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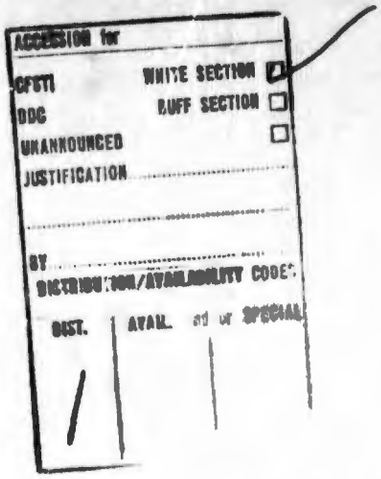

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FOREWORD

This study was accomplished in the Environmental Systems Branch under task No. 793002 and NASA Defense PR T-63615(G). The work was done between 18 July and 24 September 1967. The revised paper was submitted for publication on 4 October 1968.

The Biometrics Division carried out analysis of variance on the data presented. The authors are deeply indebted to the personnel of the Environmental Systems Branch and the participating subjects for their dedicated support of this study. They were informed volunteers as required in all our research (USAFSAM Regulation 80-2).

This report has been reviewed and is approved.

GEORGE E. SCHAFER
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Commander

ABSTRACT

Trained volunteers performed steady-state moderate exercise (one-half of maximum $\dot{V}O_2$) and heavy exercise (two-thirds of maximum $\dot{V}O_2$) in 0, 8, 15, 21, and 30 mm. Hg $P_{I_{CO_2}}$ for 30 minutes on a bicycle ergometer. At CO_2 levels of 8 and 15 mm. Hg, no difficulty was encountered by the subjects. The higher levels of hypercapnia caused some respiratory symptoms of "air-hunger" and intercostal muscle pain, but were of mild enough degree to permit all subjects to complete the exercise. Incremental exercise up to workloads producing maximum $\dot{V}O_2$ was also performed. The tolerance at maximum exercise in 21 mm. Hg $P_{I_{CO_2}}$ resembled that at two-thirds workload in 30 mm. Hg $P_{I_{CO_2}}$. $\dot{V}_E$ during maximum exercise did not vary with the level of inspired CO_2, whereas at submaximal workloads, $\dot{V}_E$ increased as $P_{I_{CO_2}}$ increased. At two-thirds and maximum workloads, $\dot{V}CO_2$ during exercise fell progressively with increasing $P_{I_{CO_2}}$. The ineffective CO_2 removal is explained by the decreased alveolar-inspired CO_2 gradient with increasing $P_{I_{CO_2}}$. Inadequate elimination of CO_2 caused respiratory acidosis to be superimposed on the metabolic acidosis normally present during exercise.

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I. INTRODUCTION

Space and undersea exploration have placed man in sealed environmental situations which require highly efficient gaseous control systems. With the ever-present possibility of malfunction of the system for CO_2 removal, it is imperative to know the extent of man's tolerance and adaptability to increased concentrations of this waste product of metabolism. Considerable effort has been directed to the study of physiologic adjustments of resting man to acute and chronic exposure to increased CO_2 levels (5, 13, 14, 25, 26, 32, 33), and a concept of maximum limits is emerging. Little knowledge has been acquired. however, regarding the interplay of hypercapnia and active or exercising man. The few previous studies which have been directed at the impact of the simultaneous stresses of exercise and hypercapnia have focused upon expired gas volumes (2, 8, 16). Schaefer (25) studied the effects of low levels of exercise in 3% CO_2, acutely and chronically, while Hickman et al. (16) exercised untrained subjects in 5% CO_2. Oxygen and carbon dioxide transport along with blood gas data during hypercapnia and exercise have not been given due emphasis. Dripps and Comroe (9) compared the cardiovascular responses in high CO_2 levels of 7.6% and 10.4% and in heavy exercise, but did not study the effect of combined stress. The following experiment was designed to evaluate man's responses to steady-state and exhaustive exercise programs in 0, 8, 15, 21, and 30 mm. Hg inspired carbon dioxide ($P_{I_{CO_2}}$).[1]

[1] $P_{I_{CO_2}} = (P_B - 47) F_{I_{CO_2}}$

II. METHODS

Eight United States Air Force airmen having just completed basic training served as volunteer subjects for this experiment. They ranged in age between 18 and 21 years and were determined to be in excellent physical condition.

A 3.6 x 3.6 x 2.4 m. environmental room equipped with a control system for inspired O_2 ($P_{I_{O_2}}$), $P_{I_{CO_2}}$, and temperature was utilized. Oxygen and carbon dioxide were continuously monitored with a Beckman model F-3 paramagnetic analyzer and a Beckman LB-1 infrared analyzer, respectively. Both analyzers were calibrated with gases which had been cross-checked for accuracy by Scholander and gas chromatographic technics. Barometric pressure was monitored by a Wallace and Tiernan absolute pressure gage and water vapor was measured by a Cambridge dew point hygrometer. A standard window air-conditioner was used for temperature control.

The desired atmospheric composition was established early each morning and maintained throughout the day or changed to a second CO_2 level after the morning experiments. Approximately one hour was required for the stabilization of a new atmosphere. Subjects and investigators entered the environmental room through a 1.0 x 1.5 x 2.4 m. transfer lock which prevented disturbance of the internal environment.

In table I, the data show the mean resting (time 0) and exercise (time 30 minutes), O_2 and CO_2 inspired concentrations for all exercise

TABLE I

Atmospheric conditions

		Carbon dioxide levels (mm. Hg)				
		0	8	15	21	30
		$P_{I_{O_2}}$ (mm. Hg)				
	Rest	142	145	144	137	133
A	Exercise	139	145	143	136	133
	P	<.001	N.S.	N.S.	N.S.	N.S.
		$P_{I_{CO_2}}$ (mm. Hg)				
	Rest	.89	8.2	15.1	20.9	30.2
B	Exercise	2.5	8.3	15.0	20.9	30.0
	P	<.001	N.S.	N.S.	N.S.	N.S.

A—O_2 tensions were significantly different at only the 0 mm. Hg P_{ICO_2} level between the rest and exercise states.

B—CO_2 tensions were significantly different at only the 0 mm. Hg P_{ICO_2} level between rest and exercise.

N.S.—$P > .05$.

tests in the study. There was a significant difference in the chamber O_2 and CO_2 atmosphere only for the 0 mm. Hg $P_{I_{CO_2}}$ studies. This was due to the slow progressive rise in CO_2 and fall in O_2 produced by the breathing of five people in a closed environmental room. Analysis was also done comparing the atmospheres for the different exercise levels tested and revealed no significant difference. The $P_{I_{O_2}}$ was reduced at the higher CO_2 levels to prevent the full increase in alveolar O_2 tension that would be associated with the hypercapnic hyperventilation. Room temperature was held at 68° to 72° C. and the relative humidity ranged between 65% and 85%.

