP, torr		TPR, dyn·sec cm^{-5}	CW, kg·m/min	$D_{L_{CO}}$, ml/min·torr	$\dot{V}_A/\dot{Q}$	Diff. Perf.
			SP	DP					
Code 1 (Filtered Air)	5	108.6±4.0	123±3	72±3	465±31	25.94±1.35	46.4±2.5	1.75±0.17	3.02±0.14
	35	112.5±4.6	135±4	75±4	508±41	27.90±2.24	50.0±4.1	1.78±0.17	3.31±0.29
	65	112.0±4.4	131±4	72±3	478±35	27.85±2.56	51.9±3.9	1.80±0.13	3.38±0.30
	95	115.2±4.7	130±2	71±4	478±32	27.06±1.26	50.0±4.1	1.79±0.15	3.26±0.20
Code 2 (Nitrogen Dioxide)	5	110.2±4.6	114±5	74±4	406±33°	27.14±2.46	49.8±5.2	1.70±0.25	3.07±0.22
	35	109.2±5.0	128±5	75±6	432±23°	30.51±3.57	51.9±4.9	1.64±0.26	3.10±0.41
	65	112.2±5.7	129±4	74±4	466±41°	28.50±3.15	50.6±5.3	1.66±0.22	3.13±0.18
	95	113.7±5.6	132±3	75±4	442±23°	30.88±2.59	50.1±3.9	1.65±0.25	2.95±0.24

° $P < 0.01$ (NO_2 < FA).

Group C

The subjects in this group performed exercise only in the fourth of the eight 15-min periods and measurements were repeated at 15-min intervals following exercise. The pulmonary function measurements made in the pre-exposure and post-exposure periods are shown in Table 11. No pulmonary function change occurred which could be attributed to nitrogen dioxide exposure. The FEF 50% was greater before than after the exposure on the filtered air day. There is no apparent reason for this and it is probably due to random variation. None of cardiovascular or metabolic parameters measured during exposure showed any significant variation due to nitrogen dioxide exposure (Table 12). Similarly, pulmonary function tests made during the chamber exposure were not affected by nitrogen dioxide (Table 13).

All Groups

The pre- and post-exposure pulmonary function data of the three groups of subjects ($n = 16$) were analyzed collectively for the effect of 0.62 ppm NO_2 (Table 14). Overall, there was a trend ($P < 0.10$) for vital capacity to decrease slightly following NO_2 exposure but this change was small (approximately 80 ml) and is of doubtful physiological importance. Expiratory reserve volume was smaller ($P < 0.05$) following exposure to either filtered air or NO_2 apparently as a result of a decrease in end expiratory position due to a larger tidal volume ($P < 0.05$). This may reflect some anticipation on the part of the subject as a result of the large number of respiratory maneuvers already performed. Closing volumes were too variable and erratic preventing us from performing any statistical analysis. There was a fall in maximum voluntary ventilation post-exposure apparently reflecting the fatigue and perhaps decreased motivation in the subjects.

Symptomatology

Individual subjective responses to nitrogen dioxide exposure were determined from reported symptoms and answers to our questionnaire.

Table 11. PULMONARY FUNCTION CHANGES BEFORE AND AFTER EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP C)

	Filtered Air (Code 1)		Nitrogen Dioxide (Code 2)	
	Pre	Post	Pre	Post
FVC, ml	5680±239	5718±195	5718±317	5675±299
$FEV_{1.0}$, ml	4783±332	4771±232	4964±260	4935±288
FEF25-75%, liters/sec	5.59±0.73	5.47±0.65	5.88±0.55	5.78±0.57
FEF50%, liters/sec	6.38±0.79	5.36±0.30[a]	5.80±0.64	5.94±0.36
FEF75%, liters/sec	2.95±0.64	2.61±0.50	3.17±0.52	2.86±0.54
IC, ml	3637±222	3688±126	3574±160	3657±203
ERV, ml	2043±262	2029±167	2145±209	2017±232
FRC, ml	3840±421	3688±462	3700±421	3755±489
RV, ml	1797±203	1659±387	1555±317	1738±340
TLC, ml	7477±323	7378±377	7273±410	7412±389
R_{aw}, cm H_2O/liters·sec	1.78±0.24	1.64±0.11	1.93±0.36	2.16±0.53
MVV, liters/min	204±14	210±9	213±13	221±19

[a] $P < 0.05$.

Table 12. PULMONARY FUNCTION CHANGES DURING 2-HOUR EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP C)
(NOTE: Exercise at 45% $\dot{V}_{O_2\ max}$ during minutes 45-60.)

	Time, min	FVC, ml	$FEV_{1.0}$, ml	$FEV_{2.0}$, ml	$FEV_{3.0}$, ml	FEF25-75%, liters/sec	FEF50%, liters/sec	FEF75%, liters/sec
Code 1 (Filtered Air)	12	5767±312	4732±290	5443±281	5638±276	5.39±0.67	5.65±0.45	2.98±0.30
	43	5670±242	4803±214	5453±202	5607±231	5.53±0.57	6.01±0.25	3.41±0.40
	72	5642±257	4776±282	5333±207	5567±229	4.96±0.69	5.53±0.76	2.65±0.52
	87	5712±219	4540±254	5423±183	5601±196	4.61±0.57	5.25±0.62	2.63±0.26
	100	5605±278	4555±246	5285±203	5515±251	5.04±0.61	5.72±0.36	2.37±0.32
	117	5550±234	4547±337	5191±229	5457±220[a]	4.30±0.38	5.16±0.61	2.27±0.38
Code 2 (Nitrogen Dioxide)	12	5698±284	4683±326	5482±287	5651±275	5.19±0.51	5.79±0.73	2.93±0.53
	43	5722±244	4747±285	5502±247	5666±246	4.99±0.68	5.39±0.87	2.74±0.75
	72	5679±273	4616±241	5392±210	5587±252	5.25±0.55	5.60±0.36	2.79±0.30
	87	5761±279	4738±324	5502±227	5692±254	5.26±0.75	5.28±0.58	3.26±0.56
	100	5671±273	4692±425	5384±291	5605±268	4.74±0.72	5.66±0.81	2.82±0.56
	117	5646±304	4597±358	5331±300	5477±271	4.82±0.62	5.48±0.70	3.07±0.59

[a] P6 and P13 > P18 (87 and 100 min > 117 min).

