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Human Response to Carbon Dioxide in the Low-Pressure, Oxygen-Rich Atmosphere

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ABSTRACT

Eight subjects were successively exposed to an inspired carbon dioxide partial pressure of 21 mm. Hg, equivalent to 3 per cent at sea level, in an atmosphere of 700 mm. Hg total pressure and in an oxygen atmosphere of 200 mm. Hg total pressure. The duration of exposure to carbon dioxide was 4 days in each case. Response to carbon dioxide was nearly the same at the two different pressures as measured by the degree of hyperventilation and hypercapnia produced. Respiratory acidosis reached a maximum after 2 days CO_2 exposure at each pressure and was followed by a pH shift on the third and fourth days due to renal or metabolic compensation. There was no objective evidence in the respiratory studies of an adaptive acclimatization to carbon doxide during the 4-day exposures. The subjective ability to detect carbon dioxide in the atmosphere was not always reliable, especially after prolonged exposure. No performance deterioration was measured and, in fact, operator efficiency was maintained at a remarkably even level.

THE ADVENT of prolonged manned space missions and the necessary utilization of the sealed atmosphere have increased the requirement for knowledge of man's response to the various environmental factors comprising his atmosphere. One such factor, the carbon dioxide concentration in the spacecraft atmosphere, requires further study and definition of tolerance limits even though the present design limits established for nominal operation (5-7 mm. Hg. P_{CO_2} are well within human tolerance.[14] The utilization of CO_2 removing systems which operate more efficiently at higher CO_2 concentrations, the possibility of mechanical failure of the CO_2 removal system, and the probability of increased CO_2 levels resulting from overloads on the CO_2 removal system during rendezvous flights and emergencies, all exemplify the need for accurate, thorough knowledge of human tolerance limits for CO_2 in various spacecraft atmospheres.

Tolerance to chronic exposure to CO_2 in the sea level atmosphere has been the subject of a number of studies and has been discussed by Schaefer[14] and reviewed by others.[3, 6, 7, 15] Reports of alterations of CO_2 tolerance at altitude where hypoxic hyperventilation is superimposed upon the effect of CO_2 have also been published;[1] however, the studies are not applicable to the low pressure, O_2 enriched, artificial atmosphere. Other data might lead one to believe that CO_2 tolerance would vary with gas density or atmospheric pressure. Lanphier[8] reports elevated alveolar P_{CO_2} levels (P_ACO_2) in working subjects breathing air under 4 atmospheres of pressure, but no elevation of P_ACO_2 when subjects breathed He_2-O_2 mixtures at that pressure, the latter atmospheres being less dense. Unpublished studies by our own group indicate reduction of P_ACO_2 with barometric pressure, possibly due to ventilatory changes related to gas density, could influence response to CO_2. Moreover, studies by Otis and Bembower[4] demonstrated decreased work of breathing at reduced barometric pressures. The present study was undertaken to obtain additional data regarding man's response to elevated CO_2 concentrations, particularly

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comparing response at 700 mm. Hg to those at 200 mm. Hg total pressure.

MATERIALS AND METHODS

Experimental Sequence. All 8 subjects were healthy, young Air Force pilots who volunteered for the studies. They were carefully screened prior to the experiments by the USAF School of Aerospace Medicine Consultation Services for medical and psychiatric abnormalities.

The 8 subjects were divided into groups of four. The first four were carried through the experimental sequence in late 1962 and will be noted as 21, 22, 23, and 24. The group of 4 subjects in the early 1963 experiment will be noted as 25, 26, 27, and 28 throughout the remainder of the paper. The 1962 and 1963 experiments will be noted as 62-6 and 63-1, respectively.

In daily medical evaluation, a survey of symptoms was made by an attending physician who entered the chamber by means of a lock and examined the subjects. The daily routine of the subjects in the chamber was uniform with a 5-hour sleep period supplemented by 2-hour rest periods. Programmed activity was limited to 2-hour shifts on a psychomotor testing panel. The remainder of the time was spent in reading, study, hygiene, personal care, and maintenance of internal chamber facilities. During this experiment, the subjects were fed a standardized diet designed by Scrimshaw [16] for study of aspects to be reported elsewhere. Caloric intake was metered out at 30-40 Kcal./kg.