Experimental profile

Upon completion of the preliminary medical evaluation studies, the subjects began a 14-day exercise training program using a Collins bicycle ergometer. The workload was progressively increased each day during the training period starting at 50 w. at 60 r.p.m. for 30 minutes twice daily. By the end of their training, they were pedaling at 250 w., a workload which exceeded that in all the steady-state studies. Following completion of the training period, each subject performed maximum exertion tests on the ergometer. These tests consisted of a stepwise increase in workload of 10 w. every 3 minutes starting at 120 w. and maintenance of a constant pedal speed of 60 r.p.m. Heart rate, respiratory rate, and expired air collections were taken at various workloads to determine the maximum oxygen uptake ($\dot{V}O_2$). Watt load/$\dot{V}O_2$ curves were then constructed for each subject. To insure the attainment of exhaustion and maximum $\dot{V}O_2$, each man performed two or three tests and the highest $\dot{V}O_2$ obtained was used. Once the curves were established, workloads in watts were selected for each man which would yield one-half and two-thirds their maximum $\dot{V}O_2$. The steady-state exercise experiments in CO_2 were then performed at these empirical workloads. The mean workloads for all 8 subjects for the one-half and two-thirds levels[2] averaged 130 w. ($\approx$ 800 kgm./min.) and 180 w. ($\approx$ 1,100 kgm./min.), respectively. The one-half work level was associated with a mean heart rate of 128 beats/minute while the two-thirds load produced an average heart rate of 168 beats/minute

[2]The terms one-half and two-thirds work levels or states used throughout this text refer to that exercise in which one-half and two-thirds of maximum $\dot{V}O_2$ was obtained on the pre-experimental maximum exertion test.

Steady-state exercise

The one-half maximum $\dot{V}O_2$ runs were conducted in 0 (air), 8, 15, and 21 mm. Hg $P_{I_{CO_2}}$ while the two-thirds maximum $\dot{V}O_2$ tests were carried out in the same atmospheres plus 30 mm. Hg $P_{I_{CO_2}}$ (see table II). Each subject performed only one steady-state run on a given day. Note that 6 of 8 and 7 of 8 subjects performed in the one-half and two-thirds studies, respectively. The experimental protocol was the same for all exercise experiments. The subject, in the postabsorptive state, and investigators entered the environmental room together via the transfer lock system. While sitting quietly on the bicycle ergometer, the subject was immediately integrated with the recording system including a modified lead II ECG, rectal temperature, and ventilatory measurement apparatus. ECG electrodes and rectal probe were placed on the subjects before they entered the environmental facility. Three-minute expired air samples were collected in plastic 100-liter Douglas bags using a Collins Triple "J" low resistance valve (< 2 cm. H_2O at 200 liters/min.), wide bore tubing (1½ in. I.D.), and a dual-bag collection system. All bags were flushed for 30 seconds with the subjects' expired air prior to sample collection. Glass syringes (100 cc.) lubricated with lithium chloride were used to collect duplicate air samples from each Douglas bag. These samples were measured for expired O_2 and CO_2 content using the E-2 and LB-1 gas analyzers, respectively, and the results were corrected for water vapor. Air volumes were measured using a 120-liter Tissot spirometer. Using the values for expired minute volume, $F_{E_{CO_2}}$ and $F_{E_{O_2}}$, the $F_{E_{N_2}}$, inspired minute volume ($\dot{V}I$), $\dot{V}O_2$, and $\dot{V}CO_2$ were calculated and the latter two corrected to STPD. Respiratory rate was measured by a thermistor positioned in the expiratory circuit of the breathing apparatus with readout on a Beckman oscillograph. Rectal temperature was recorded on a United Systems Corporation digital thermometer.

Approximately 10 minutes after the subject entered the chamber, a resting arterial blood sample was obtained by a percutaneous brachial arterial puncture with a 19-gage needle. The sample was collected in a 10 cc. heparinized glass syringe. Five minutes later, resting cardiopulmonary measurements were recorded. The exercise program was started immediately following these procedures and the workload was increased to the predetermined level within the first 45 seconds. The subject exercised at this workload for the next 30 minutes. No recovery measurements were made.

Respiratory and cardiac rates, blood pressure, and body temperature were recorded every 5 minutes during exercise, and expired air collections were made at the 7- to 10- and 27- to 30-minute periods. A second arterial

TABLE II

Experimental profile

$P_{I_{CO_2}}$ (mm. Hg)	Work level		
	180 w. 800 kgm./min.	180 w. 1,100 kgm./min.	330 w. 2,000 kgm./min.
0	½ max.	⅔ max.	Max.
8	½ max.	⅔ max.	Max.
15	½ max.	⅔ max.	—
21	½ max.	⅔ max.	Max.
30	—	⅔ max.	—
Number of subjects	6/8	7/8	8/8

sample was obtained during the 26th and 27th minute of exercise. Blood gas data were obtained for the two-thirds maximum $\dot{V}O_2$ experiments only. No significant differences were observed for $\dot{V}E$, $\dot{V}O_2$, $\dot{V}CO_2$, and HR between the 10th minute and 30th minute of exercise, indicating that a steady state had been achieved. Therefore, only the data collected during the 27- to 30-minute period of steady-state exercise were tested. In all cases, nonsignificance (N.S.) is indicated when $P > .05$.

Arterial oxygen tension (PaO_2) and carbon dioxide tension ($PaCO_2$) were measured at 35.6° C. using Instrumentation Laboratories ultra-microelectrodes (model 113), while pH was measured with the Radiometer AME-1. All results were corrected to body temperature using the revised correction factors of Nunn (21) and Severinghaus (28). Bicarbonates were calculated using the Henderson-Hasselbalch equation assuming a pK of 6.10 and solubility coefficient of 0.03 for carbon dioxide. The performance of one-half and two-thirds exercise workloads at different inspired PCO_2 levels was randomized for all subjects in order to prevent adaptation and training effects.

Maximum exercise tests

After completion of all phases of the steady-state exercise study, all 8 subjects also participated in maximum exertion tests in 0 (air) and in 8 and 21 mm. Hg PCO_2 to determine the effect of hypercapnia on maximum work performance.[3] The profile of these maximum runs involved a stepwise increase until exhaustion, of 15 w. each minute, starting at 50 w. while maintaining a steady pedal speed of 60 r.p.m. Heart rate, respiratory rate, and expired air collections for volume, $\dot{V}CO_2$ and $\dot{V}O_2$, were the only measurements obtained during these studies. The preliminary procedures for chamber entry and equipment-subject integration were the same as for the steady-state experiments. Expired air was measured over a 45-second period after 15 seconds of adjustment to each step-up in watt load. Collections occurred at rest, 95 w., 125 w., 155 w., and at workloads near maximum $\dot{V}O_2$.

[3]Maximum work performance was judged by total exhaustion and in all cases was associated with plateauing of the heart rate greater than 190 beats per minute.

III. RESULTS

General observations

The subjects completed all 30-minute steady-state and maximum exercise runs at all workloads and CO_2 levels tested. No difficulty was noticed by the subjects exercising at any of the work levels below 21 mm. Hg PI_{CO_2}. However, at the 21 mm. level and above, there were noticeable subjective respiratory symptoms during exercise at two-thirds maximum and maximum $\dot{V}O_2$, and the subjects were well aware of their increased ventilation (table III).