Table 13. METABOLIC AND CARDIOVASCULAR CHANGES DURING EXPOSURE TO FILTERED AIR OR 0.6 ppm NITROGEN DIOXIDE (GROUP C)

	Time, min	$\dot{V}_{BTPS}$, liters/min	$\dot{V}_A$, liters/min	RR, breaths/min	$\dot{V}_{O_2}$, liters/min	% $\dot{V}_{O_2}$ max	R	O_2 Pulse, ml/beat	CI, liters/min·m^2
Code 1 (Filtered Air)	5	9.1±1.34	5.82±1.17	13.6±1.4	0.31±0.04	8±1	0.73±0.04	4.17±0.57	2.95±0.16
	35	9.14±0.82	5.61±0.69	15.6±2.5	0.3±0.04	8±1	0.77±0.05	4.38±0.38	2.85±0.24
	50	36.96±1.93	31.24±1.22	21.2±2.9	1.60±0.06	43±1	0.88±0.03	14.23±0.96	10.07±1.01
	65	11.91±1.07	9.01±0.78	14.2±2.3	0.38±0.02	10±1	0.88±0.04	4.73±0.16	3.70±0.28
	80	10.77±0.89	7.34±1.14	14.0±1.4	0.37±0.03	10±1	0.74±0.06	5.19±0.16	3.22±0.20
	95	9.55±0.66	6.27±0.89	14.2±1.8	0.34±0.03	9±1	0.73±0.06	5.03±0.25	2.93±0.16
	110	9.73±0.58	6.41±1.0	14.0±2.4	0.32±0.02	9±1	0.74±0.05	4.74±0.33	3.07±0.37
Code 2 (Nitrogen Dioxide)	5	9.79±0.79	6.59±0.64	13.6±1.6	0.29±0.03	8±1	0.87±0.05	4.14±0.30	2.80±0.18
	35	9.28±0.94	5.95±0.74	15.4±1.9	0.28±0.03	8±1	0.83±0.04	4.27±0.47	2.82±0.05
	50	34.51±4.33	27.78±3.67	21.2±3.3	1.35±0.15	36±3	0.92±0.03	13.17±2.13	10.84±0.91
	65	10.72±0.64	8.20±0.63	15.6±2.4	0.34±0.02	9±1	0.94±0.05	4.06±0.41	4.08±0.51
	80	9.39±0.61	6.13±0.29	14.2±1.8	0.30±0.01	8±1	0.81±0.05	4.17±0.29	3.13±0.38
	95	8.52±0.50	5.26±0.36	14.8±1.8	0.27±0.01	7±1	0.80±0.06	3.74±0.30	2.93±0.29
	110	7.93±0.26	4.67±0.19	14.8±1.8	0.26±0.01	7±1	0.73±0.03	3.68±0.12	2.87±0.39

Continued on next page

Table 13. (Continued)

	Time, min	HR, beats/min	BP, torr		TPR, dyn·sec cm^{-5}	CW, kg·m/min	$D_{L_{CO}}$, ml/min·torr	$\dot{V}_A/\dot{Q}$	Diff. Perf.
			SP	DP					
Code 1 (Filtered Air)	5	72.8±4.2	118±7	80±6	1326±94	8.95±0.61	25.4±2.5	1.02±0.16	4.52±0.33
	35	67.8±3.3	121±6	82±5	1440±17	8.91±0.68	---	1.04±0.14	---
	50	112.0±3.2	134±9	82±4	427±48	34.81±3.51	50.0±3.6	1.70±0.21	2.67±0.25
	65	81.2±2.8	124±6	81±3	1100±75	11.86±1.19	---	1.28±0.19	---
	80	72.2±4.0	119±7	77±4	1196±68	9.97±0.96	---	1.18±0.14	---
	95	67.6±4.2	121±5	85±7	1406±96	9.17±0.49	---	1.13±0.15	---
	110	67.8±2.8	118±7	81±6	1349±19	9.28±0.76	25.4±3.0	1.16±0.22	4.46±0.58
Code 2 (Nitrogen Dioxide)	5	70.8±1.6	121±5	81±4	1437±10	8.70±0.54	27.0±4.8	1.27±0.16	5.23±1.12
	35	66.6±2.3	118±6	80±7	1387±97	8.57±0.45	---	1.11±0.17	---
	50	116.2±6.7	133±7	81±8	395±54	36.77±1.36	54.5±2.3	1.38±0.24	2.72±0.28
	65	84.2±5.8	126±6	79±7	1041±17	13.07±1.10	---	1.06±0.15	---
	80	73.6±3.0	123±5	82±6	1359±21	9.84±0.99	---	1.09±0.18	---
	95	69.0±2.7	117±5	79±6	1365±16	8.82±0.85	---	0.95±0.13	---
	110	70.0±3.2	119±5	80±7	1421±15	8.84±1.22	26.2±2.7	0.91±0.12	5.43±0.66

Table 14. PULMONARY FUNCTION CHANGES FOLLOWING NO_2 EXPOSURE: POOLED DATA FROM GROUPS A, B, AND C (n = 16).