These studies were conducted in an altitude chamber at the USAF School of Aerospace Medicine which had been adapted for atmospheric control. Carbon dioxide was monitored by a Beckman LB-1 infrared CO_2 analyzer, oxygen was monitored by a Beckman F-3 analyzer, and nitrogen by a Nitralyzer 300 AR. Calibration of all instruments was carried out every 12 hours. Readings were taken every 15 minutes and average readings are presented in Table I.

The subjects were successively exposed to the four gaseous environmental compositions presented in Table I. The duration of exposure was 4 days in each atmosphere carried out in the same sequence as shown in Table I. Following exposure to the CO_2-rich, 700 mm. Hg atmosphere, the subjects were removed from the chamber for 4 days to permit recovery prior to exposure to 200 mm. Hg pressure. Carbon dioxide levels were maintained to provide comparable tracheal partial pressure of CO_2 ($P_ICO_2 = 21$ mm. Hg). This P_ICO_2 is equivalent to that obtained when breathing 3 per cent CO_2 at sea level.

Inspired partial pressure of oxygen (P_IO_2) was held to similar levels in each of the four atmospheres so that the results would not be influenced by gross differences in PO_2. Chamber temperature was selected by the subjects. In transition from the CO_2-low to the CO_2-rich atmosphere, the CO_2 level was gradually increased over a 4-hour period. The subjects were not told when or how much the CO_2 levels would be elevated, nor what symptoms might be anticipated.

Respiratory Studies. Basal respiratory studies were performed with the subjects fasting and recumbent after they had awakened from a 5-hour sleep period.

Inspiratory minute volume ($\dot{V}_I$) was measured in experiment 62-6, using a Servo spirometer made by Custom Engineering and Development Company. In experiment 63-1, $\dot{V}_I$ was measured with a Tissot spirometer. Both methods gave comparable results. Subjects breathed from 7 to 10 minutes for each of the samples.

Expiratory minute volume ($\dot{V}_E$) was measured by collecting exhaled air in a Douglas bag during the $\dot{V}_I$ measurement, using the Servo spirometer in experiment 62-6 and a Tissot spirometer in experiment 63-1. From these measurements $\dot{V}_I$ and $\dot{V}_E$ were calculated for the BTPS state. End tidal air (alveolar air) was collected by the Rahn Sampler technique [12] with the subject recumbent immediately following the $\dot{V}_I$ and $\dot{V}_E$ collections. Samples of alveolar air, expired air, and cabin atmosphere were collected in syringes lubricated with saturated LiCl and were then analyzed. In experiment 62-6, the oxygen and carbon dioxide fractions were determined by the Scholander micro-gas analyzer.[17] In experiment 63-1, these gas fractions were determined by the Beckman E-2 oxygen analyzer and the Liston-Becker-1 infrared carbon dioxide analyzer. From these results, CO_2

TABLE I. SUMMARY OF ENVIRONMENTAL CONDITIONS

	Type of Atmosphere				
	Control	CO_2 Rich	San Antonio Ambient	Control Low Pressure	CO2 Rich Low Pressure
	Days of Experiment				
	1 thru 4	5 thru 8	9 thru 12	13 thru 16	17 thru 20
Total Barometric Pressure (mm. Hg)	700 ±	700 ±	Ambient*	200 ±	200 ±
P_ICO_2 (mm. Hg)	2.5 ± .6	21.3 ± .9		2.5 ± .7	20.9 ± 1.0
P_IO_2 (mm. Hg)	148.5 ± 3.7	155.1 ± 3.4		142.1 ± 3.6	127.0 ± 1.0
P_IN_2 (mm. Hg)	493.7 ± 11.4	437.2 ± 11.0		2.7 ± 2.3	2.7 ± 1.4
% Relative Humidity	64	80		43	47
Temperature (°C.)	24.8	24.2		22.5	22.2

* Average ambient barometric pressure at San Antonio, Texas is 747 mm. Hg.

