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Environmental Health Effects Research Series

EFFECTS OF LOW LEVEL CARBON MONOXIDE EXPOSURE
Blood Lipids and Coagulation Parameters

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

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EFFECTS OF LOW LEVEL CARBON MONOXIDE EXPOSURE

Blood Lipids and Coagulation Parameters

by

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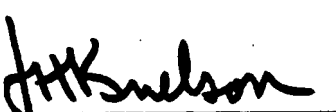
FOREWORD

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 report that follows is part of the Laboratory's research to refine health information on exposure effects to pollutants for which ambient air quality standards have been developed.



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ABSTRACT

This study examined the effects of carbon monoxide (CO) in 50 and 100 ppm doses on response to treadmill exercise, blood coagulation and blood lipids in normal men. Twenty-three men were exposed to CO or to air in a double-blind protocol. After exposure, each underwent a graded exercise treadmill test which was terminated at 85% maximal heart rate. Blood for measurement of carboxyhemoglobin (COHb), hematocrit, platelet count, prothrombin time, partial thromboplastin time, thrombin time, fibrin split products, factor VIII, platelet aggregation, serum cholesterol and triglycerides was drawn at baseline, preexercise and postexercise. COHb did not change on air days but reached a mean of 2.17% on 50 ppm days and 4.15% on 100 ppm days. The mean duration of exercise was 19 sec shorter on CO days than on air days ($f = 4.93$). The greatest effect was on 100 ppm days ($f = 8.00$). Coagulation parameters and cholesterol and triglyceride measurements were not significantly affected by CO exposure. Over the week of testing the cholesterol and triglyceride levels fell significantly and exercise was regularly associated with increased factor VIII activity. CO levels of 50 and 100 ppm significantly reduced the duration of exercise to attainment of a target heart rate in normal men. No effect of CO at these levels on coagulation parameters or on serum cholesterol and triglycerides was detected.

INTRODUCTION

The goal of this study was to detect the effects of carbon monoxide in 50 ppm and 100 ppm doses on response to treadmill exercise in normal young men on certain parameters of blood coagulation and on blood lipids.

METHODS

Patient selection: Informed consent was obtained from all subjects. Twnety-three men less than 38 years of age were included in the study. Each was given a physical examination, and chest x-ray and electrocardiograms were performed on every subject. Men with evidence of organic heart disease of any kind were excluded from the study. Additionally, all subjects were asked to refrain from cigarette smoking during the 12 hours before the beginning of each exposure period. Each subject was shown to have normal hematocrit, platelet count, prothrombin time, partial thromboplastin time, thrombin clotting time and factor VIII levels.

Experimental protocol: (Fig. 1) Each subject was studied on weekday mornings. Each fasted except for water during the 8 hours before the test was performed. At the beginning of the day, blood was drawn for baseline coagulation and lipid determinations. The subject then was exposed to air with or without carbon monoxide via a closed system which included a tank of gas with pressure regulators, a Douglas bag reservoir, and a tightly fitting mask. The exposure period was 4 hours. On Monday and Friday mornings the subjects were exposed to air only. Tuesday through Thursday the gas was air, air with carbon monoxide (CO) at 50 ppm or air with CO at 100 ppm as determined by one of the investigators. The physician, the technicians and the subject were unaware of the content of the gas while the experiment was progressing and when the electrocardiograms were analyzed.

At the end of the 4 hours of exposure, blood was again drawn for carboxyhemoglobin (COHb), coagulation factor and lipid analyses. The subject was then asked to walk on a treadmill until 85% maximal heart rate had been achieved. The treadmill was a programmed instrument set to advance at 3-minute intervals from a speed of 2 mph to 10 mph and from no incline to an incline of 16°. Heart rate was monitored by a Hewlett-Packard three-channel monitor which recorded 12 leads of ECG at 1-minute intervals and by a telemetered rate counter which computed the rate from the R-R interval. When the latter instrument indicated that 85% maximal heart rate as determined by the standard tables was reached, the time and stage of exercise were recorded and the treadmill was stopped. The subject again donated blood for analysis and the ECG was continued until the baseline heart rate was achieved. The ECG was analyzed for heart rate and time. Each subject was used as his own control from day to day and the Monday and Friday tests were included to document any training effect.