Intercostal muscle pain resulting from the very large ventilations (approximately 140 liters/min.) occurred in 2 of 8 subjects during the maximum exercise runs in 21 mm. Hg PI_{CO_2}. These subjects felt this chest pain to be the limiting factor to continuing the exercise step-up. Three other subjects felt that respiratory exhaustion, rather than muscle fatigue, had definitely limited their performance.

At 30 mm. Hg PI_{CO_2}, 6 of the 7 subjects experienced mild to moderate frontal headaches. These varied considerably in onset and

TABLE III

General observations

PI_{CO_2} (mm. Hg)	Workloads		
	½ max.	⅔ max.	Max.
0	0	0	0
8	0	0	0
15	0	0	--
21	1	1	1, 2, 3
30	—	1, 3, 4	—

Legend: 0—No awareness or symptoms.
1—Awareness of CO_2.
2—Intercostal muscle pain.
3—"Air Hunger."
4—Headache.

duration, occurring usually in the final minutes of the exercise run and disappearing within one hour after exposure.

Ectopic foci on the precordial ECG's were seen in 4 of 8 subjects on nine different occasions. In all cases but one (a premature atrial contraction), these foci originated from below the A-V node. These premature ventricular contractions (PVC's) varied in frequency from three per minute to a trigeminy rhythm alternating with two sinus beats. The occurrence of PVC's was not related to the level of exercise or the inspired CO_2 environment. In no case were the subjects aware of these ECG changes, nor did they complain of cardiovascular symptoms.

Steady-state studies

Ventilation. For any given inspired CO_2 tension, the average $\dot{V}_E$ was greater for the two-thirds exercise level than for the one-half level. The results in table IV show that at rest, the exercise one-half or two-thirds level, $\dot{V}_E$ increased significantly with $P_{I_{CO_2}}$ elevation. However, this rise was of a smaller magnitude than the increase in $\dot{V}_E$ which accompanies the change in exercise state. The rise in $\dot{V}_E$ with different exercise loads was brought about by increases in both respiratory rate and tidal volume (V_T), while the rise related to $P_{I_{CO_2}}$ reflects chiefly tidal volume changes. The rest values in table IV belong to the two-thirds exercise level.

$\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, R. At the one-half and two-thirds exercise levels, the $\dot{V}_{O_2}$ did not vary significantly with the CO_2 atmosphere (table V). $\dot{V}_{CO_2}$ decreased significantly from 2.43 liters/min. (STPD) to 1.84 liters/min. over the 0 and 30 mm. Hg $P_{I_{CO_2}}$ range in the two-thirds run (table IV). The one-half exercise study did not show a significant drop in $\dot{V}_{CO_2}$; however, this may be true only because this work level was not performed in 30 mm. Hg $P_{I_{CO_2}}$. Paralleling the $\dot{V}_{CO_2}$ results, the respiratory quotient (R) fell from 0.94 to 0.72 at the one-half exercise level.

Pulse rates and rectal temperature. Resting and exercise pulse rates at both the two work levels did not change with $P_{I_{CO_2}}$. Rectal temperature also shows no variation. However, both parameters did increase at the higher work level.

Acid-base changes. Blood gas data were recorded only for the 30-minute two-thirds exercise runs (table VI). The delta values refer to changes between the exercise and resting measurements at each $P_{I_{CO_2}}$ level. The mean resting P_{aO_2} ranged from 95 mm. Hg in 0 $P_{I_{CO_2}}$ to 115 mm. Hg in 30 mm. Hg $P_{I_{CO_2}}$. The latter was the result of hyperventilation induced by CO_2 and explains why, in all cases, the mean blood oxygen tension remained greater than 93 mm. Hg during exercise. The lowest calculated oxygen saturation was 95%. Arterial P_{CO_2} increased during exercise from the resting value in the 15, 21, and 30 mm. Hg $P_{I_{CO_2}}$ environments. Analysis of variance shows a linear increase of the ΔP_{aCO_2} with high $P_{I_{CO_2}}$ levels. At all CO_2 levels the pH fell during exercise, with the magnitude of the change linear with increasing $P_{I_{CO_2}}$. Calculated bicarbonate declined during exercise in all $P_{I_{CO_2}}$ atmospheres, but the mean values were not proportional to the level of $P_{I_{CO_2}}$.

Maximum exercise runs

During maximum exercise at various $P_{I_{CO_2}}$ levels only $\dot{V}_{CO_2}$ and R changed significantly (see table VII). These two parameters decreased in a manner similar to the 30-minute steady-state two-thirds work run. The $\dot{V}_E$ during maximum $\dot{V}_{O_2}$ did not change with increasing $P_{I_{CO_2}}$. This is in marked contrast to the $\dot{V}_E$ at 155 w. ($\sim$ one-half $\dot{V}_{O_2}$) which was 19.7 liters higher in 21 mm. Hg $P_{I_{CO_2}}$ than in air (see table VIII). On the average, the duration of the maximum study in 21 mm. Hg $P_{I_{CO_2}}$ was 1 minute shorter and the total workload 120 kgm. (20 w.) less than in 0 mm. Hg $P_{I_{CO_2}}$ although statistically this was not found to be significant.

IV. DISCUSSION

Headaches have occurred in acute and chronic hypercapnia studies with varying frequency, depending on the level of $P_{I_{CO_2}}$ (5, 25,

