JOURNAL OF APPLIED PHYSIOLOGY
Vol. 38, No. 2, February 1975. *Printed in U.S.A.*

Maximal aerobic capacity at different levels of carboxyhemoglobin

STEVEN M. HORVATH, PETER B. RAVEN, THOMAS E. DAHMS, AND DAVID J. GRAY
Institute of Environmental Stress, University of California, Santa Barbara, California 93106

HORVATH, STEVEN M., PETER B. RAVEN, THOMAS E. DAHMS, AND DAVID J. GRAY. *Maximal aerobic capacity at different levels of carboxyhemoglobin.* J. Appl. Physiol. 38(2): 300–303. 1975.—Previous studies had indicated that maximum aerobic power ($\dot{V}O_{2\,max}$) would be seriously impaired when HbCO levels were above 7% but was not altered if HbCO was around 2.7%. The present studies indicated that the critical level at which HbCO influenced $\dot{V}O_{2\,max}$ was approximately 4.3%. This was accompanied as in the above-noted studies with a reduction in total work time to the attainment of $\dot{V}O_{2\,max}$. Two procedures to raise HbCO to appropriate levels were employed, i.e., a buildup wherein HbCO was incrementally increased by breathing ambient air containing 75 or 100 ppm CO and a bolus plus maintenance procedure. In the latter, HbCO was raised to the level attained in the buildup test by giving a "bolus" of CO followed by the continued inhalation of CO at a level to just maintain this level of HbCO regardless of the magnitude of the ventilation. Regardless of the mode of presentation, the decrement in $\dot{V}O_{2\,max}$ occurred at the same level of HbCO. These observations are of considerable significance, since it indicated that even low ambient levels of CO (23.7 ppm) would result in lowering maximum aerobic power if the individual had been previously exposed to CO such that the level was raised to this critical point.

maximum aerobic power; air pollution

PREVIOUS INVESTIGATIONS (10, 13, 14, 19, 20) suggested that a linear decline in aerobic power ($\dot{V}O_{2\,max}$) occurred with a progressive increase in carboxyhemoglobin (%HbCO) levels. The requisite HbCO levels were obtained prior to the maximum aerobic power test by breathing a high concentration of carbon monoxide—a "bolus" (BO) presentation. The resultant HbCO levels were between 7 and 33%. Several studies (9, 15, 16) during which young and middle-aged men, smokers and nonsmokers, continuously breathed air containing 50 ppm of CO—a "buildup" (BU) presentation—failed to demonstrate any significant decrease in $\dot{V}O_{2\,max}$, although the duration of effort in this progressive test was significantly shortened. The HbCO levels in these studies were 2.7% for nonsmokers and 4.5 and 5.2%, respectively, for young and middle-aged smokers. Several possibilities exist to explain these differences. The mode of presentation of CO may be a factor or the level of ambient inspired CO may not have been high enough to have interfered with oxygen transport. There is a necessity to determine the precise level of HbCO at which aerobic capacity is impaired and to relate this level to the ambient concentrations of CO present in our air environment.

METHODS

Four healthy adult male volunteers aged 24–33 yr were subjects for the present investigation. Three were nonsmokers and the fourth abstained from his pipe smoking for a minimum of 12 h prior to each test. They had been engaged in numerous previous studies and were well versed in the experimental procedures. All subjects were screened for cardiovascular and pulmonary abnormalities.

The maximum aerobic capacity was determined utilizing the progressive test described by Drinkwater and Horvath (8). Each subject performed three $\dot{V}O_{2\,max}$ tests for the buildup experiments (BU), which consisted of breathing either filtered air (*A*), 75 ppm CO in filtered air (*B*), or 100 ppm CO in filtered air (*C*). The conditions were presented in random order and in a single-blind mode so that the subjects were unaware of the conditions of the exposure. The inspired level of CO was maintained within ±3 ppm of the required level for the entire exposure condition leading to a gradual increase in HbCO over time. There was 1 wk between each exposure. The subjects then repeated the three exposures in a different random order with the exception that a preliminary bolus (BO) inhalation of CO was given to bring the preexercise HbCO level to that obtained at the end of the previous BU tests. During this second series the HbCO levels were maintained at the required levels throughout the entire test within 0.1% during *B* tests and 0.12% during *C* exposures. The technique employed to maintain these levels has been described elsewhere (7).