	Filtered Air		Nitrogen Dioxide	
	Pre	Post	Pre	Post
FVC, ml	5983±900	5963±908	6037±928	5951±963[b]
$FEV_{1.0}$, ml	4816±639	4876±670	4931±729	4955±656
FEF25-75%, liters/sec	5.05±1.36	5.05±1.21	5.06±1.45	4.85±1.34
FEF50%, liters/sec	5.37±1.41	5.27±1.18	5.17±1.16	5.22±1.16
FEF75%, liters/sec	2.42±0.90	2.48±0.89	2.61±0.95	2.55±0.86
IC, ml	3756±674	3824±626	3759±602	3745±643
ERV, ml	2226±435	2138±425[a]	2278±468	2206±455[a]
FRC, ml	4028±715	3998±875	3911±598	3946±717
V_T, ml	868±304	964±317[a]	859±252	894±274[a]
TLC, ml	7784±1057	7823±1227	7670±968	7691±1108
R_{aw}, cm H_2O/liters·sec	1.80±0.38	1.83±0.42	1.73±0.55	1.88±0.72
MVV, liters/min	200±33	196±36[b]	201±40	195±42[b]

[a] $P < 0.05$.
[b] $P < 0.10$.
(See text.)

No significantly different responses were reported between NO_2 and filtered air exposure. Occasionally symptoms were noted primarily associated with the exercise stress and included fatigue and slight dizziness. The subjects reported that they were "more tired" after the Group B exposures which was anticipated since this group exercised for a greater amount of time during the 2 h than in the other two experimental sessions. No physical signs related to NO_2 exposures were detected by the physician's examination.

DISCUSSION

A 2-h exposure to nitrogen dioxide at a concentration of 0.62 ppm had no profound effects on either the cardiovascular or pulmonary function of young men. The few and unrelated changes which did occur following NO_2 exposure showed no consistent pattern. The few instances where statistically significant changes were found should, therefore, be regarded with some skepticism since they could not be related to concomitant changes in associated parameters.

In Group A, the decrease in MVV following NO_2 exposure was not accompanied by any change in vital capacity or maximum expiratory flow. Such a change in MVV could possibly occur if there was a marked increase in laryngeal resistance but this is unlikely as the subjects reported no symptoms indicative of this increased resistance. In Group B, the slight decrease in total peripheral resistance during ozone exposure was not accompanied by other alterations in circulatory function. When data from all subjects was pooled, the only overall trend was for a small decrease in vital capacity. This was surprising because most studies evaluating the effect of higher concentrations of NO_2 on pulmonary function (1,4,9,10,17) have suggested that following exposure to NO_2 there was an increase of airway resistance or a decrease of maximum expiratory flow but that there was usually no effect on lung volumes. These effects have been shown with concentrations of NO_2 greater than 1 ppm and the lack of a change in maximum expiratory flow in our subjects was not unexpected.

In a study of exercising subjects, Rokaw (47) found an increased airway resistance at 1.5 and 3.0 ppm NO_2. They found no change at 0.5 ppm NO_2 which is in agreement with our results. Although the toxicity of NO_2 has been demonstrated when humans (1,5,8) or animals (19,22,24) have been exposed to concentrations which exceed present ambient levels (> 1.0 ppm), the effect of exposure to ambient levels (0.20 - 0.50 ppm) is minimal (4,10,14,15,16,17). These limited effects of ambient levels of NO_2 are in striking contrast to the effects of ozone on pulmonary function at present ambient concentrations that we (46) and others (2,3,15,16) have observed.

Several factors in these present experiments differ from those usually employed in studies on the effects of NO_2 on man. None of our subjects were smokers and thus they had not been previously exposed to the NO_2 arising from cigarette smoking. It has been suggested that the potential ill effects from NO_2 exposure would be greater in smokers. The ambient exposure concentrations were relatively low, being at levels which occur primarily during heavy smog days where hourly averages of about 0.6 ppm have been reported. However, some of the exposed subjects exercised for up to one-half of their exposure time to NO_2. Consequently since their alveolar ventilations had been increased by four to five fold by the exercise, they would have been exposed to relatively higher levels of inhaled NO_2. Nonetheless, only minimal alterations in pulmonary functions were observed and these did not show a consistent pattern indicative of an overall effect of the nitrogen dioxide exposure.

SECTION VIII
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SECTION IX

GLOSSARY OF TERMS, ABBREVIATIONS, AND SYMBOLS

(1) RESPIRATORY MEASUREMENTS

Parameter and Formula	Abbreviation	Units
1. Ventilatory Volume		
(a) $\dot{V}_E$ (uncorrected volume)	$\dot{V}_E$	liters/min
(b) $\dot{V}_E\ BTPS = \dot{V}_E \times \frac{310}{273 + \text{gas temp.}} \times \frac{BP - WVP}{BP - 47}$	$\dot{V}_E$ BTPS	liters/min
(c) $\dot{V}_E\ STPD = \dot{V}_E \times \frac{P_{bar} - P_w}{760} \times \frac{273}{273 + \text{gas temp.}}$	$\dot{V}_E$ STPD	liters/min
	P_{bar} = barometric pressure	
	P_w = water vapor pressure at the gas temp.	
2. Respiratory Rate	RR or f_R	breaths/min
3. Tidal Volume		
$\frac{\dot{V}_E}{RR}$	V_T	ml/breath
4. Ventilatory Equivalence Ratio		
$\frac{\dot{V}_E\ BTPS}{\text{Oxygen Uptake}}$	$\dot{V}_E$ BTPS/$\dot{V}_{O_2}$	$\frac{\text{liters breathed}}{\text{liters } O_2}$