Coagulation factor assays: Baseline blood samples were drawn at 8:00 a.m. from both smokers and non-smokers prior to CO exposure. Samples were drawn into heparin for COHb levels and into a siliconized vacuum tube for blood lipids and delivered immediately to the respective laboratories. The samples for blood coagulation studies were handled as follows: blood was drawn into 3.2% sodium citrate at a ratio of 1:9 and immediately transported on ice to the laboratory. Hematocrit tubes and red cell pipettes were prepared with whole fresh blood. The hematocrit tubes were heparinized capillary tubes. The hematocrit was immediately centrifuged on a microhematocrit centrifuge for 5 minutes. Values were obtained by the scale method and recorded in duplicate. One percent ammonium oxalate was used as platelet diluting fluid.

Red cell pipettes containing the diluted blood sample were returned to the coagulation laboratory and platelet counts were made by the method of Brecher, et al (Am. J. Clin. Path., 23: 15-26, 1953).

The anticoagulated blood for coagulation analyses was spun in plastic disposable tubes (17 x 100 mm) at 150 x g in an Adams Dynac centrifuge for 10 minutes at room temperature, and sufficient platelet-rich plasma (PRP) was aspirated for platelet aggregation studies. This sample remained at room temperature and the platelet aggregating assay was performed immediately. The remaining plasma sample was re-mixed and re-centrifuged at 1500 x g in the Adams Dynac centrifuge. The plasma was immediately aspirated, aliquoted, labelled and frozen in a -70° refrigerator for other coagulation studies to be performed at a later time.

Platelet aggregating assays were performed using a Payton Dual Channel Aggregation Module and a Bausch & Lomb VO-5 Recorder. The PRP was added to the cuvette (0.45 ml) and allowed to mix for 1 minute before serial dilutions of 0.05 M epinephrine (Parke Davis Adrenalin Chloride Solution) were added. Results were tabulated, charted and recorded.

The coagulation factor assays were done on the fresh frozen samples several days later. The tests were performed using usual laboratory reagents and Hyland Reference Plasma (Hyland Laboratories, Costa Mesa, California) as a normal control.

For the prothrombin time (PT) plasma samples were removed from the -70° refrigerator and thawed in a waterbath at 37°. Simplastin (General Diagnostics, Morris Plains, N.J.) was placed in a test tube and into the waterbath. After thawing, the plasma was removed and placed at room temperature. One tenth ml of the plasma was added to a 10 x 75 mm disposable culture tube and incubated

at 37° for 30 sec. At the end of this period, 0.2 ml of Simplastin was added and the stopwatch started. The sample was immediately removed from the waterbath and tilted until fibrin strands began to form. The test and control samples were done in duplicate and recorded. The normal control PT fell between 12 and 14 sec.

For the partial thromboplastin time (PTT), plasma samples were thawed in the 37° waterbath. Test tubes of undiluted Thrombofax (Ortho Pharmaceutical, Raritan, N.H.) and 0.02 M CaCl were placed in the waterbath. After thawing, the plasma samples were held at room temperature. One tenth ml of plasma was added to a 10 x 75 mm disposable culture tube and incubated for 60 sec at 37°. At the end of 60 sec, 0.1 ml of Thrombofax and 0.1 ml of 0.02 M CaCl were added and the stopwatch started. The sample remained in the waterbath for 45 sec before being removed and tilted. The test samples and reference normals were done in duplicate and recorded. The normal clotting times fell between 40 and 60 sec.

The thrombin clotting time (TCT) was performed at room temperature with plasma which had been thawed in a 37° waterbath. Two tenths ml of plasma was added to a 10 x 75 mm disposable culture tube followed immediately by addition of 0.2 ml of thrombin (10 units/ml) (Parke, Davis, and Co., Detroit, Michigan), and the stopwatch was immediately started. This test along with the reference normal was done in duplicate. The normal TCT ranged from 12 to 14 sec.

The plasma factor VIII (antihemophilic factor) assay was based upon the observation that the PTT of hemophilic plasma is prolonged and the degree of correction of this prolonged time is proportional to the factor VIII concentration of the plasma sample added as test material. Hemophilic blood

(substrate) was drawn from a patient with severe classic hemophilia into 3.2% sodium citrate at a ratio of 1:9. The plasma was prepared by spinning the whole blood at 1500 x g for 10 minutes, RT. Hemophilic plasma samples were aliquoted and frozen at -70°.