TABLE IV

Ventilation volumes

Subject	P_{ICO_2} (mm. Hg)	$\dot{V}_E$ (liters/min. BTPS)			V_T (liters/min. BTPS)			Respiratory rate		
		Rest	½ max.	⅔ max.	Rest	½ max.	⅔ max.	Rest	½ max.	⅔ max.
130		14.3	64.0	78.8	0.841	2.133	2.627	17	30	30
131		9.4	58.5	73.0	0.448	1.773	1.738	21	33	42
132		12.1	69.1	80.0	0.864	1.772	2.051	14	39	39
133	0	10.5	59.7	86.2	0.750	2.488	2.394	14	24	36
134		9.1	47.6	65.2	0.506	1.983	2.103	18	24	31
135		7.0	43.5	70.4	0.538	2.071	2.933	13	21	24
136		7.0	—	75.0	0.368	—	2.206	19	—	34
$\bar{X}$		9.9	57.1	75.5	0.616	2.037	2.293	16.6	27.6	33.7
130		11.0	59.7	89.6	0.579	1.990	2.715	19	30	33
131		12.7	—	70.3	0.635	—	2.130	20	—	33
132		10.0	57.1	79.0	0.588	1.370	2.194	17	33	36
133	8	11.2	60.6	83.8	0.589	2.020	2.149	19	30	39
134		13.6	62.3	75.5	0.800	1.597	1.936	17	39	39
135		10.0	55.4	62.3	0.714	2.052	2.596	14	27	24
136		11.2	—	90.0	0.560	—	1.875	20	—	48
$\bar{X}$		11.4	59.5*	78.6	0.652	1.878*	2.228	18.0	31.8*	36.0
130		15.5	73.5	87.6	0.738	2.722	2.654	21	27	33
131		17.1	66.9	84.5	1.006	2.027	2.224	17	33	38
132		13.9	60.3	84.3	0.772	1.546	2.479	18	39	34
133	15	11.8	78.0	73.9	0.694	1.857	2.111	17	42	35
134		11.6	74.5	70.5	0.644	2.069	1.808	18	36	39
135		10.7	51.4	67.8	0.823	2.142	2.608	13	24	26
136		15.1	—	95.8	0.755	—	2.129	20	—	45
$\bar{X}$		13.7	67.4	80.6	0.776	2.061	2.288	17.7	33.6	35.7
130		12.4	84.6	99.1	0.590	2.563	3.003	21	33	33
131		15.5	78.0	75.3	0.775	2.600	2.282	20	30	33
132		12.5	72.7	85.1	0.694	2.203	2.025	18	33	42
133	21	12.5	85.7	92.6	0.781	2.381	2.572	16	36	36
134		12.5	67.0	92.2	1.250	2.233	2.364	10	30	39
135		14.0	46.0	83.1	1.077	1.917	3.613	13	24	23
136		10.0	—	80.7	0.476	—	1.793	21	—	45
$\bar{X}$		12.8	72.3	86.9	0.806	2.316	2.522	17.0	31.6	35.9
130		21.5	—	90.5	0.896	—	2.514	24	—	36
131		24.1	—	85.5	1.418	—	2.375	17	—	36
132		24.5	—	107.2	1.114	—	2.749	22	—	39
133	30	23.4	—	109.5	1.300	—	2.808	18	—	39
134		25.0	—	100.8	1.389	—	2.400	18	—	42
135		24.3	—	104.3	1.620	—	3.477	15	—	30
136		26.4	—	126.1	1.056	—	2.473	25	—	51
$\bar{X}$		24.2	—	103.4	1.256	—	2.685	19.9	—	39.0
P		<.001	<.025	<.001	<.001	N. S.	<.025	N. S.	N. S.	N. S.
Number of subjects		7	6	7	7	6	7	7	6	7

*These means are based on statistical estimates for subject 131.

P—Significance of variation with P_{ICO_2} (analysis of variance).

N.S.—$P > .05$

TABLE V

Oxygen and carbon dioxide exchange

Subject	$P_{I_{CO_2}}$ (mm. Hg)	$\dot{V}_{O_2}$ (liters/min. STPD)		$\dot{V}_{CO_2}$ (liters/min. STPD)		Respiratory exchange ratio	
		½ max.	⅔ max.	½ max.	⅔ max.	½ max.	⅔ max.
130		1.965	2.516	1.723	2.707	.88	1.08
131		2.087	2.579	1.849	2.454	.89	.95
132		2.087	2.462	1.736	2.270	.83	.92
133	0	2.186	2.522	2.039	2.438	.93	.97
134		1.740	2.594	1.613	2.413	.93	.93
135		2.045	2.825	1.625	2.669	.79	.94
136		—	2.466	—	2.060	—	.84
$\bar{X}$		2.005	2.566	1.747	2.430	.87	.94
130		1.835	2.871	1.574	2.402	.86	.84
131		—	2.517	—	2.164	—	.86
132		1.984	2.495	1.533	2.185	.77	.88
133	8	2.034	2.470	1.913	2.485	.94	1.00
134		1.934	2.377	1.647	2.335	.85	.98
135		2.049	2.151	1.931	2.155	.94	1.00
136		—	2.448	—	2.209	—	.90
$\bar{X}$		1.967*	2.476	1.720*	2.276	.87*	.92
130		2.082	2.287	1.848	1.943	.89	.85
131		1.981	2.920	1.770	2.689	.89	.92
132		2.053	2.566	1.708	1.634	.83	.63
133	15	2.140	2.145	1.996	2.054	.93	.96
134		2.460	2.356	2.551	2.022	1.04	.86
135		1.920	2.410	1.803	2.121	.94	.88
136		—	2.242	—	1.933	—	.86
$\bar{X}$		2.131	2.418	1.981	2.057	.92	.85
130		1.905	2.574	1.705	2.161	.90	.84
131		1.991	2.653	1.884	1.906	.95	.72
132		1.851	2.543	1.431	2.243	.77	.88
133	21	2.126	2.745	[illegible]928	2.378	.77	.87
134		2.096	2.710	1.857	2.142	.89	.79
135		1.579	2.616	1.420	2.050	.90	.78
136		—	2.266	—	1.950	—	.86
$\bar{X}$		1.914	2.587	1.608	2.119	.84	.82
130		—	2.228	—	1.668	—	.75
131		—	2.486	—	1.785	—	.72
132		—	2.615	—	1.812	—	.69
133	80	—	2.423	—	1.827	—	.75
134		—	2.675	—	1.929	—	.72
135		—	2.839	—	2.068	—	.73
136		—	2.636	—	1.799	—	.68
$\bar{X}$		—	2.557	—	1.941	—	.72
P		N. S.	N. S.	N. S.	<.001	N. S.	<.001

*These means are based on statistical estimates for subject 131.

P—Significance of variation with $P_{I_{CO_2}}$ (analysis of variance).

N.S.—$P > .05$.