(2) METABOLIC MEASUREMENTS

Parameter and Formula	Abbreviation	Units
1. Oxygen Uptake		
(a) $\frac{\dot{V}_E \text{ STPD} \times \text{True } O_2\%}{100}$	$\dot{V}_{O_2}$	liters O_2/min
(b) $\frac{\dot{V}_E \text{ STPD} \times \text{True } O_2\% \times 1000}{100 \times \text{Pre Wt}}$	$\dot{V}_{O_2}$	ml $O_2/kg \cdot min^{-1}$
(c) $\frac{\dot{V}_E \text{ STPD} \times \text{True } O_2\% \times 1000}{100 \times \text{Lean Body Mass}}$	$\dot{V}_{O_2}$	ml $O_2/LBM \cdot min^{-1}$
2. True Oxygen		
$(\%N_2 \times 0.265) - \%O_2$ in expired air	True O_2	%
3. Respiratory Exchange Ratio	R	no units
$\frac{\%\text{ Expired } CO_2}{\%\text{ Expired } O_2}$ or $\frac{CO_2 \text{ Production}}{\text{Oxygen Uptake}}$	$\frac{\dot{V}_E\ CO_2}{\dot{V}_{O_2}}$	
4. Excess Carbon Dioxide	Excess CO_2	liters
$\dot{V}_E \text{ STPD} \times \frac{(\%CO_2 \text{ Expired} - 0.03)}{100} - \dot{V}_{O_2} \times 0.75$		
5. Maximal Aerobic Power	$\dot{V}_{O_2\ max}$	liters/min
and/or		ml $O_2/kg \cdot min^{-1}$
Maximal Aerobic Capacity		ml $O_2/LBM \cdot min^{-1}$
(The largest value of oxygen uptake obtained when a subject performs maximal exhaustive work.)		

Parameter and Formula	Abbreviation	Units
6. Percent of Maximal Oxygen Uptake	$\%\dot{V}O_{2\ max}$	%
$\frac{\dot{V}O_2}{\dot{V}O_{2\ max}} \times 100$		
7. Energy Production		
cal/liter O_2 = 1.27604 × R + 3.82041		
(a) = cal/liter O_2 × 60 × liter O_2/min	M	kcal/h
(b) = $\frac{a}{\text{Pre Wt, in kg}}$	M	$kcal/kg \cdot h^{-1}$
(c) = $\frac{a}{BSA}$	M	$kcal/m^2 \cdot h^{-1}$
(d) = c × 1.163	M	$watts/m^2$

(3) CARDIOVASCULAR

1. Cardiac Output = Stroke Volume × HR	$\dot{Q}$	liters/min
$\frac{\dot{V}O_2}{C_aO_2 - C_vO_2}$		
2. Cardiac Index	CI	$liters/min \cdot m^{-2}$
$\frac{\dot{Q}}{\text{Body Surface Area, in } m^2}$	Body Surface Area = BSA	

Parameter and Formula	Abbreviation	Units
3. Cardiac Work	CW	kg·m/min
$\frac{SP \times 13.6 \times \dot{Q}}{1000}$		
4. Heart Rate	HR, f_C	beats/min
5. Stroke Volume	SV	ml/beat
$\frac{\dot{Q}}{HR}$		
6. Stroke Index	SI	ml/beat·m^{-2}
$\frac{SV}{BSA}$		
7. Stroke Work	SW	g·m/beat
$\frac{SP \times 13.6 \times SV}{1000}$		
8. Oxygen Pulse	O_2 Pulse	ml O_2/beat
$\frac{\dot{V}_{O_2} \times 1000}{HR}$		

Parameter and Formula	Abbreviation	Units
9. Arterio-Mixed Venous Oxygen Difference	$(a - \bar{v})O_2$ diff.	ml O_2/liter blood
$\frac{\dot{V}_{O_2} \times 1000}{\dot{Q}}$		
10. Systolic Pressure (Arterial)	SP, P_{sys}	torr
11. Diastolic Pressure (Arterial)	DP, P_{dias}	torr
12. Mean Blood Pressure (Arterial)	MBP, $\bar{P}_{bl}$	torr
$\frac{SP - DP}{3} + DP$		
13. Pulse Pressure	PP	torr
SP - DP		
14. Total Peripheral Resistance	TPR	dyn·sec cm^{-5}
$\frac{1.333 \times 60 \times MBP}{\dot{Q}}$		

(4) PULMONARY

1. Forced Vital Capacity	FVC	(ml, ml/kg) ml/m^2

Parameter and Formula	Abbreviation	Units
2. Timed Forced Expired Volumes (1.0, 2.0, and 3.0 seconds)	$FEV_{1.0}$ $FEV_{2.0}$ $FEV_{3.0}$	ml
3. Forced Expired Volumes as a percentage of Forced Vital Capacity $\frac{FEV_{1.0}}{FVC} \times 100$	$FEV_{1.0}/FVC\%$ $FEV_{2.0}/FVC\%$ $FEV_{3.0}/FVC\%$	%
4. Inspiratory Capacity	IC	ml
5. Expiratory Reserve Volume	ERV	ml
6. Functional Residual Capacity	FRC	ml
7. Residual Volume	RV	ml, ml/kg, ml/m^2
8. Total Lung Capacity VC + RV	TLC	ml, ml/kg, ml/m^2
9. Residual Volume/Percent Total Lung Capacity $\frac{RV}{TLC} \times 100$	RV/%TLC	%
10. Maximal Mid-Expiratory Flow	MMEF	liters/sec
or	FEF 25 - 75%	
Mean Forced Expiratory Flow during middle half of FVC	FEF 25 - 75%	

Parameter and Formula	Abbreviation	Units
11. Maximal Voluntary Ventilation	MVV	liters/min
12. Maximal Expiratory Flow @ 50% of Vital Capacity	MEF50%	liters/sec
or		
Forced Expiratory Flow @ 50% of FVC exhaled	FEF 50%	
13. Maximal Expiratory Flow @ 25% of Vital Capacity	MEF25%	liters/sec
or		
Forced Expiratory Flow @ 75% of FVC exhaled	FEF 75%	

(5) TEMPERATURE REGULATORY

1. Rectal Temperature	T_{re}	°C
2. Forehead Temperature	T_{hd}	°C
3. Arm Temperature	T_{arm}	°C
4. Finger Temperature	T_{fing}	°C
5. Thigh Temperature	T_{thi}	°C