For the factor VIII assay, Thrombofax diluted 1:10 with normal saline was used as the partial thromboplastin. Citrated saline was used as a buffered diluting fluid and referred to as the human diluent. It was composed of one part 0.2% normal saline, one part imidazole buffer (pH 7.2) and 0.4 part 3.2% trisodium citrate. Calcium was added to the system by means of calcium-imidazole-saline (C-I-S) [1.4 parts of 1.2% CaCl and one part of 0.9% saline were added to 1.2 parts imidazole buffer (pH 7.2)]. The plasma samples were activated with kaolin (Fisher Scientific Co., Fair Lawn, N.H.).

Test and hemophilic plasmas were thawed at 37°. Hyland reference plasma was prepared following container directions. Serial dilutions of 10%, 5%, 2.5% and 1.25% were made with both test and control plasmas. The plasmas were mixed with 10 mg/ml kaolin, capped and incubated at room temperature for 15 minutes, tilting every 2 minutes to keep the kaolin suspended. The C-I-S mixture and the diluted Thrombofax were placed in test tubes, labelled and incubated in the 37° waterbath. After a 15-minute waiting period, the activated plasmas were placed on ice and left for at least 5 minutes before starting the test. Determinations of the PTT's of the plasma samples began with the 10% dilution of control followed by the 10% dilution of the test, etc. All testing was done in duplicate.

Two tenths ml of plasma mixture was placed in a 37° waterbath in a 10 x 75 mm tube and incubated for 30 sec. Upon completion of the 30 sec, 0.1 Thrombofax and 0.1 ml C-I-S mixture were added and a stopwatch started. The tubes remained

in the waterbath for 60 sec but were tilted after the first 30 sec. At the end of 60 sec the tubes were removed and tilted until the fibrin formation began. The stopwatch was stopped and times recorded when fibrin strands were noted. The duplicate PTT's were averaged. Using semilogarithmic paper, the plasma concentrations were plotted on the logarithmic scale against the PTT's on the arithmetic scale. The control points were connected forming a straight line. Factor VIII activity was calculated by comparing the relative concentrations of normal and test plasmas at time points on the parallel graphic lines.

Fibrin split products were assayed by a latex particle agglutination method. Five ml of whole blood was drawn at baseline, preexercise and postexercise and allowed to clot. EACA was present in the tube to prevent fibrinolysis. The serum was allowed to incubate at room temperature for 24 hours. At the end of this period the sample was centrifuged and the serum aspirated, aliquoted and frozen. At the time of testing the samples were thawed and diluted with glycine saline buffer in serial dilutions from 1:1 - 1:64. Special glass slides obtained from Burroughs-Wellcome Co., Research Triangle Park, N.C., were for checking agglutination. One drop of patient serum was placed on a glass slide and one drop of latex suspension (Burroughs-Wellcome Co., Research Triangle Park, N.C.) added. The glass slide was tilted back and forth checking for agglutinating particles. Agglutination in samples diluted more than 1:8 was considered positive and reported as the highest dilution at which agglutination occurred.

RESULTS

A total of 23 normal young men were studied. There were 15 men who denied use of more than five cigarettes per day. This group will be referred

to as nonsmokers. Eight subjects were smokers. These two groups of subjects will for the most part be considered separately. In the group of nonsmokers the mean age was 26.2 years with a median of 25 years and a range from 20 to 38 years. The smokers had a mean age of 24.25 years with a median of 26 years and a range of 20 to 33 years.

Carbon monoxide levels: Nonsmokers had baseline carboxyhemoglobin levels which ranged from zero to 1.55% with a mean of 0.52%. The baseline levels were not significantly different from day to day (Table 1).

On days when the nonsmoking subjects were exposed to air containing no CO the COHb levels did not significantly change during the exposure period. Immediately after the period of exposure to CO at 50 ppm the mean COHb level in the nonsmokers was 2.75 ± 0.90%. After exposure to 100 ppm the level in nonsmokers was 4.72 ± 1.49%. The levels in nonsmokers after exercise on days when exposure was to air only were not significantly changed. Postexercise levels on days when the subjects were exposed to 50 and 100 ppm had decreased from preexercise values slightly to 2.53 ± 0.74% and 4.27 ± 1.21% respectively. This slight decrease was statistically significant.