TABLE VI

Mean rest-exercise blood gas changes

Subject	$P_{I_{CO_2}}$	P_{O_2}(R)	P_{O_2}(E)	ΔP_{O_2}	P_{CO_2}(R)	P_{CO_2}(E)	ΔP_{CO_2}	pH(R)	pH(E)	ΔpH	Calculated HCO_3(R) (mEq/liter)	Calculated HCO_3(E) (mEq/liter)	ΔHCO_3 (mEq/liter)
		(mm. Hg)											
130		93.1	94.6	+1.5	38.5	35.4	−3.1	7.388	7.324	−.064	22.5	17.8	−4.7
131		88.4	84.8	−3.6	51.9	45.9	−6.0	7.398	7.344	−.054	31.0	24.2	−6.8
132		98.7	96.2	−2.5	37.5	37.4	−0.1	7.399	7.356	−.033	22.5	20.3	−2.2
133	4	108.8	94.3	−14.5	34.5	36.9	+2.4	7.385	7.310	−.075	20.0	18.0	−2.0
134		97.2	99.8	+2.6	36.8	37.8	+1.0	7.385	7.390	+.005	21.3	22.2	+1.9
135		86.4	95.9	+9.5	42.7	39.5	−3.2	7.373	7.341	−.032	24.1	20.7	−3.4
136		91.8	90.6	−1.2	38.3	39.6	+1.3	7.397	7.311	−.086	22.8	19.4	−3.4
$\bar{X}$		94.9	93.7	−1.2	40.0	38.9	−1.1	7.389	7.339	−.048	23.5	20.4	−2.9
S.D.		7.5	4.8	7.3	5.8	3.4	3.1	0.01	0.028	−.031	3.6	2.3	2.7
P'			N. S.			N. S.			P<.01				
130		108.7	110.4	+1.7	40.3	37.4	−2.9	7.378	7.270	−.106	23.0	16.6	−6.4
131		98.6	100.8	+2.2	40.2	39.5	−0.7	7.389	7.341	−.045	23.5	20.7	−2.8
132		105.6	104.2	−1.4	38.6	44.3	+5.7	7.401	7.319	−.082	23.2	22.1	−1.1
133	8	98.4	101.5	+3.1	42.7	43.7	+1.0	7.374	7.339	−.035	24.2	22.8	−1.4
134		103.1	98.0	−5.1	37.9	44.2	+6.3	7.371	7.320	−.051	21.3	22.1	+0.8
135		98.3	99.5	+1.2	42.3	39.7	−2.6	7.360	7.322	−.038	23.2	19.9	−3.3
136		103.1	114.7	+11.6	40.2	36.7	−3.5	7.392	7.359	−.033	23.7	20.1	−3.6
$\bar{X}$		102.3	104.2	+1.9	40.3	40.5	+0.47	7.381	7.324	−.056	23.2	20.6	−2.5
S.D.		4.0	6.2	5.1	1.8	3.3	4.1	0.01	0.028	.028	0.9	2.0	2.3
P'			N. S.			N. S.			P<.01				
130		116.7	118.9	+2.2	47.1	47.2	+0.1	7.347	7.326	−.021	25.0	23.9	−1.1
131		96.5	84.2	−12.3	41.3	52.0	+10.7	7.371	7.263	−.108	23.2	22.8	−0.4
132		102.9	99.4	−3.5	37.3	45.1	+7.8	7.348	7.277	−.071	19.9	20.4	+0.5
133	15	107.8	103.6	−4.2	46.3	49.4	+3.1	7.348	7.301	−.047	24.7	23.6	−1.1
134		109.7	104.2	−5.5	43.5	50.0	+6.5	7.367	7.316	−.051	24.2	24.7	+0.5
135		116.3	110.5	−5.8	46.7	50.2	+3.5	7.360	7.320	−.040	25.6	25.1	−0.5
136		116.7	101.9	−14.8	40.6	40.5	−0.1	7.406	7.318	−.088	24.7	20.1	−4.6
$\bar{X}$		109.5	103.2	−6.3	43.3	47.8	+4.5	7.364	7.303	−.061	23.9	22.9	−1.0
S.D.		7.8	10.6	5.7	3.7	3.9	4.0	0.02	0.024	.030	1.9	2.0	1.7
P'			.05>P>.02			.05>P>.02			P<.01				

TABLE VI (contd.)

Subject	$P_{I_{CO_2}}$	P_{O_2}(R)	P_{O_2}(E)	ΔP_{O_2}	P_{CO_2}(R)	P_{CO_2}(E)	ΔP_{CO_2}	pH(R)	pH(E)	ΔpH	Calculated HCO_3(R) (mEq/liter)	Calculated HCO_3(E) (mEq/liter)	ΔHCO_3 (mEq/liter)
		(mm. Hg)											
130		110.2	105.2	−5.0	42.8	48.6	+5.8	7.375	7.266	−.109	24.3	21.4	−2.9
131		105.4	95.6	−9.8	45.2	55.3	+10.1	7.382	7.278	−.104	26.0	25.1	−0.9
132		108.0	97.3	−10.7	41.2	51.1	+9.9	7.384	7.250	−.134	23.8	21.7	−2.1
133	21	113.1	103.0	−10.1	39.4	49.7	+10.3	7.367	7.308	−.059	21.9	24.2	+2.3
134		112.2	101.5	−10.7	41.9	53.8	+11.9	7.371	7.279	−.092	23.8	24.4	+0.6
135		111.3	102.6	−8.7	45.4	52.4	+7.0	7.367	7.286	−.081	25.6	24.4	−1.2
136		117.9	106.4	−11.5	44.3	49.3	+5.0	7.387	7.285	−.102	25.8	22.7	−3.1
X		111.2*	101.7*	−9.5*	42.9*	51.5*	+8.6*	7.376*	7.279*	−.097*	24.4*	23.4*	−1.0*
S.D.		4.0	3.9	2.2	2.2	2.5	2.6	0.01	0.01	.023	1.7	1.6	2.0
P′			P<.01			P<.01			P<.01				
130		110.2	104.9	−5.3	46.4	57.2	+10.8	7.388	7.249	−.089	24.2	24.3	+0.1
131		106.6	95.6	−11.0	47.3	57.0	+9.7	7.364	7.291	−.073	26.1	26.6	+0.5
132		113.3	107.4	−5.9	45.2	54.3	+9.1	7.337	7.222	−.115	23.5	21.6	−1.9
133	30	118.2	104.4	−13.8	45.0	59.0	+14.0	7.353	7.262	−.091	24.2	25.8	+1.6
134		115.7	104.6	−11.1	47.3	61.6	+14.3	7.346	7.179	−.167	25.1	22.2	−2.9
135		120.8	104.9	−15.9	47.8	58.4	+10.6	7.359	7.249	−.100	26.1	24.8	−1.3
136		117.8	119.7	+1.9	42.9	48.7	+5.8	7.390	7.210	−.180	25.2	18.9	−6.3
X		114.7	105.9	−8.7	46.0	56.6	+10.6	7.355	7.237	−.116	24.9	23.5	−1.5
S.D.		5.0	7.1	6.1	1.7	4.1	2.9	0.02	0.037	.041	1.0	2.7	2.6
P′			P<.01			P<.01			P<.01				
P″		<.001	<.01	<.01	<.025	<.001	<.001	<.001	<.001	<.005			

*Mean based on estimated values for subject 134 and subject 135.

P′—Significance of rest-exercise change (paired observation t-test).

P″—Significance of variation with $P_{I_{CO_2}}$ (analysis of variance).

N.S.—P > .05

TABLE VII

Maximum exercise runs

Subject	$P_{I_{CO_2}}$ (mm. Hg)	Workload (kgm./min.)	$\dot{V}_E$	Resp. rate	Pulse rate	Max. $\dot{V}O_2$	$\dot{V}CO_2$	R	Metabolic rate (kcal./hr.)
130		2,233	143.9	48	192	3.627	3.604	.99	1,088
131		1,957	90.3	45	192	2.917	3.432	1.25	875
132		1,957	143.8	54	189	3.593	3.419	.95	1,078
133	0	1,866	144.8	51	198	3.374	3.811	1.13	1,012
134		2,141	147.5	51	180	3.567	4.241	1.19	1,070
135		2,416	163.0	51	201	4.396	4.688	1.07	1,319
136		2,019	152.5	65	195	3.486	3.765	1.08	1,046
137		1,866	110.9	33	195	3.358	3.775	1.12	1,007
$\bar{X}$		2,057	137.1	49.7	192.7	3.540	3.841	1.09	1,062
130		2,141	159.3	48	192	3.422	3.675	1.07	1,027
131		2,141	117.5	36	195	4.103	4.368	1.06	1,231
132		2,141	140.0	51	189	3.330	3.632	1.09	999
133	8	1,866	134.2	48	204	3.503	3.738	1.07	1,051
134		1,866	136.8	48	173	3.680	3.928	1.07	1,104
135		2,233	152.6	48	204	4.266	4.139	.97	1,280
136		1,957	156.3	60	195	3.207	3.541	1.10	962
137		1,988	133.9	42	195	3.689	3.643	.99	1,107
$\bar{X}$		2,042	141.3	47.6	193.6	3.650	3.834	1.05	1,095
130		2,049	169.1	48	192	3.436	3.308	.96	1,031
131		2,049	119.6	36	192	3.451	3,583	1.04	1,035
132		1,957	144.7	51	192	3.511	3.368	.96	1,053
133	21	2,049	146.8	45	195	3.440	3.380	.98	1,032
134		1,682	125.9	54	177	3.123	3.073	.98	937
135		2,141	156.0	48	192	3.807	3.589	.94	1,142
136		1,774	149.1	60	195	3.186	3.448	1.08	956
137		1,774	117.4	36	192	3.047	2.882	.95	914
$\bar{X}$		1,934	141.1	47.2	190.9	3.375	3.329	.99	1,013
P		N. S.	N. S.	N. S.	N. S.	N. S.	<.005	<.025	
Number of subjects		8	8	8	8	8	8	8	