Parameter and Formula	Abbreviation	Units
6. Calf Temperature	T_{calf}	°C
7. Chest Temperature	T_{ch}	°C
8. Toe Temperature	T_{toe}	°C
9. Room Temperature	T_{rm}	°C
10. Air Temperature	T_a	°C
11. Radiant Temperature	T_r	°C
12. Globe Black Temperature	T_g	°C
13. Wall Temperature	T_{wall}	°C
14. Wet Bulb Temperature	T_{wb}	°C
15. Mean Skin Temperature	$\overline{T}_{sk}$	°C

$$\overline{T}_{sk} = 0.07\ T_{hd} + 0.36\ T_{ch} + 0.05\ T_{fing} + 0.14\ T_{arm} + 0.05\ T_{toe} + 0.13\ T_{calf} + 0.20\ T_{thi}$$

16. Mean Body Temperature	$\overline{T}_b$	°C

$$0.65\ T_{re} + 0.35\ \overline{T}_{sk}$$

17. Body Heat Content	BHC	$kcal/m^2$

$$\frac{\text{Pre Wt} \times 0.83\ \overline{T}_b}{\text{BSA}}$$

Parameter and Formula	Abbreviation	Units
18. Wet Bulb Globe Temperature Index	WBGT	°C(°F)
$0.3\ T_g + 0.7\ T_{wb}$		
19. Tissue Conductance	K	$kcal/m^2 \cdot h^{-1}\ °C^{-1}$
$\frac{kcal/m^2 \cdot h^{-1}}{T_{re} - \overline{T}_{sk}} = \frac{\text{Energy Prod}}{T_{re} - \overline{T}_{sk}}$		
20. Respiratory Evaporative Water Loss	Resp. H_2O Loss	g/h
$\dot{V}_E$ BTPS × factor × 60		
(The factor is determined from density steam tables and is dependent on temp. of expired gases.)		
21. Respiratory Evaporative Heat Loss	Resp. Heat Loss ($-E_r$)	$kcal/m^2 \cdot h^{-1}$
$\frac{\text{Resp. } H_2O \text{ Loss} \times 0.58}{\text{BSA}}$		
22. Skin Evaporative Heat Loss	Evap. Heat Loss ($-E_{sk}$)	$kcal/m^2 \cdot h^{-1}$
$\frac{[\text{Pre Wt} - \text{Post Wt} - \text{Resp. } H_2O \text{ Loss} - \text{Excess } CO_2\ (g)] \times 0.580}{\text{BSA}}$		

ALPHABETICAL LIST OF ABBREVIATIONS AND SYMBOLS USED

$(a - \bar{v})O_2$ diff.	arterio-mixed venous oxygen difference
alveol. (A)	alveolar
AQS	air quality standards
BHC	body heat content
BMR	basal metabolic rate
BP	blood pressure
BSA	body surface area
BTPS	body temperature and pressure, saturated with water vapor
cal	calorie(s)
C_aO_2	arterial oxygen content
CI	cardiac index
cm	centimeter(s)
CNS	central nervous system
CO	carbon monoxide
CO_2	carbon dioxide
CV	closing volume
C_vO_2	venous oxygen content
CW	cardiac work
°C	degree(s) Celsius
°F	degree(s) Fahrenheit
diff.	difference
diff. perf.	diffusion perfusion
$D_{L_{CO}}$	diffusion capacity to carbon monoxide

DP	diastolic pressure
dyn	dyne(s)
ERV	expiratory reserve volume
evap.	evaporative
FA	filtered air
f_C	cardiac frequency (same as HR)
FEF 50%	forced expiratory flow after 50% of FVC exhaled
FEF 75%	forced expiratory flow after 75% of FVC exhaled
FEF 25 - 75%	forced expiratory flow during middle half of FVC
ΔFEF 75%	difference between FEF 75% on helium and air flow volume curve
FEV	forced expired volume
$FEV_{1.0}$	forced expired volume (1.0 second)
$FEV_{2.0}$	forced expired volume (2.0 seconds)
$FEV_{3.0}$	forced expired volume (3.0 seconds)
f_R	respiratory frequency
FRC	functional residual capacity
FVC	forced vital capacity
g	gram(s)
h	hour(s)
H, ht	height
Hb	hemoglobin
HbCO	carboxyhemoglobin
Hct	hematocrit
HLa	lactate

H_2O	water
HR	heart rate (same as f_C)
IC	inspiratory capacity
K	tissue conductance
kg	kilogram(s)
LBM	lean body mass
m	meter(s)
M	energy production
max	maximal, maximum
MBP	mean blood pressure
MEF	maximal expiratory flow
MEF25%	maximal expiratory flow at 25% of vital capacity
MEF50%	maximal expiratory flow at 50% of vital capacity
mEq	milliequivalent(s)
min	minute(s)
ml	milliliter(s)
MMEF	maximal mid expiratory flow
mMoles	millimoles
MVV	maximum voluntary ventilation
N_2	nitrogen
NO_x	oxides of nitrogen
O_2	oxygen
O_3	ozone
P	probability of wrongfully rejecting the null hypothesis (level of significance)

P_{bar}	barometric pressure
P_w	water vapor pressure
$P\bar{v}CO_2$	mixed venous carbon dioxide partial pressure
PAN	peroxyacetylnitrate
%	percent
perf.	perfusion
PIF	point of identical flow on helium and air flow volume curves
PP	pulse pressure
ppm	parts per million
press.	pressure
prod.	production
$\dot{Q}$	cardiac output
R	respiratory exchange ratio
R_{aw}	airway resistance
RBC	red blood cell
resp.	respiratory
RH	relative humidity
RR	respiratory rate (same as f_R)
RV	residual volume
s, sec	second(s)
SD	standard deviation
SE	standard error
SI	stroke index
SO_x	sulfur oxides
SP	systolic pressure