Blood volumes were measured to obtain total body hemoglobin (7). On the day of the BU tests the subject was seated and a blood sample taken for analysis of its hemoglobin, lactate (18), hematocrit, plasma protein, and CO content (6). The subject was then connected to the ECG monitoring leads (V4) and started breathing through an open-circuit system, at which time CO administration was initiated. Thirteen minutes later another blood sample was obtained and analyzed as above. At the 15th min the subject began walking on the treadmill at 3.4 mph with the grade automatically being increased 1% each minute. Immediately upon exhaustion the subject was seated in a chair for a 15-min recovery to determine the oxygen debt. A third blood sample was secured at the 4th min of recovery. In the BO studies the subject was connected to a closed-circuit system for a preliminary seated rest period of 15 min while his HbCO levels were brought to the required level. He breathed 100% oxygen, and 10% of the previously determined quantity of CO for filtered air was injected

Downloaded from http://jap.physiology.org/ by 10.220.33.2 on January 16, 2017

into the system each minute for the first 10 min. Blood samples were obtained to determine the HbCO levels. At the end of this 15-min period he then transferred to the open-circuit system which provided the maintenance level of ambient CO (7). Additional blood samples were taken as for the BU tests and the same protocol of rest, exercise, and recovery followed.

During rest, exercise, and recovery, ventilatory volumes, respiratory rates, and oxygen and carbon dioxide contents of expired air were continuously monitored, averaged, and recorded by a PDP-12 computer connected on line to the respective analyzers. Oxygen percentage was analyzed using a Servomex analyzer, and CO_2 by an infrared analyzer. Ventilatory volumes were monitored with a dry gas meter, and respiratory rate was obtained using a thermistor in the mouthpiece. Aliquot expired air samples were obtained at intervals for direct analysis by gas chromatography as an independent check on the computerized data. Inspired CO was continuously monitored using a long-path IR analyzer (Beckman 315B). The electrocardiogram was monitored on an oscilloscope with heart rates obtained from the ECG recorded during the last 10 s of each minute.

Data were analyzed using a two-factor analysis of variance with repeated measures across exposure conditions and CO presentation modes. Where significant interactions were found a further analysis was made of simple main effects followed by a Newman-Keuls test of ordered means at the 0.05 and 0.10 levels of confidence (21). Variables selected for analysis included all physiological variables measured at $\dot{V}O_{2\,max}$ and blood parameter values obtained prior to and following the exercise tests.

RESULTS

The subjects' physical characteristics, including their blood volumes and CO dilution spaces, are presented in Table 1. The values were within the range of the normal population with the exception that the plasma volumes of all subjects were greater than the average (2). Table 2 summarizes the average $\dot{V}O_{2\,max}$ and total exercise time obtained during each condition as well as the ventilatory volumes and heart rates at $\dot{V}O_{2\,max}$. Regardless of the mode of presentation of CO, the $\dot{V}O_{2\,max}$ was lower ($P < 0.10$) when HbCO was over 4.0%. All four subjects exhibited decreased aerobic power under these conditions. No significant differences in $\dot{V}O_{2\,max}$ from control conditions were observed when subjects breathed 75 ppm CO or attained the same level of carboxyhemoglobin (3.2–3.4% by the bolus and maintenance procedure). However, ventilatory volumes were significantly lower during all four CO exposures than during the filtered air tests. It should be noted that the subjects walked 1–2 min longer

TABLE 1. *Physical characteristics of subjects*

Subj No.	Age, yr	Wt, kg	SA, m²	Blood Volumes, liters			THb, g	CO Dilution,* liters
				Total	RBC	Plasma		
1	24	61.1	1.65	5.40	2.09	3.32	698	0.970
2	28	76.8	2.00	6.26	2.37	3.90	747	1.038
3	29	77.0	2.04	6.69	2.86	3.83	882	1.225
4	33	79.3	1.96	6.31	2.29	4.02	781	1.085

* Total Hb × 1.389.

TABLE 2. *Average $\dot{V}O_{2\,max}$ and ventilation and heart rates at $\dot{V}O_{2\,max}$ as well as total time walked during the three conditions of exposure and two modes of presentation*

Condition	$\dot{V}O_{2\,max}$, l/min		$\dot{V}_{EBTPS}$, l/min		Heart Rate, beats/min		Time Walked, min	
	BU	BO	BU	BO	BU	BO	BU	BO
A	3.69 ±0.16	3.73 ±0.10	119.6 ±6.6	119.4 ±2.6	189.0 ±8.4	190.0 ±5.3	24.0 0.47	24.0 0.47
B	3.51 ±0.16	3.80 ±0.14	103.0 ±5.9	116.5 ±3.1	185.5 ±5.6	186.8 ±4.0	22.8 ±0.29	23.0 ±1.2
C	3.43 ±0.08	3.46 ±0.06	109.4 ±4.8	102.9 ±5.2	189.3 ±8.4	183.3 ±3.4	22.6 ±0.28	21.5 ±0.75
	C < *A* and *B* $P < 0.10$		*A* > *B* and *C* $P < 0.05$		No signif diff		*A* > *B* and *C* $P < 0.05$	