P—Significance of variation with $P_{I_{CO_2}}$ (analysis of variance).

N.S.—$P > .05$

26, 32). Glatte (13) reported occurrence in 4 of 7 subjects exposed to 21 mm. Hg $P_{I_{CO_2}}$ for 5 days and in 6 out of 7 subjects exposed to a 30 mm. Hg $P_{I_{CO_2}}$ environment for the same period. These occurred in the first 24 hours of exposure and disappeared by the second day in CO_2. The headaches were of a throbbing nature, aggravated by the recumbent position and the Valsalva maneuver and were probably due to cerebral vascular dilation. Measurements of cerebral vascular dynamics during hypercapnia by others support this concept. Patterson et al. (23) found a significant decrease in cerebral vascular resistance and a 10% increase in cerebral blood flow in subjects breathing $P_{I_{CO_2}}$ of 24.5 mm. Hg. In the present study, the added factor of exercise and sudden (rather than gradual) exposure to CO_2

TABLE VIII

Submaximum and maximum $\dot{V}_E$ comparison during maximum exercise testing

Subject	½ max. $\dot{V}o_2$		Max. $\dot{V}o_2$	
	0	21	0	21
130	51.1	89.4	143.9	169.1
131	23.4	60.4	90.3	119.6
132	54.0*	83.0	143.8	144.7
133	57.4	62.0*	144.8	146.8
134	47.4	58.2	147.5	125.9
135	46.6	50.5	163.0	156.0
136	58.9	72.3	152.5	149.1
137	35.9	56.4	110.9	117.4
$\bar{X}$	46.8	66.5	137.1	141.1
S.D.	11.9	18.7	24.0	18.4
P	<.01		N. S.	

*Estimated values from subjects $\dot{V}_E$/watt load curve.

P—Significance of rest-exercise change (paired observation t-test).

N.S.—$P > .05$

may have modified the headache pattern. No associated prodromata of the migraine symptom complex were present. The headaches occurred at the 30 mm. Hg P_{ICO_2} level only, but they did not appear or disappear in any pattern. In no case were they severe enough to interfere with the subjects' performance of exercise.

Premature ventricular contractions are the most common ECG arrhythmia and are a frequent finding in normal men during exercise. The incidence at the USAF School of Aerospace Medicine among apparently healthy pilots during maximum treadmill testing is over 30%. PVC's have not been reported during human hypercapnia studies in resting man with the P_{ICO_2} below 35 mm. Hg (13, 26). Horwitz et al. (18) exposing nonanesthetized dogs to 42 mm. Hg P_{ICO_2} and Brackett et al. (5) exposing humans to 71 mm. Hg P_{ICO_2} for 15 to 25 minutes showed no ECG changes. Sechzer et al. (27) did find four incidents of PVC's with $Paco_2$ over 50 mm. Hg $Paco_2$ in 27 exposures (27). These occurred in 53, 75, 86, and 101 mm. Hg $Paco_2$. Others have reported PVC's too, but these occurred in patients with $Paco_2 \sim 100$ mm. Hg, although the actual level was not measured (24). These, however, were in resting-state studies; therefore, the significance of the findings in this present exercise study is unclear. One subject contributed to five of the nine incidents of ectopic foci, probably representing an individual unusually prone to exercise arrhythmia. If elevated CO_2 was playing a factor in the ECG changes, these ectopic beats should have occurred with greatest frequency at the highest level ($P_{ICO_2} = 30$ mm. Hg). This trend did not occur.

In contrast to the benign nature of the ECG changes and headaches seen with exercise and hypercapnia, ventilation limitations may have altered the work capacity of the subjects and led to physiologic abnormalities. During maximum work runs when minute ventilation exceeded 130 liters/min. ($\sim$ 70% of maximum voluntary ventilation [MVV]), the subjects experienced intercostal muscle pain and dyspnea only when the P_{ICO_2} was 21 mm. Hg. These symptoms may have led to the slight decrease in exercise time in the 21 mm. Hg P_{ICO_2} atmosphere. Although the same level of ventilation was reached in 0 and 8 mm. Hg P_{ICO_2}, respiratory distress did not occur and generalized fatigue was the determining factor in ending these runs. It appears that the magnitude of the ventilation itself was not the only cause for the subjective feeling of respiratory embarrassment and that the level of P_{ICO_2} played a major role since the steady-state exercise in 30 mm. Hg P_{ICO_2}, when the $\dot{V}_E$ reached only 50% of MVV ($\sim$ 100 liters/min.), was accompanied by complaints of dyspnea on two occasions. In addition, Dripps and Comroe (9) reported the observation that several of their subjects having $\dot{V}_E$ greater than 100 liters/min. insisted that they had no dyspnea.

The significant increase in $\dot{V}_E$ during exercise with hypercapnia was not surprising and has been reported by others (2, 3, 8, 9, 12, 16). $\dot{V}_E$'s ten times resting ambient levels were successfully maintained for the entire 30-minute

exercise period at the two-thirds workload in 30 mm. Hg $P_{I_{CO_2}}$. While the $\dot{V}_E$ level is only 50% of the subjects' MVV, it should be remembered that the MVV test usually is performed over only a 20-second period. Freedman (11) has stated that, after 4 minutes of hyperventilation, the maximum $\dot{V}_E$ is only 61% of the 15-second MVV. In a recent study on MVV during exercise, Shephard (29) reported that, while working at 80% of aerobic work capacity and simultaneously undergoing hypercapnic hyperventilation of 2% CO_2, men attained, on the average, only 80%, 74%, and 75% of MVV in the 5th, 10th, and 15th minute of exercise, respectively. In addition, the mechanics of breathing while exercising on a bicycle have been found to be altered from the normal situation, even if the exercise is carried out in an ambient environment (15). Normally, abdominal muscle excursion (diaphragmatic component) does contribute a small part at end inspiration to increasing one's tidal volume; the major contribution is made by rib-cage expansion. Grimby (15) found that, while exercising on a bicycle, abdominal component at end-inspiration may actually decrease, thereby placing added burden on rib-cage expansion to account solely for the increased V_T of exercise. Dripps and Comroe (9) reported their subjects attained, on the average, only 66% of their MVV while performing strenuous muscular exercise on a stationary bicycle. How these findings are affected by the added stress of hypercapnia is not known, but it appears that some limitation on further tidal volume increases was present in our subjects during the two-thirds exercise level in 30 mm. Hg $P_{I_{CO_2}}$. This limitation may have led to the drop in $\dot{V}_{CO_2}$ observed.