STPD	standard temperature and pressure, dry
SV	stroke volume
SVC	slow vital capacity
SW	stroke work
syst.	systolic
T_a	ambient air temperature
T_{arm}	arm temperature
$\overline{T}_b$	mean body temperature
T_{calf}	calf temperature
T_{ch}	chest temperature
T_{fing}	finger temperature
T_g	globe temperature
T_{hd}	forehead temperature
T_r	radiant temperature
T_{re}	rectal temperature
T_{rm}	room temperature
$\overline{T}_{sk}$	mean skin temperature
T_{thi}	thigh temperature
T_{toe}	toe temperature
T_{wall}	wall temperature
T_{wb}	wet bulb temperature
temp.	temperature
TGV	thoracic gas volume
TLC	total lung capacity
TLV	threshold limit values
TPR	total peripheral resistance

V	volume
$\dot{V}$	timed ventilatory volume
$\dot{V}_A$	alveolar ventilation
$\dot{V}_A/\dot{Q}$	ventilation perfusion ratio
$\dot{V}_E$	ventilatory volume, expired
$\dot{V}_{O_2}$	oxygen uptake
$\dot{V}_{O_2\ max}$	maximal aerobic capacity (maximal aerobic power)
V_T	tidal volume
VC	vital capacity
W, wt	weight
WBGT	wet bulb globe temperature index
yr	year(s)
x^2	statistical datum derived in the chi-square test

SECTION X

APPENDIX

PRINTOUT OF METABOLIC, CARDIOVASCULAR AND PULMONARY FUNCTION DATA

EX.NO.	STUD.	DATE	AGE	SEX	PRE WT.	POST WT.	HT.CM	BSA	BF	PRE TEMP	POST TEMP	HRS.PA	RM TEMP	REL.HUM	B.	TIME
7940	NUXBJX	05-05-75	20	M	78.00	77.20	175.0	1.91	.00	37.10	37.70	1	25.0	45	755	930

PERIOD	EVENT	V/MIN	HR	% O2	% CO2	GAS TEMP	CT COL	V STPD	V BTPS	T O2	L/O2/MIN	ML O2/KG	O2 P	VE	% MAX	HR
1	P1	0-8	41.4	24	16.11	4.65	21.5	5.02	37.36	45.28	4.89	1.83	23.41	17.39	24.79	0.45	103
6	P3	0-8	40.4	24	16.07	4.55	21.5	5.05	36.45	44.18	4.97	1.81	23.21	17.57	24.41	0.42	103
11	P5	0-8	39.0	24	15.99	4.51	21.5	5.03	35.73	43.31	5.08	1.81	23.26	17.61	23.87	0.42	103
16	P7	0-8	40.2	26	15.92	4.41	21.5	5.48	36.27	43.96	5.19	1.88	24.15	18.33	23.34	0.44	106

MAXIMUM OXYGEN UPTAKE = 4.28

METABOLIC DATA: EX. NO. 7940

	R	EXCESS CO2	KCAL/KG-HR	KCAL/HR	V ALVEOLAR	DEAD SPACE	WATTS/M2	TIDAL VOL. ML
[illegible]	0.95	0.3292	6.99	545.55	37.40	0.326	332.185	1886.56
6	0.91	0.2901	6.87	536.13	35.58	0.358	326.450	1840.99
11	0.88	0.2401	6.84	533.62	34.09	0.359	324.921	1804.53
16	0.84	0.1761	7.05	543.65	35.38	0.330	334.045	1690.56

TEMPERATURES: 7940

EVENT		RECTAL	FOREHEAD	ARM	FINGER	THIGH	CALF	CHEST	ABDOMEN	_____	RADIANT	WALL	RMSA
P1	2-4	37.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	22.5	0.0	22.4
P2	2-4	37.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	23.9	0.0	24.2
P3	2-4	37.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	23.2	0.0	23.0
P4	2-4	37.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	26.5	0.0	26.3
P5	2-4	37.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	25.8	0.0	25.7
P6	2-4	37.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	27.2	0.0	27.1
P7	2-4	37.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	27.1	0.0	27.1
P8	2-4	37.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	27.7	0.0	27.7
POST	2-4	37.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	26.8	0.0	26.7

ROOM TEMP. MEAN 25.58 RADIANT TEMP. MEAN 25.63

EVENT		MEAN SKIN TEMP.	MEAN BODY TEMP.	BODY HEAT KCAL/M2	RADIATION KCAL/M2-HR	TISSUE CONDUCT.	RESP.EVAP. KCAL/M2-HR	SKIN EVAP. KCAL/M2-HR	EXCESS CO2 GRAMS/HR	RESP. H2O GM/HR
P1	2-4	0.0	0.0	0.0	0.0	0.0	24.0	78.4	49.03	82.0
P2	2-4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.00	0.0
P3	2-4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.00	0.0
P4	2-4	0.0	0.0	0.0	0.0	0.0	24.2	81.4	41.75	80.4
P5	2-4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.00	0.0
P6	2-4	0.0	0.0	0.0	0.0	0.0	23.8	83.7	35.80	78.8
P7	2-4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.00	0.0
P8	2-4	0.0	0.0	0.0	0.0	0.0	24.1	85.6	28.46	80.0
POST	2-4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.00	0.0

EX.NO.	STS	DATE	AGE	SEX	PRE WT.	POST WT.	HT.CM	BSA	BF	PRE TEMP	POST TEMP	HRS.PA	RM TEMP	REL.HUM	B	TIME
7943	NUXBJA	06-03-75	20	M	78.0	77.2	176.0	1.91	.00	37.1	37.7	1	25.0	45	755	900