Smokers had a mean COHb at the baseline that was 1.06 units higher than that of nonsmokers on the average (Table 2). After exposure to 50 ppm the mean COHb level was 3.42 ± 0.94% and after 100 ppm it was 5.32 ± 1.23%. These levels dropped slightly to 3.07 ± 0.79% and 5.04 ± 1.26% after exercise.

Table 3 shows the combined data on smokers and nonsmokers and indicates the significantly increased levels of COHb on the CO exposure days. The average increase in COHb from baseline to preexercise for the two CO days was 3.16% more than for the three air days. On the 50 ppm day this increase was 2.17% while on the 100 ppm day it was 4.15%. The 1.98% increase on the 100 ppm day over the 50 ppm day was significant.

Exercise tolerance: Figure 4 shows the exercise tolerance in seconds on the 5 days of the study for nonsmokers. The data concerning exercise tolerance in smokers is shown in Figure 5. There was no significant difference between smokers and nonsmokers with respect to time required to reach 85% of predicted maximal heart rate.

Comparison of exercise tolerance on days when subjects were exposed to CO with that on days when the exposure was to air only shows a significantly shorter duration of exercise to achievement of 85% maximal heart rate on CO days. On CO days the mean exercise time was 488 sec as compared with 507 sec on air days. The difference between exercise times on air days and on days with exposure to 50 ppm was not significant while that between air days and CO days with 100 ppm was significant.

Blood lipids: No differences in cholesterol levels were noted to be related to CO exposure (Table 6). There was, however, a significantly lower level on Friday than on Monday. This difference was an average of 9 mg %. The triglyceride level also fell by an average 17 mg % across the 5-day period. No change in triglyceride levels could be related to CO exposure (Table 7).

Blood coagulation parameters: Prothrombin times, partial thromboplastin times, thrombin clotting times and fibrin split product titers were never outside the range of normal and daily variation in our tests made it impossible to correlate changes with exercise or presence or absence of carbon monoxide in the inspired air.

Factor VIII: The factor VIII levels increased significantly from preexercise to postexercise values (Table 8). There was, however, no significantly greater increase on CO days than on air days. Although not significant ($p = 0.157$) the difference between smokers and nonsmokers was

rather large. The mean for smokers was 85.7% and the mean for nonsmokers was 100.6%. This apparent difference deserves further study.

Hematocrit: On the three air days, the mean hematocrit increased 0.8% from preexercise to postexercise (Table 9). This increase was significant. On the CO days, this increase was 0.9% which again was significant. There was an increase of 1.3% on the 50 ppm day which makes it unlikely that an effect of CO exposure on the differences in hematocrit levels before and after exercise can be implied.

Platelet count: There was a large but not significant ($p = 0.075$) difference between the platelet counts of smokers and nonsmokers. The mean count for nonsmokers was 225,000/mm^3, that for smokers was 253,000/mm^3. Additionally, there was significant increase in platelet counts in all groups between the preexercise and postexercise sampling periods (Table 10). The mean increase on the three air days was 15,300/mm^3, the increase on the 50 ppm day was an average of 37,000/mm^3 and the increase on 100 ppm days was 19,300/mm^3. The difference between the increase on air days and the increase on the 50 ppm day, 22,500/mm^3, was significant.

Platelet aggregation studies were performed on 5 subjects. These studies showed no effect of exercise or carbon monoxide on platelet aggregation to ADP or epinephrine in our system.

DISCUSSION

The validity of this study is dependent to a great extent upon the comparability of the study subjects and, therefore, is potentially threatened by the presence among the study group of both smokers and nonsmokers. Smokers, for instance, had an average baseline COHb level that was 1.06% higher than that of the nonsmokers. Subsequent measurements were proportionally

different between the smokers and nonsmokers. This problem has been significantly abated, however, by the use of paired t analysis allowing comparison of each variant in a single subject. Even though variability between subjects prevented the description of an effect of smoking on the parameters measured, within each subject there was measured an effect of carbon monoxide exposure over and above that attributable to the smoking.