Values are means ± SE. BU = buildup exposures with *A* = filtered air, *B* = breathing 75 ppm CO, and *C* = breathing 100 ppm CO. BO = bolus exposures plus maintenance at 17.7 ppm CO (*B*), and at 23.6 ppm CO (*C*).

in the latter condition. These lower times in which CO was being breathed were significantly lower ($P < 0.05$). The difference in work time between the lower and higher final HbCO levels was also significant. No significant differences between conditions were obtained for heart rate, ventilatory equivalent ratio, or excess carbon dioxide at $\dot{V}O_{2\,max}$. Oxygen debt was similar under all conditions. At $\dot{V}O_{2\,max}$ the only differences observed between bolus and buildup presentations of CO were for the respiratory exchange ratio (R), which was lower in BO ($\bar{X}$ = 1.02) than in BU ($\bar{X}$ = 1.04), $P < 0.10$, and for tidal volume, which was higher in BO ($\bar{X}$ = 2.73 liters) than in BU ($\bar{X}$ = 2.66 liters), $P < 0.05$. No consistent differences in any of the measured parameters were observed during the submaximal levels of work during the progression to maximum.

The HbCO levels followed the anticipated pattern of the experimental design and clearly demonstrated the ability of the techniques utilized to obtain and maintain the predicted values (Table 3). There was no difference in HbCO levels at rest (control) in any of the six tests. The second blood sample (Pre 2) reflected the changes in HbCO due to either the BO or BU condition. In the BU experiments the HbCO values while breathing 75 or 100 ppm CO were not significantly different over the short time period of quiet sitting. Blood carboxyhemoglobin levels at the end of the rest period in the BO state were not significantly different from the final postexercise value obtained during the BU experiments. The 4-min postexercise HbCO levels for each condition were significantly different ($P < 0.01$) from each other ($A < B < C$) but there were no differences (*B* and *C*) between BO and BU modes of presentation of CO. This latter occurred despite the progressive increase in ventilatory volumes from 6 to 120 l/min under the conditions of the exercise test. Although no differences were observed in resting lactates, the postexercise blood lactates were significantly higher ($P < 0.01$) following the filtered air studies than in any of those in which blood HbCO was increased regardless of the mode of presentation of CO.

Downloaded from http://jap.physiology.org/ by 10.220.33.2 on January 16, 2017

TABLE 3. *Mean values for blood parameters during all conditions*

Condition*		Hemoglobin, mmol/l BU	Hemoglobin, mmol/l BO	Carboxyhemoglobin, % BU	Carboxyhemoglobin, % BO	Lactate mEq/l BU	Lactate mEq/l BO
A	Pre 1	8.88 ±0.15	8.65 ±0.15	0.35 ±0.06	0.50 ±0.11	1.82 ±0.21	1.62 ±0.24
	Pre 2	8.70 ±0.13	8.70 ±0.12	0.35 ±0.03	0.50 ±0.11		
	Post	9.25 ±0.10	9.35 ±0.14	0.33 ±0.06	0.35 ±0.11	11.05 ±1.77	11.28 ±0.45
B	Pre 1	8.70 ±0.21	8.88 ±0.12	0.38 ±0.05	0.50 ±0.16	1.48 ±0.17	1.24 ±0.22
	Pre 2	8.53 ±0.13	8.83 ±0.13	0.75 ±0.03	3.28 ±0.12		
	Post	9.10 ±0.08	9.40 ±0.13	3.35 ±0.14	3.18 ±0.16	9.94 ±0.65	9.59 ±1.23
C	Pre 1	8.83 ±0.13	8.93 ±0.10	0.40 ±0.07	0.48 ±0.12	1.79 ±0.22	1.38 ±0.26
	Pre 2	8.78 ±0.20	8.88 ±0.12	0.90 ±0.05	4.43 ±0.28		
	Post	9.30 ±0.15	9.38 ±0.10	4.30 ±0.30	4.25 ±0.29	10.10 ±0.88	8.23 ±1.21

Values are means ± SE. BU = buildup exposures. BO = bolus exposures. * *A* = filtered air (FA); *B* = 75 ppm CO; *C* = 100 ppm CO.