Average of readings taken every 15 minutes. Standard deviations follow the average readings. Data from Experiment 62-6 and 63-1 were combined. $P_{I_X} = (P_B - P_{H_2O_t})F_{I_X}$.

production ($\dot{V}CO_2$), O_2 consumption ($\dot{V}O_2$), and alveolar ventilation were calculated from equations presented by Rahn.[13] The respiratory studies for the 8 subjects were then subjected to a repeated, measurement-type analysis of variance and the statistical significance of differences occurring in the CO_2-rich atmospheres was computed.

Blood Studies. Venous samples were collected anaerobically and analyzed for pH and P_{CO_2} by using pH and P_{CO_2} electrodes made by Instrumentation Laboratories, Inc. After 4 days exposure of the subjects to each artificial atmosphere, arterial samples were obtained by brachial artery puncture. Analysis of P_{O_2} was made without delay by means of a P_{O_2} electrode, and the pH and P_{CO_2} were measured and treated in the same fashion as for the venous blood. End tidal alveolar samples were drawn at the time of arterial puncture by the Rahn Sampler for analysis of alveolar gas and alveolar-arterial oxygen gradients were computed.

Electrolyte Studies. Although these experiments were not specifically designed to study acid-base balance, urinary electrolytes were analyzed to investigate possible metabolic compensations for the expected respiratory acidosis. Chlorides were measured by the Cotlove amperometric method,[2] inorganic phosphates by the method of Bodansky,[16] and sodium and potassium were analyzed using a Beckman DU flame photometer.

Psychomotor Performance Studies. Five tasks were performed as follows: 1) a vigilance task in which the subject monitors three meters for deflections from the null position (the score on this task was taken in response time in fifths of a second); 2) an arithmetic encoding task involving simple addition and encoding the digits in the obtained sum (scored in terms of response time); 3) a compensatory tracking task wherein the subject tracks a meter displaying a signal derived from a generated sine wave, plus the algebraic sum of his own response signal. The task is programmed in 1-minute trials, is time-shared, and is scored in terms of errors about a set point of ± 8 microamperes scale deviation from the null position; 4) a short-term memory task requiring monitoring the number of light flashes presented randomly on three separate lights independently for 40 seconds and then reporting the result via switch operation after the delayed (10 sec.) command (the measure of performance is the percentage of errors); 5) a problem-solving task wherein the sequential operation of 4 lighted push button switches indicates a preprogrammed relationship between either 2 or 3 of the 4 "elements." The relationship is a conjunctive one; that is, if button 2 lights 4, and 3 lights 4, the solution is 2 and 3. Both positive and negative inference may be used (this task is scored in terms of percentage error, only one trial per problem being allowed). The complete task system will be described in a subsequent paper.[9]

Each subject worked at the tasks on a fixed schedule for a 2-hour period twice each 24 hours. Scores were recorded hourly. Prior to the experiment, each subject was coached for one-half hour on the various tasks and given 4 distributed practice sessions of 1 hour each to obtain a reasonable equality of performance and to attenuate as much of the learning effect as possible. The signal rate was held constant throughout the experiment by operating the semi-random programmer at 1800 steps per hour. The compensatory tracking task was time-shared during its 1-minute trial period. This resulted in a loss of 1500 signals per hour so that 300 signals per hour were available for operator processing.

RESULTS

Subjective Responses. Though the subjects were not told when CO_2 was added to the atmosphere, their acuity was augmented by talking to each other and they were not oblivious to changes in gas injection patterns necessary to alter the chamber atmospheres. In spite of such clues, one subject (27) thought CO_2 was not elevated at all at 700 mm. Hg. Another subject (25) suspected CO_2 elevation one day before actual introduction at 200 mm. Hg.

Awareness of hyperventilation was the most helpful physiologic clue and 7 subjects (21, 22, 23, 24, 25, 26, and 28) noted this symptom, particularly in the first 2 or 3 days of each CO_2-rich atmosphere. Thereafter, they became less aware of hyperventilating except for subject 22 who was equally aware of it throughout the 4 days of CO_2-rich atmosphere exposure. Some subjects noted hyperventilation only intermittently during certain activities such as when in bed (21 and 22), or while sitting, working at the psychomotor panel in the evenings (23 and 24), or when fatigued (25, 26, 27, and 28). This variable awareness of hyperventilating led subjects to suspect that CO_2 levels were intermittently elevated.