Carbon monoxide exposure primarily influenced exercise tolerance. A significantly decreased time to attainment of 85% of maximal heart rate was demonstrated on days when the subjects had been exposed to carbon monoxide. The carboxyhemoglobin level at which this effect was noted was 4.93%. These results are similar to those reported by others and imply that carbon monoxide even in relatively small doses will decrease the peak work production of normal young men. Of special note is a demonstrable effect of added CO in smokers similar to that of nonsmokers.

These findings show a physiologic effect of carboxyhemoglobin at very low levels. The effect is possibly related to an increased requirement for peripheral blood flow because of a decreased availability of oxygen for respiration. The exact mechanism by which increased heart rate precipitated by carbon monoxide exposure at a certain level of exertion is mediated is, of course, unknown. The fact that such an effect can be measured at submaximal exertion, however, implies that the workload to be met by the cardiovascular system can be significantly augmented by even very small doses of carbon monoxide.

To further characterize the physiologic effects of carbon monoxide, blood lipids and coagulation measures were determined. The serum cholesterol and triglyceride levels were not affected by exposure to carbon monoxide or by submaximal exercise following carbon monoxide exposure.

Previous studies on animals have shown increased serum cholesterol levels after weeks of exposure to carbon monoxide. It has also been shown that cigarette smokers have slightly higher cholesterol levels than do nonsmokers. The fact that no change was observed in our subjects may mean that CO has no hyperlipidemic effect in humans. More likely is the possibility that such an effect cannot be demonstrated after an exposure period of only 4 hours and at levels as low as those used in this study.

To study the effects of carbon monoxide on the coagulation system we chose to examine the routinely used clotting "screening tests" which include prothrombin time, partial thromboplastin time, thrombin clotting time and fibrin split products. Additionally, we examined the phase reactant and "consumable" factor VIII because of its known variability in response to a number of interventions. Specifically we wished to determine if the known increase in plasma factor VIII levels caused by exercise would be augmented by the presence of carboxyhemoglobin. The screening tests showed no change with either CO exposure or exercise. This result was related to the poor sensitivity of the test procedure. It should be remembered for instance that more than a 20% fall in a clotting factor is required before it can be detected by the screening tests. Finally the use of screening tests to measure "hypercoagulability" is unacceptable because of the known variability among laboratories and the absence of consensus as to the definition of the term "hypercoagulability". Therefore, there is no major alteration in the clotting system attributable to short-term, low-dose carbon monoxide exposure.

Factor VIII assays, unlike screening assays, are relatively sensitive to small changes in the plasma level of this factor. Additionally, the plasma factor VIII is known to decrease rapidly in the face of intravascular coagulation

and to increase with exercise, catacholamine infusions or infection. This study shows that chronic smoking is associated with a slight but not statistically significant decrease in factor VIII levels below the normal level. This difference between smokers and nonsmokers has not been previously described and deserves further study. There was a significant increase in factor VIII levels between the preexercise period and the postexercise period as expected. However, no difference was noted between the increases recorded on air days and those which occurred on CO days. These studies do not rule out the possibility that at higher doses of CO some effect on factor VIII might be noted. They do indicate that no demonstrable effect occurs at levels which are of interest to environmental planners.

Finally, an attempt was made to measure the effects of carbon monoxide exposure and exercise on platelet function. Platelet counts were made on each blood sample. There was a large but not statistically significant difference between smokers and nonsmokers with the mean level among the smokers being 28,000 platelets/mm^3 higher. This difference has not been noted in the past. There was a singificant increase in platelet counts between the preexercise and postexercise measurements, but no reproducible effect of carbon monoxide was noted. The low-dose and short-term of exposure to carbon monoxide may have allowed potential effects on platelet concentration to go undetected. There was, however, no marked effect demonstrated by this study.