DISCUSSION

No significant decreases in maximal aerobic capacity were noted until HbCO levels exceeded 4.3%. Previously it had been shown that $\dot{V}O_{2\,max}$ was unchanged when HbCO levels were approximately 2.7% (9, 16). On the other hand Ekblom and Huot (10) reported a 9% decrease in $\dot{V}O_{2\,max}$ when HbCO was 7.0%. It would appear that a certain increment in HbCO was necessary to modify maximal aerobic capacity. It is interesting to note that certain central nervous system functions (11, 12) are also depressed at approximately this same level (4–5% HbCO). These altered capacities have been observed to occur in young nonsmokers. Smokers generally have HbCO values around 4–7% and their performances may not be affected in the same manner or to the same degree (4, 5, 11). Further investigations utilizing smokers as subjects may indicate that it would be more meaningful to relate the decline in $\dot{V}O_{2\,max}$ to a change in HbCO from control levels rather than the absolute value present. Roughton and Darling (17) suggested on theoretical grounds that work capacity would be reduced to zero when HbCO reached 45–50%. Although the effect of these higher levels of HbCO cannot be confirmed, a review of available data, including that available from this study, indicated that a linear decline in $\dot{V}O_{2\,max}$ does occur when HbCO levels range from approximately 4 to 35% (11, 16) and that this change can be expressed as percent decrease in $\dot{V}O_{2\,max}$ = 0.91 (%HbCO) + 2.2.

In the present study there occurred a reduction in work time to exhaustion, 4.9 and 7.0% decreases when HbCO levels had attained 3.3 and 4.3%, respectively. A similar but more marked reduction in maximum work time had been previously reported (10), a 38% decrease at 7% HbCO. The forms of exercise utilized to obtain $\dot{V}O_{2\,max}$, walking vs. running, 20–24 vs. 3–5 min, may partially explain the larger differences observed by the latter investigators. In the walking tests, although the subjects were unaware of the composition of the inspired gases, they subjectively reported a greater feeling of tiredness in the legs and considerable cramping when exercising while breathing CO. Whether these subjective impressions were responsible for the earlier termination of the tests could not be determined but the subjects were accustomed to these maximum performances and apparently ceased activity only when completely exhausted. It was observed that the postexercise blood lactates were significantly lower in the CO tests than in the filtered air conditions in contrast to Ekblom and Huot's (10) findings of no change regardless of level of HbCO up to 20%. The different test procedures may provide the only explanation, since in short running maximum tests blood lactates are generally higher than in the more prolonged walking tests. The shorter performance time during CO exposures may also explain the lower lactate levels. It is also possible that the decreased work capacity may be a function of the decreased availability of oxygen to metabolic tissues, since increasing levels of HbCO result in concomitant decreases in arterial oxygen saturation and raised levels of venous oxygen saturation (1, 3). Vogel et al. (19) have indicated that at $\dot{V}O_{2\,max}$ with 20% HbCO, the cardiac output had attained the same maximal level as that of the higher $\dot{V}O_{2\,max}$ when breathing air containing no CO. This high cardiac output was attained through a higher heart rate. In the present study as well as those of others (17, 20, 21), maximum heart rates were observed even though HbCO varied between 4.3 and 20%. These results do not agree with Ekblom and Huot (10), who found significant decrement in maximum heart rate with increasing levels of HbCO. Again this may reflect some differences consequent to different test procedures, in particular their method of administering CO which was not continuous as was ours but was interrupted and by bolus.

Although some concern must still be held as to methodology of producing elevated HbCO levels, it was with some surprise that in the present studies no difference in eventual response was noted in the two modes of presentation of CO. This may be due to our slower presentation of the bolus or it may be that the effect of decreased oxygen delivery is demonstrable only at or near the maximal capabilities of the subjects. We observed no consistently significant ventilatory or heart rate differences during the progressive increases in energy expenditure of this walking test regardless of the mode of presentation of CO. Both Vogel et al. (19, 20) and Pirnay et al. (14) reported consistently higher heart rates for given selected submaximal work loads and increased ventilatory volume exchange per unit of oxygen uptake.

The results of the present study suggest that a critical level of HbCO must be present before significant physiological alterations could be demonstrated. They further exhibited that the absolute level may be more important than the mode of presentation, at least at low levels of HbCO and in nonsmokers. The coincidence of deteriorated

Downloaded from http://jap.physiology.org/ by 10.220.33.2 on January 16, 2017

performance as indicated by decreased maximal aerobic power and depression of certain central nervous system functions when HbCO levels are about 4–5% may be more than suggestive.

We express our appreciation and thanks to the subjects who again willingly agreed to participate in these strenuous tests.

This work was supported in part by the California Air Resources Board through Grant ARB-2098.

Received for publication 24 June 1974.