Tingling and numbness of extremities, symptoms usually suggestive of excessive hyperventilation, were seen on one occasion in 2 subjects (25 and 28) during

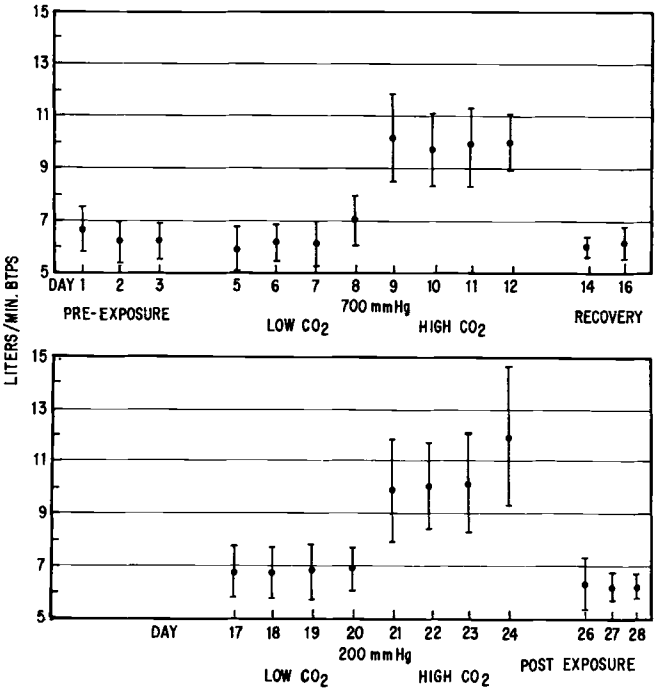

Fig. 1. Inspiratory minute volume. Each value is the daily average of 8 subjects. The vertical bars represent one standard deviation on either side of the mean.

the first day of CO_2 enrichment at 700 mm. Hg. Subject 28 noted lightheadedness at the same time. One subject (22) developed a headache on the first day of exposure to the CO_2-rich atmosphere at 700 mm. Hg. Five subjects (21, 22, 25, 27 and 28) developed headaches on the first day of exposure to the low pressure, CO_2-rich atmosphere. Three (21, 22, and 25) of the five had intermittent headaches for the next 2 days. The headaches were mild and generally lasted for 1 or 2 hours. No headaches were reported during the low CO_2 periods.

Inspiratory Minute Volume (V_I). The day-to-day averages for the 8 subjects (Fig. 1) show that there was no appreciable change from the pre-experiment control values to the low CO_2, 700 mm. Hg atmosphere. However, upon addition of CO_2, $\dot{V}_I$ increased and remained elevated throughout the 4-day, CO_2 rich period with no upward or downward trend. Upon return to San Antonio ambient atmosphere, $\dot{V}_I$ returned to baseline values. Throughout the low CO_2, 200 mm. Hg atmosphere, 4 of the subjects (25, 26, 27, and 28) demonstrated moderate hyperventilation, raising the averages during that period to somewhat higher than control values. Again, upon addition of CO_2 to the atmosphere, $\dot{V}_I$ increased markedly.

Four-day averages for all 8 subjects (Table II) show

TABLE II. INSPIRATORY MINUTE VOLUME ($\dot{V}_I$)

	Low CO_2	High CO_2	High CO_2 Minus Low CO_2	% Increase
$\dot{V}_I$ @ 700 mm. Hg	6.32*	9.93*	3.61	57
$\dot{V}_I$ @ 200 mm. Hg	6.81*	10.53	3.72	55
Increase due to reduced pressure (L.)	0.49	0.60		
% increase due to reduced pressure	8	6		

* Represents liters/minute, BTPS, and is the average of 8 subjects over 4 days.

that although subjects began with moderate hyperventilation in the low CO_2, 200 mm. Hg atmosphere, their $\dot{V}_I$ increment upon addition of CO_2 was nearly the same as in the 700 mm. Hg atmosphere. Analysis of variance of the $\dot{V}_I$ values indicated: 1) a highly significant increase in $\dot{V}_I$ upon addition of CO_2 ($P<.001$); 2) a possibly significant increase $\dot{V}_I$ due to the lower pressure alone ($P<.025$); 3) no significant changes between the pre- and post-experiment values.