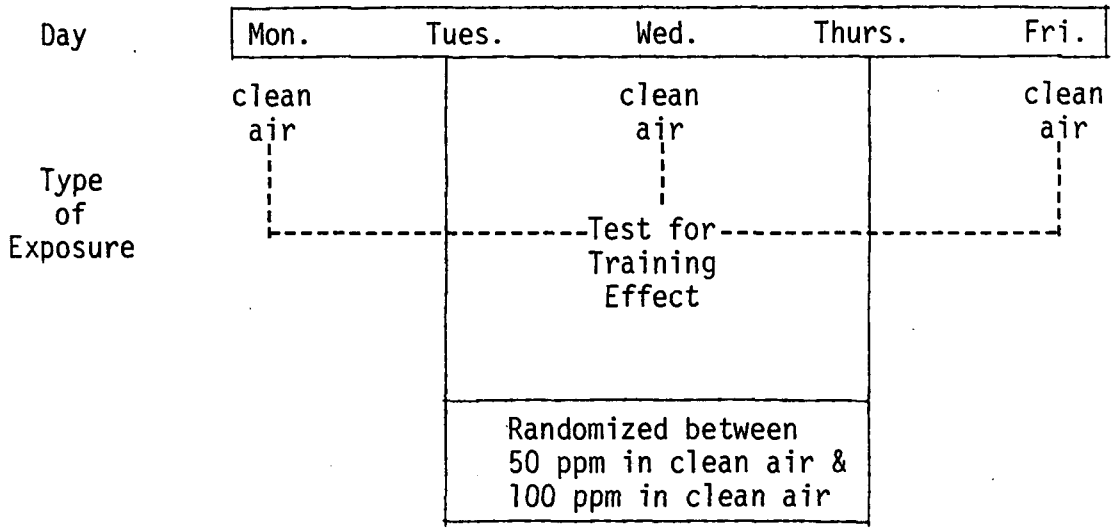
Platelet aggregometry was attempted on the first several study subjects. The blood sample size, the need for collection of simultaneous control studies and the long period of uninterrupted testing necessary to do these studies prohibited the assay of this variable in all subjects. No effect on platelet aggregation of either exercise or CO was detected.

Study of patients with coronary heart disease was begun during the first half of 1976. At that time two studies were completed. The second patient suffered an episode of prolonged chest pain which required admission to the coronary care unit. Because of this occurrence, the study was suspended until the Protection of the Rights of Human Subjects authorization could be reviewed and reevaluated. This review is presently in process.

In summary, these studies have demonstrated a dose-related increase in heart rate with standardized exercise in normal young men. This effect was noted at carboxyhemoglobin levels of 4% on the average which was accumulated over a 4-hour period. The study was sound in that double-blind administration of air and air containing carbon monoxide prohibited the prejudicial performance of subjects and the prior knowledge of investigators. Additionally, the study was conducted over a 5-day period which allowed for the evaluation of training effect. Simultaneous studies of blood lipids and coagulation screening tests as well as more sensitive measures of coagulation failed to link changes in these parameters to the presence in the inspired air of carbon monoxide. These results indicate that levels of carbon monoxide in the atmosphere as low as 50 to 100 ppm limit the ability to perform submaximal activity. There is, however, no detectable effect of carbon monoxide at these levels on blood lipids or coagulation parameters. The possibility that effects may exist after exposure to higher doses of carbon monoxide for longer periods cannot be ruled out by our study.

Figure 1. PROTOCOL

Gas Exposure: 4-hour exposure via closed face mask with subject sitting in a chair.



Typical Day:

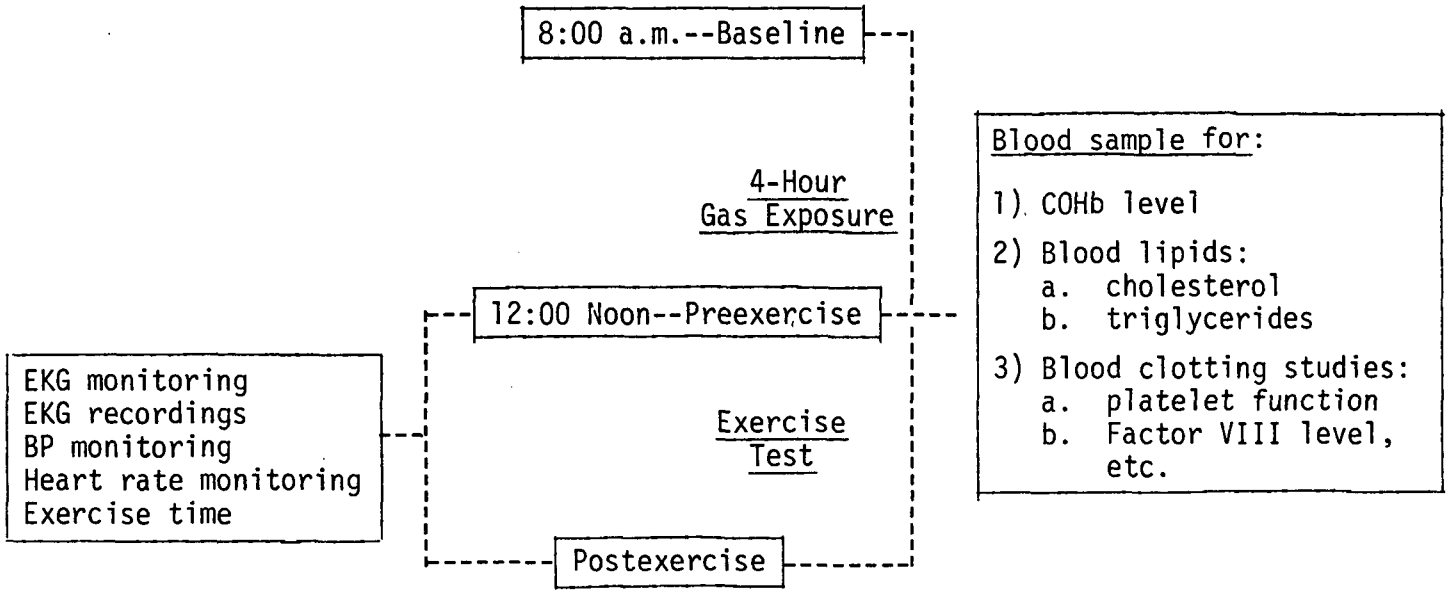


Table 1

COHb (Nonsmokers)

	Monday	X	Friday	50 ppm	100 ppm
Baseline	0.47	0.64	0.52	0.54	0.52
S.D.	0.54	0.47	0.30	0.47	0.46
Preexercise	0.31	0.70	0.51	2.75	4.72
S.D.	0.36	0.42	0.32	0.90	1.49
Postexercise	0.48	0.61	0.62	2.53	4.27
S.D.	0.29	0.41	0.31	0.74	1.21

Table 2

COHb (Smokers)

	Monday	X	Friday	50 ppm	100 ppm
Baseline	2.06	2.18	2.28	1.88	1.82
S.D.	1.50	0.87	0.97	1.13	0.80
Preexercise	1.51	1.65	1.70	3.42	5.32
S.D.	0.88	0.59	0.90	0.94	1.23
Postexercise	1.38	1.47	1.51	3.07	5.04
S.D.	0.95	0.72	0.65	0.79	1.26

Table 3

COHb (Combined)

		Monday	X	Friday	50 ppm	100 ppm
Baseline	Mean	1.02	1.17	1.07	1.00	0.97
	S.D.	1.22	0.97	0.99	0.99	0.86
Preexercise	Mean	0.72	1.03	0.93	2.98	4.93
	S.D.	0.82	0.66	0.81	0.95	1.40
Postexercise	Mean	0.79	0.91	0.93	2.72	4.54
	S.D.	0.73	0.67	0.62	0.78	1.25

Table 4

Nonsmokers

Subject	Age	Peak H.R.	Exercise Time (sec)				
			Mon	X	Fri	50 ppm	100 ppm
J.W.	31	165	410	315	330	305	305
J.L.	29	165	615	615	590	560	625
G.W.	38	160	590	610	580	600	590
S.G.	24	170	434	470	576	511	350
N.W.	22	175	515	535	510	500	500
T.H.	29	175	533	523	543	575	493
S.R.	20	180	510	501	503	501	472
A.D.	23	175	501	469	465	492	495
B.Y.	24	170	339	327	360	300	285
M.P.	20	180	590	554	467	513	538
T.E.	30	165	394	495	405	431	385
L.E.	22	180	690	750	750	720	605
W.R.	25	170	410	614	672	499	616
C.S.	26	170	447	470	520	405	424
T.M.	30	165	395	410	430	420	397
Mean	26.2	Mean	492	511	513	489	472
Median	25	S.D.	99	113	112	108	112