PERIOD	EVENT	CARDIAC OUTPUT L/MIN.	HEART RATE BEATS/MIN.	L O2/MIN.	SYSTOLIC PRESSURE	DIASTOLIC PRESSURE	STROKE VOL. ML/BEAT	STROKE INDEX ML/BEAT-M2
1	P1 4-5	16.100	94.0	1.83	110.0	60.0	171.28	89.67
2	10-11	0.000	105.0	0.00	0.0	0.0	0.00	0.00
3	14-15	0.000	113.0	0.00	132.0	72.0	0.00	0.00
4	P2 4-5	0.000	66.0	0.00	118.0	60.0	0.00	0.00
5	14-15	0.000	58.0	0.00	110.0	70.0	0.00	0.00
6	P3 4-5	14.700	93.0	1.81	132.0	76.0	158.06	82.76
7	10-11	0.000	103.0	0.00	134.0	60.0	0.00	0.00
8	14-15	0.000	114.0	0.00	128.0	64.0	0.00	0.00
9	P4 4-5	0.000	76.0	0.00	111.0	78.0	0.00	0.00
10	14-15	0.000	69.0	0.00	112.0	70.0	0.00	0.00
11	P5 4-5	16.500	97.0	1.81	120.0	60.0	170.10	89.06
12	10-11	0.000	103.0	0.00	120.0	60.0	0.00	0.00
13	14-15	0.000	115.0	0.00	118.0	68.0	0.00	0.00
14	P6 4-5	0.000	65.0	0.00	110.0	78.0	0.00	0.00
15	14-15	0.000	74.0	0.00	117.0	64.0	0.00	0.00
16	P7 4-5	15.300	100.0	1.83	127.0	54.0	153.00	80.10
17	10-11	0.000	100.0	0.00	122.0	56.0	0.00	0.00
18	14-15	0.000	113.0	0.00	128.0	58.0	0.00	0.00
19	P8 4-5	0.000	66.0	0.00	113.0	72.0	0.00	0.00
20	14-15	0.000	61.0	0.00	115.0	70.0	0.00	0.00

EX.NO. 7940

PERIOD	EVENT	CARDIAC INDEX L/MIN-M2	A-V O2 DIFF. ML O2/L	TOT.PERIPH.RES. DYNES.SEC.CM-5	PULSE PRESS.	MEAN BLOOD PRESSURE	STROKE WORK GRAMS-M/BEAT	CARDIAC WORK KG-M/MIN.	SYST. INDEX
1	P1 4-5	8.43	113.42	380.36	50.00	76.67	256.229	24.086	10340
2	10-11	0.00	0.00	0.00	0.00	0.00	0.000	0.000	0
3	14-15	0.00	0.00	0.00	60.00	92.00	0.000	0.000	14916
4	P2 4-5	0.00	0.00	0.00	38.00	92.67	0.000	0.000	7788
5	14-15	0.00	0.00	0.00	40.00	83.33	0.000	0.000	6380
6	P3 4-5	7.70	123.14	515.06	56.00	94.67	283.757	26.389	12276
7	10-11	0.00	0.00	0.00	74.00	84.67	0.000	0.000	13802
8	14-15	0.00	0.00	0.00	64.00	85.33	0.000	0.000	14592
9	P4 4-5	0.00	0.00	0.00	33.00	89.00	0.000	0.000	8456
10	14-15	0.00	0.00	0.00	42.00	84.00	0.000	0.000	7726
11	P5 4-5	8.64	109.95	387.78	60.00	80.00	277.608	26.928	11640
12	10-11	0.00	0.00	0.00	60.00	80.00	0.000	0.000	12360
13	14-15	0.00	0.00	0.00	50.00	84.67	0.000	0.000	13570
14	P6 4-5	0.00	0.00	0.00	32.00	88.67	0.000	0.000	7150
15	14-15	0.00	0.00	0.00	53.00	81.67	0.000	0.000	8658
16	P7 4-5	8.01	123.10	409.43	73.00	78.33	264.261	26.426	12700
17	10-11	0.00	0.00	0.00	66.00	78.00	0.000	0.000	12200
18	14-15	0.00	0.00	0.00	70.00	81.33	0.000	0.000	14464
19	P8 4-5	0.00	0.00	0.00	41.00	85.67	0.000	0.000	7458
20	14-15	0.00	0.00	0.00	45.00	85.00	0.000	0.000	7015

EX.NO.	STUDY	DATE	AGE	SEX	PRE WT.	POST WT.	HT.CM	BSA	BF	PRE TEMP	POST TEMP	HRS.PA	RM TEMP	REL.HUM	BP	TIME
7940	NOXBOX	06-05-75	20	M	78.0	77.2	176.5	1.91	.00	37.1	37.7	1	25.0	45	755	930

PERIOD	EVENT	TLV ML	FVC ML	1 SEC ML	1 SEC % FVC	2 SEC ML	2 SEC % FVC	3 SEC ML	3 SEC % FVC	50% L/SEC	25% L/SEC
1	PRE EXP	7700	6635	5078	76.53	6039	91.02	6370	96.01	3.66	2.32
2	P1	0	0	0	0.00	0	0.00	0	0.00	0.00	0.00
4	P2 (B)	0	6540	4674	71.53	5927	90.63	6300	96.33	4.20	2.07
6	P3	0	0	0	0.00	0	0.00	0	0.00	0.00	0.00
8	P4 (B)	0	6709	4815	71.77	5995	89.36	6441	96.01	4.55	2.02
11	P5	0	0	0	0.00	0	0.00	0	0.00	0.00	0.00
13	P6 (B)	0	6736	4783	71.01	6045	89.74	6441	95.62	4.18	1.95
16	P7	0	0	0	0.00	0	0.00	0	0.00	0.00	0.00
18	P8 (B)	0	6808	4855	71.31	6173	90.67	6581	96.67	4.54	2.13
19	POST EXP	7660	6514	5112	78.48	6050	92.88	6348	97.45	4.20	2.08
PREDICTED		7081	5425	4382						5.25	
% PREDICTED		108.74	122.31	115.89						73.52	