The fall in CO_2 respiratory exchange ($\dot{V}_{CO_2}$) with progressive rise in inspired CO_2 levels caused a rise in CO_2 body stores. Since the respiratory system is the chief organ of CO_2 excretion, this buildup in stores does represent a failure of fully adequate ventilation. It should be understood that the drop in $\dot{V}_{CO_2}$ in the face of rising P_{aCO_2} is not a drop in production by the tissues, but a decrease in the amount which leaves the body. Fall in $\dot{V}_{CO_2}$ with increasing $P_{I_{CO_2}}$ has also been observed by Finkelstein et al. (unpublished data) in exposures of men in 0 and 15 mm. Hg $P_{I_{CO_2}}$. Sinclair et al. (manuscript in preparation) studied dogs exercising on a treadmill in 0, 15, 30, 42, and 56 mm. Hg $P_{I_{CO_2}}$ and found a progressive decrease in $\dot{V}_{CO_2}$ from 40 to 29 cc./kg. body weight. The explanation of why a higher level of ventilation (100 liters/min.) in 30 mm. Hg $P_{I_{CO_2}}$ would be inadequate to prevent body CO_2 buildup while a lower ventilation (75 liters/min.) in air would be fully adequate may be found if the alveolar-inspired gradient for CO_2 is examined. In the ambient atmosphere of 0.03% CO_2, the lungs operate under a 38 to 42 mm. Hg P_{CO_2} alveolar-inspired gradient. $P_{A_{CO_2}}$ is dependent upon the CO_2 production and alveolar ventilation ($\dot{V}_A$) as described by Otis (22):

$$P_{A_{CO_2}} = \frac{.863\ \dot{V}_{CO_2}}{\dot{V}_A} + P_{I_{CO_2}} \qquad (1)$$

A constant $\dot{V}_{CO_2}$ of 250 cc./min. STPD and a $\dot{V}_A$ of 5.5 liters/min. BTPS will maintain the $P_{A_{CO_2}}$ at 40 mm. Hg. The importance of the alveolar-inspired CO_2 gradient is shown in the relationship of Kao et al. (19).

$$(P_{A_{CO_2}} - P_{I_{CO_2}})\dot{V}_E = \dot{V}_{CO_2}(V_T/V_A)\ .863 \qquad (2)$$

Assuming a constant for the tidal volume/alveolar volume ratio (V_T/V_A),[4] the relationship between the gradient and $\dot{V}_E$ is described by an isometabolic hyperbola (19). If a decrease in the gradient is not accompanied by an appropriate increase in $\dot{V}_E$, $\dot{V}_{CO_2}$ will decrease proportionally. During hypercapnic breathing at the 30 mm. Hg $P_{I_{CO_2}}$ levels, the normal alveolar-inspired gradient of 38 mm. Hg is reduced to 16 mm. Hg during rest and to 26 mm. Hg during exercise (fig. 1). Therefore, a liter of alveolar ventilation is not as effective in removing CO_2 and body stores increase. Bullard (6) asserted that during heavy exercise with $\dot{V}_{CO_2}$ of 3.5 liters/min., a $\dot{V}_E$ of 88 liters/min. is sufficient to keep P_{CO_2} at 40 mm. Hg in normocapnic atmospheres. Disproportionately higher ventilations are needed

[4] It has been found that V_T/V_A will slightly decrease during exercise (1) and hypercapnic hyperventilation (26) since the rise in dead space is always proportionally smaller than the rise in tidal volume (V_T).

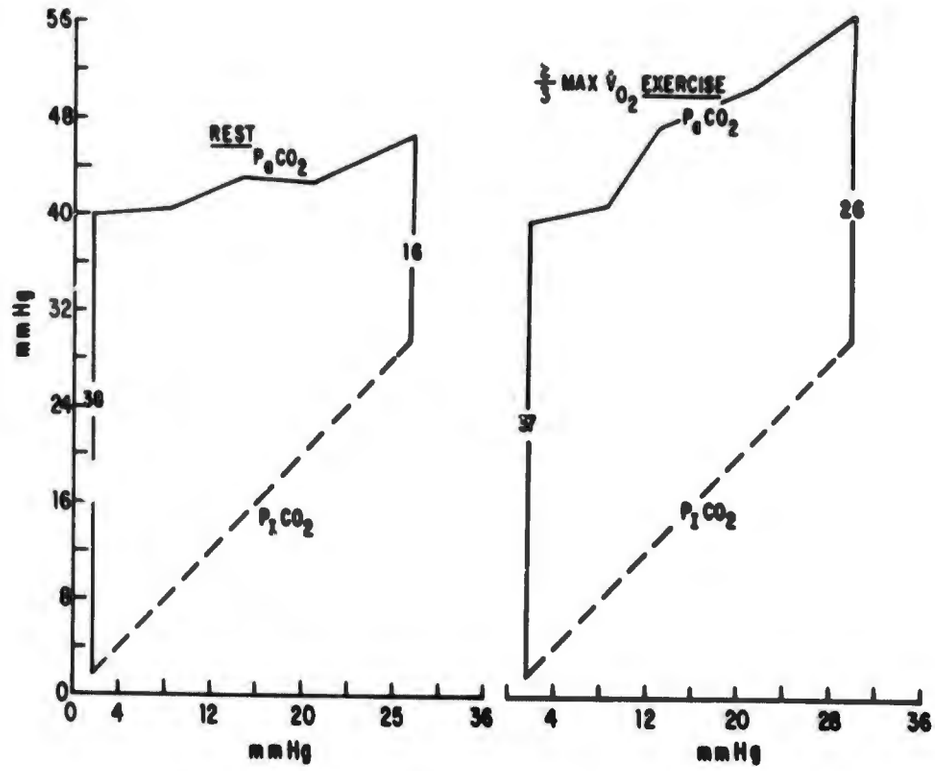

FIGURE 1

Arterial-inspired P_{CO_2} gradient.

to prevent P_{aCO_2} and CO_2 stores from rising in hypercapnic atmospheres, but for those reasons mentioned above, our subjects were unable to achieve them.