Table 5

Smokers

Subject	Age	Peak H.R.	Exercise Time (sec)				
			Air Days			CO Exposure Days	
			Mon	X	Fri	50 ppm	100 ppm
H.R.	33	165	470	505	512	485	480
J.H.	22	180	---	435	435	433	440
C.S.	24	170	315	310	300	317	265
W.N.	25	(159-149)					
D.F.	26	170	529	405	480	515	462
D.P.	22	180	577	531	558	499	516
C.K.	20	180	594	544	605	615	533
B.F.	22	180	617	760	780	786	699
Mean	24.25	Mean	517	499	524	521	485
Median	24	S.D.	112	141	149	147	129

Table 6

Cholesterol

		Monday	X	Friday	50 ppm	100 ppm
Baseline	Mean	196	198	192	205	197
	S.D.	39	32	28	33	37
Preexercise	Mean	206	203	194	200	205
	S.D.	45	36	32	31	42
Postexercise	Mean	210	206	199	206	198
	S.D.	41	45	24	29	33

Table 7

Triglycerides

		Monday	X	Friday	50 ppm	100 ppm
Baseline	Mean	115	128	109	117	125
	S.D.	52	59	45	50	65
Preexercise	Mean	118	106	97	100	111
	S.D.	61	56	44	50	62
Postexercise	Mean	124	107	99	103	115
	S.D.	64	49	46	47	56

Table 8

Factor VIII

		Monday	X	Friday	50 ppm	100 ppm
Baseline	Mean	93	87	91	89	90
	S.D.	33	23	29	24	34
Preexercise	Mean	89	82	85	88	84
	S.D.	34	32	33	29	25
Postexercise	Mean	111	106	110	109	114
	S.D.	36	34	34	29	31

Table 9

Hematocrit

		Monday	X	Friday	50 ppm	100 ppm
Baseline	Mean	45.5	44.5	42.9	44.5	45.0
	S.D.	3.2	2.6	2.3	3.3	3.5
Preexercise	Mean	46.3	44.8	43.0	44.0	45.1
	S.D.	3.3	3.3	2.5	3.4	3.2
Postexercise	Mean	47.7	45.3	43.5	45.3	45.5
	S.D.	3.2	2.9	3.2	3.6	3.1

Table 10

Platelet Count

(per mm^3 in thousands)

		Monday	X	Friday	50 ppm	100 ppm
Baseline	Mean	233	225	236	235	235
	S.D.	54	41	53	47	39
Preexercise	Mean	231	231	228	217	227
	S.D.	52	43	41	39	41
Postexercise	Mean	238	240	258	255	246
	S.D.	46	40	55	55	39

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4. TITLE AND SUBTITLE	5. REPORT DATE
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16. ABSTRACT

This study examined the effects of carbon monoxide (CO) in 50 and 100 ppm doses on response to treadmill exercise, blood coagulation and blood lipids in normal men. Twenty-three men were exposed to CO or to air in a double-blind protocol. After exposure, each underwent a graded exercise treadmill test which was terminated at 85% maximal heart rate. Blood for measurement of carboxyhemoglobin (COHb), hematocrit, platelet count, prothrombin time, partial thromboplastin time, thrombin time, fibrin split products, factor VIII, platelet aggregation, serum cholesterol and triglycerides was drawn at baseline, preexercise and postexercise. COHb did not change on air days but reached a mean of 2.17% on 50 ppm days and 4.15% on 100 ppm days. The mean duration of exercise was 19 sec shorter on CO days than on air days ($f = 4.93$). The greatest effect was on 100 ppm days ($f = 8.00$). Coagulation parameters and cholesterol and triglyceride measurements were not significantly affected by CO exposure. Over the week of testing the cholesterol and triglyceride levels fell significantly and exercise was regularly associated with increased factor VIII activity. CO levels of 50 and 100 ppm significantly reduced the duration of exercise to attainment of a target heart rate in normal men. No effect of CO at these levels on coagulation parameters or on serum cholesterol and triglycerides was detected.

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a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
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18. DISTRIBUTION STATEMENT	19. SECURITY CLASS *(This Report)*	21. NO. OF PAGES
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