REFERENCES

1. Adams, J. D., H. H. Erickson, and H. L. Stone. Myocardial metabolism during exposure to carbon monoxide in the conscious dog. *J. Appl. Physiol.* 34: 238–242, 1973.
2. Altman, P. L. and D. S. Dittmer (Editors). *Blood and Other Body Fluids* (3rd ed). Bethesda, Md.: *Fed. Am. Soc. Exptl. Biol.*, 1971, p. 1–2.
3. Ayers, S. M., S. Granelli, and H. Mueller. Myocardial and systemic responses to carboxyhemoglobin. *Ann. N.Y. Acad. Sci.* 17: 268–293, 1970.
4. Chevalier, R. B., J. A. Bowers, S. Bondurant, and J. C. Ross. Circulatory and ventilatory effects of exercise in smokers and nonsmokers. *J. Appl. Physiol.* 18: 357–360, 1963.
5. Chevalier, R. B., R. A. Krumholz, and J. C. Ross. Reaction of nonsmokers to carbon monoxide inhalation. *J. Am. Med. Assoc.* 198: 135–138, 1966.
6. Dahms, T. E., and S. M. Horvath. Rapid, accurate technique for determination of carbon monoxide in blood. *Clin. Chem.* 20: 533–537, 1974.
7. Dahms, T. E., S. M. Horvath, and D. J. Gray. Technique for accurately producing desired carboxyhemoglobin levels during rest and exercise. *J. Appl. Physiol.* 38: 366–368, 1975.
8. Drinkwater, B. L., and S. M. Horvath. Responses of young female track athletes to exercise. *Med. Sci. Sports* 3: 56–62, 1971.
9. Drinkwater, B. L., P. B. Raven, S. M. Horvath, J. A. Gliner, R. O. Ruhling, N. W. Bolduan, and S. Taguchi. Air pollution, exercise, and heat stress. *Arch. Environ. Health* 28: 177–181, 1974.
10. Ekblom, B., and R. Huot. Response to submaximal and maximal exercise at different levels of carboxyhemoglobin. *Acta Physiol. Scand.* 86: 474–482, 1972.
11. Horvath, S. M. Effects of carbon monoxide on human behavior. In: *Proceedings of the Conference on Health Effects of Air Pollutants.* Washington, D. C.: Assembly of Life Sciences, Natl. Acad. Sci.-Natl. Res. Council, October 3–5, 1973, pp. 127–144.
12. Horvath, S. M., T. E. Dahms, and J. F. O'Hanlon, Jr. Carbon monoxide and human vigilance: a deleterious effect of present urban concentrations. *Arch. Environ. Health* 23: 343–347, 1971.
13. Nielsen, B. Exercise temperature plateau shifted by a moderate carbon monoxide poisoning. *J. Physiol., Paris* 63: 362–365, 1971.
14. Pirnay, F., J. Dujardin, R. Deroanne, and J. M. Petit. Muscular exercise during intoxication by carbon monoxide. *J. Appl. Physiol.* 31: 573–575, 1971.
15. Raven, P. B., B. L. Drinkwater, S. M. Horvath, R. O. Ruhling, J. A. Gliner, J. C. Sutton, and N. W. Bolduan. Age, smoking habits, heat stress, and their interactive effects with carbon monoxide and peroxyacetylnitrate on man's aerobic power. *Intern. J. Biometeorol.* 18, 1974.
16. Raven, P. B., B. L. Drinkwater, R. O. Ruhling, N. W. Bolduan, S. Taguchi, J. A. Gliner, and S. M. Horvath. Effect of carbon monoxide and peroxyacetylnitrate on man's maximal aerobic capacity. *J. Appl. Physiol.* 36: 288–293, 1974.
17. Roughton, F. J. W., and R. C. Darling. The effects of carbon monoxide on the oxyhemoglobin dissociation curve. *Am. J. Physiol.* 141: 17–31, 1944.
18. Ström, G. The influence of anoxia on lactate utilization in man after prolonged muscular work. *Acta Physiol. Scand.* 17: 440–451, 1949.
19. Vogel, J. A., and M. A. Gleser. Effect of carbon monoxide on oxygen transport during exercise. *J. Appl. Physiol.* 32: 234–239, 1972.
20. Vogel, J. A., M. A. Gleser, R. C. Wheeler, and B. K. Witten. Carbon monoxide and physical work capacity. *Arch. Environ. Health* 24: 198–203, 1972.
21. Winer, B. J. *Statistical Principles in Experimental Design.* New York: McGraw, 1962, p. 309.

Downloaded from http://jap.physiology.org/ by 10.220.33.2 on January 16, 2017