The rise in P_{aCO_2} from rest to exercise seen in this study is not the usual finding in the literature. While small increases of 2.5 to 5.0 mm. Hg during light exercise have been described (4, 16, 30), the majority of studies have found no change (1, 17) in moderate exercise nor a decrease in P_{aCO_2} (1, 10, 17, 31) in heavy exercise. Normocapnia during exercise has been used as evidence of the respiratory competence even when maximum $\dot{V}O_2$ is peaking and the cardiovascular system has reached its limit. The above studies, however, were at ambient conditions. Data of Hickam et al. (16) on untrained men in 5% CO_2 (~ 36 mm. Hg P_{ICO_2}) show a rise in P_{aCO_2} of 12.8 mm. Hg between rest and exercise as opposed to a 4.5 mm. Hg rise in 0% CO_2. In this 30 mm. Hg P_{ICO_2} atmosphere, a 10.6 mm. Hg rise in P_{aCO_2} does occur in spite of a $\dot{V}E$ of 103 liters/min.—considerably higher than Bullard's figure of 88 liters/min. By calculation our subjects would have had to raise their $\dot{V}E$'s to 125 liters/min. to prevent the decrease in $\dot{V}CO_2$ observed.[5] The ensuing respiratory acidosis due to elevation of P_{aCO_2} that results should account for a drop of 0.08 pH units. Instead a 0.118 unit decrease was observed (see table VI). The added pH drop is secondary to metabolic acidosis, probably due to lactate formation.

The finding of no change in $\dot{V}O_2$ with increasing P_{ICO_2} indicates that the metabolic cost of work is not influenced by hypercapnia. It

[5]This calculation was made using the formula of Kao et al. (19) with a 16 mm. Hg P_{CO_2} gradient and a value of 1.14 for the V_T/V_A ratio based on data by Asmussen (1).

should be noted that the ventilation equivalent ($\dot{V}_E$ BTPS/$\dot{V}O_2$ STPD) did increase for increasing $P_{I_{CO_2}}$; however, this ventilation equivalent increase is due to $\dot{V}_E$ changes. No $\dot{V}O_2$ change was seen in 6 subjects exercising at 100 w. in 0 and 8 mm. Hg $P_{I_{CO_2}}$ in a report by Krasnogor (20). Craig's study (8) at submaximal work levels reported data on one subject which suggested an increase in $\dot{V}O_2$ with increasing $P_{I_{CO_2}}$. A recent study by Finkelstein et al. (unpublished data) of maximum exercise on a bicycle ergometer at 0 and 16 mm. Hg $P_{I_{CO_2}}$ did show, however, significant decreases in maximum $\dot{V}O_2$ in hypercapnia.

In general, the results of the maximum effort agree with the steady-state tests. The $\dot{V}_E$ results at maximum $\dot{V}O_2$, however, are different in that they do not vary with $P_{I_{CO_2}}$ and suggest that a ventilation limitation has been reached at these levels of 135 to 145 liters/min. BTPS. Again, this may represent a mechanical limitation of breathing while exercising on the bicycle ergometer. $\dot{V}_E$ below this limitation at submaximal levels (~ one-half $\dot{V}O_2$) did vary with inspired CO_2 levels. The subjective symptom of the subjects indicating that maximal work in 21 mm. Hg P_{CO_2} was far more difficult than at 0 or 8 mm. Hg P_{CO_2} was supported objectively by the slightly decreased time on the ergometer. Blood gas studies were not carried out, but the possibility, based on the steady-state findings, that marked hypercapnia and acidosis occurred during the 21 mm. Hg $P_{I_{CO_2}}$ phase is real.

V. SUMMARY AND CONCLUSIONS

Well-trained volunteers were able to perform moderate exercise (one-half maximum $\dot{V}O_2$) in 0, 8, 15, and 21 mm. Hg $P_{I_{CO_2}}$, and heavy exercise (two-thirds maximum $\dot{V}O_2$) in 0, 8, 15, 21, and 30 mm. Hg $P_{I_{CO_2}}$. The exercise consisted of 30 minutes of steady-state pedaling (60 r.p.m.) on a bicycle ergometer at workloads of 800 and 1,100 kgm./min. At low CO_2 levels of 8 and 15 mm. Hg, no difficulty was encountered by the subjects. Higher levels of hypercapnia (21 and 30 mm. Hg $P_{I_{CO_2}}$) caused some respiratory symptoms of "air-hunger" and intercostal muscle pain, but were of mild enough degree to permit all subjects to complete the exercise. Stepwise exercise up to workloads producing maximum $\dot{V}O_2$ (2,000 kgm.) were also performed in 0, 8, and 21 mm. Hg $P_{I_{CO_2}}$. The tolerance at maximum exercise in 21 mm. Hg $P_{I_{CO_2}}$ resembled that at two-thirds workload in 30 mm. Hg $P_{I_{CO_2}}$. Maximum $\dot{V}_E$ of ~ 140 liters/min. did not vary with the level of inspired CO_2, whereas at submaximal workloads $\dot{V}_E$ was greater at the higher $P_{I_{CO_2}}$ level. Maximum and submaximal oxygen uptake were not altered by the CO_2 environment. In spite of large ventilations approaching 50% to 70% of MVV, $\dot{V}CO_2$ showed a progressive fall at the higher $P_{I_{CO_2}}$'s, indicating a buildup of body CO_2 stores. This buildup suggests that the pulmonary system has reached a limit for effective CO_2 removal because of the decreased alveolar-inspired CO_2 gradient with increasing $P_{I_{CO_2}}$. Larger tidal volumes and, therefore, increased alveolar ventilation may be restricted by mechanical limitations of breathing while exercising on an ergometer. The rise in body stores of CO_2 caused elevations in P_{ACO_2} during exercise. This arterial hypercapnia produces a respiratory acidosis adding to the metabolic acidosis of exercise.

Therefore, it appears that exercise in hypercapnia does stress the respiratory system, unlike the situation of normal exercising man in ambient conditions. However, man can perform for short periods even in these high CO_2 atmospheres without great distress, and the authors conclude that the existing CO_2 tolerance levels for resting man in confined cabin atmospheres (approximately 8 mm. Hg) are also adequate for the working individual.

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13. ABSTRACT

Trained volunteers performed steady-state moderate exercise (one-half of maximum $\dot{V}_{O_2}$) and heavy exercise (two-thirds of maximum $\dot{V}_{O_2}$) in 0, 8, 15, 21 and 30 mm. Hg $P_{I_{CO_2}}$ for 30 minutes on a bicycle ergometer. At CO_2 levels of 8 and 15 mm. Hg, no difficulty was encountered by the subjects. The higher levels of hypercapnia caused some respiratory symptoms of "air-hunger" and intercostal muscle pain, but were of mild enough degree to permit all subjects to complete the exercise. Incremental exercise up to workloads producing maximum $\dot{V}_{O_2}$ was also performed. The tolerance at maximum exercise in 21 mm. Hg $P_{I_{CO_2}}$ resembled that at two-thirds workload in 30 mm. Hg $P_{I_{CO_2}}$. $\dot{V}_E$ during maximum exercise did not vary with the level of inspired CO_2, whereas at submaximal workloads, $\dot{V}_E$ increased as $P_{I_{CO_2}}$ increased. At two-thirds and maximum workloads, $\dot{V}_{CO_2}$ during exercise fell progressively with increasing $P_{I_{CO_2}}$. The ineffective CO_2 removal is explained by the decreased alveolar-inspired CO_2 gradient with increasing $P_{I_{CO_2}}$. Inadequate elimination of CO_2 caused respiratory acidosis to be superimposed on the metabolic acidosis normally present during exercise.

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