PERIOD	EVENT	IC ML	ERV ML	FRC ML	RV ML	RV/TLV %	MAP L/SEC	MSC L/MIN	RR B/MIN	TV ML	TLV/HT ML/CM	VC/HT ML/CM	TLV/KG ML/KG	VC/KG ML/KG	DLCO ML/MIN/MM H
1	PRE EXP	4323	2307	3372	1065	13.0	4.25	165.0	14	800	43.02	37.59	98.72	85.06	56.50
2	P1	0	0	0	0	0.0	0.00	0.0	0	0	0.00	0.00	0.00	0.00	0.00
4	P2 (B)	0	0	0	0	0.0	3.89	0.0	0	0	0.00	37.05	0.00	83.85	0.00
6	P3	0	0	0	0	0.0	0.00	0.0	0	0	0.00	0.00	0.00	0.00	63.80
8	P4 (B)	0	0	0	0	0.0	3.88	0.0	0	0	0.00	38.00	0.00	86.01	0.00
11	P5	0	0	0	0	0.0	0.00	0.0	0	0	0.00	0.00	0.00	0.00	56.40
13	P6 (B)	0	0	0	0	0.0	3.88	0.0	0	0	0.00	38.16	0.00	86.36	0.00
16	P7	0	0	0	0	0.0	0.00	0.0	0	0	0.00	0.00	0.00	0.00	59.90
18	P8 (B)	0	0	0	0	0.0	4.01	0.0	0	0	0.00	38.57	0.00	87.28	0.00
19	POST EXP	4001	1912	3058	1146	15.0	4.75	181.1	14	800	43.39	36.90	98.21	83.51	0.00
PREDICTED		3315	2110	3766	1656	23.4	4.89	190.0							
% PREDICTED		130.56	109.34	89.53	64.30	59.13	86.85	97.39							

PERIOD	EVT	SVC 1 ML	CV 1 ML	PIF L	SVC 2 ML	CV 2 ML	DELTA_V25 L/SEC	CLOS.CAP1 ML	CC %TLV	CLOS.CAP2 ML	%TLV
1	PRE EXP	0	0	0.00	0	0	0.00	0	0.0	0	0.0
2	P1	0	0	0.00	0	0	0.00	0	0.0	0	0.0
4	P2 (B)	6427	818	0.82	6359	500	0.75	1883	24.3	1565	20.3
6	P3	0	0	0.00	0	0	0.00	0	0.0	0	0.0
8	P4 (B)	6041	545	0.56	6313	0	0.59	1610	20.9	0	0.0
11	P5	0	0	0.00	0	0	0.00	0	0.0	0	0.0
13	P6 (B)	6540	863	0.56	6631	0	0.66	1928	25.0	0	0.0
16	P7	0	0	0.00	0	0	0.00	0	0.0	0	0.0
18	P8 (B)	6722	636	0.51	6177	661	0.41	1701	22.1	1746	22.7
19	POST EXP	0	0	0.00	0	0	0.00	0	0.0	0	0.0

PERIOD	EVENT	SIT ERV ML	SIT FRC ML	SIT RV ML	BOX FRC ML	BOX RV ML	AIR.RES. CM H2O S/L	PUL.COMP.	NAR	VENT.PERF.	DIFF.PERF.	V ALV L/MIN
1	PRE EXP	2147	3437	1290	3531	1434	2.17	0.000	0.00	0.00	0.00	0.00
2	P1	0	0	0	0	0	0.00	0.000	0.00	2.33	0.00	37.46
4	P2 (B)	0	0	0	0	0	0.00	0.000	0.00	0.00	0.00	0.00
6	P3	0	0	0	0	0	0.00	0.000	0.00	2.42	4.34	35.58
8	P4 (B)	0	0	0	0	0	0.00	0.000	0.00	0.00	0.00	0.00
11	P5	0	0	0	0	0	0.00	0.000	0.00	2.10	3.42	34.69
13	P6 (B)	0	0	0	0	0	0.00	0.000	0.00	0.00	0.00	0.00
16	P7	0	0	0	0	0	0.00	0.000	0.00	2.31	3.92	35.38
18	P8 (B)	0	0	0	0	0	0.00	0.000	0.00	0.00	0.00	0.00
19	POST EXP	2231	3379	1148	3035	804	2.19	0.000	0.00	0.00	0.00	0.00

EVENT	PERIOD	STAND IC ML	STAND EKV ML	STAND RV ML
1	PRE EXP	4115	2163	1212
19	POST EXP	4400	1887	1171

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO. EPA-600/1-78-006	2.	3. RECIPIENT'S ACCESSION NO.
4. TITLE AND SUBTITLE THE EFFECT OF NITROGEN DIOXIDE ON LUNG FUNCTION IN NORMAL SUBJECTS		5. REPORT DATE January 1978
		6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S) Steven M. Horvath and Lawrence J. Folinsbee		8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS Institute of Environmental Stress University of California Santa Barbara, California 93106		10. PROGRAM ELEMENT NO. 1AA601
		11. CONTRACT/GRANT NO. 68-02-1757
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15. SUPPLEMENTARY NOTES		

16. ABSTRACT

Cardiopulmonary and metabolic responses of three groups, each consisting of five adult males (age 19 - 29) were determined before, during, and after a 2 hour exposure to 0.0.62 $\pm$ 0.12 ppm NO_2 at 25°C and 45% RH. The three groups exercised during exposure at 40% of $V_{O_2\ max}$ for either 12, 30, or 60 min. for groups C, A, and B, respectively. During the exercise periods the ventilation was about 33 liters/min, a four-fold increase over the resting level. There were no physiologically significant cardiovascular, metabolic, or pulmonary function changes which could be attributed to exposure to this level of NO_2 (0.62 ppm). There were no differences between the groups in their response despite the fact that groups A and B received more NO_2 as a result of 28% and 84% greater ventilations, respectively.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
lung nitrogen dioxide air pollution		06 F, P, T

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