Alveolar Carbon Dioxide (P_ACO_2). The day-to-day averages for the 8 subjects (Fig. 2) show that changes in alveolar carbon dioxide corresponded to changes in inspiratory minute volume. P_ACO_2 increased upon addition of CO_2 and decreased when CO_2 was removed. There were no significant upward or downward trends during the CO_2 exposure periods. Four-day averages for all 8 subjects are tabulated in Table III. Corresponding to the relatively greater ventilation during both phases

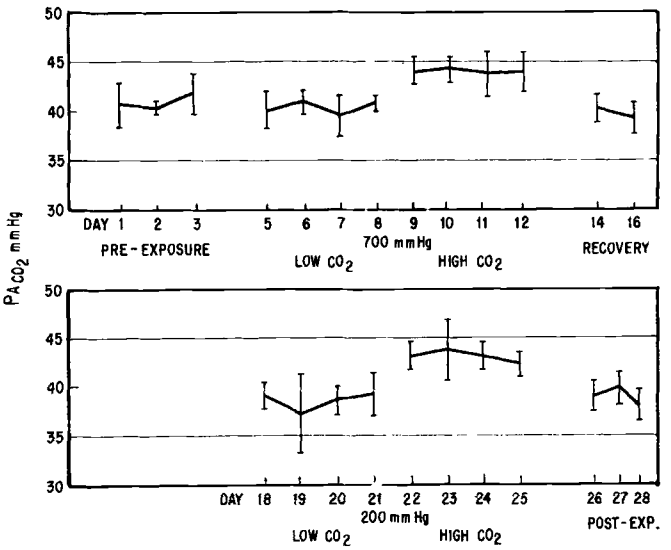

Fig. 2. Alveolar P_{CO_2}. Each value is the daily average of 8 subjects. The vertical bars represent one standard deviation on either side of the mean.

TABLE III. ALVEOLAR P_{CO_2} (P_ACO_2) mm. Hg

	Low CO_2	High CO_2	High CO_2 Minus Low CO_2	% Increase
P_ACO_2 @ 700 mm. Hg	40.6*	44.3*	3.7	9
P_ACO_2 @ 200 mm. Hg	38.6*	43.3*	4.7	12
Decrease due to reduced pressure	2.0	1.0		
% decrease due to reduced pressure	5	2		

*Represents mm. Hg and is the average of 8 subjects over 4 days.

at 200 mm. Hg, P_ACO_2 was slightly less during both phases at that pressure than those observed at 700 mm. Hg. However, the P_{CO_2} increment on addition of CO_2 was nearly the same at 200 mm. Hg as at 700 mm. Hg.

Analysis of variance of the P_ACO_2 values indicated: 1) a highly significant increase in P_ACO_2 upon addition of CO_2 ($P<.001$); 2) no significant day-to-day trends within any 4-day period; 3) a significant decrease in

TABLE IV. TIDAL VOLUME AND RESPIRATORY RATE

	Low CO_2	High CO_2	Increment	% Increase
Tidal volume @ 700 mm. Hg	.791	1.058	.267	34
Tidal volume @ 200 mm. Hg	.737	.996	.259	35
Respiratory rate @ 700 mm. Hg	9.3	10.6	1.3	14
Respiratory rate @ 200 mm. Hg	10.2	11.1	.9	9

The above figures are averages of 8 subjects over each 4-day period. Tidal volume is expressed in liter, BTPS. Respiratory rate is expressed in cycles per minute.

P_ACO_2 associated with the lower presure ($P < .005$); 4) possibly significant decrease in the post-experiment P_ACO_2 values compared with the pre-experiment P_ACO_2 values ($P < .05$).

Other Respiratory Values. It can be seen (Table IV) that respiratory rate changed only slightly in response to the CO_2-rich atmosphere whereas tidal volume increased by one-third, accounting for most of the increase seen in inspiratory minute volume. This is consistent with results of other investigators for this level of CO_2.[14] The daily averages for tidal volume and respiratory rate for all 8 subjects (Fig. 3) were significantly

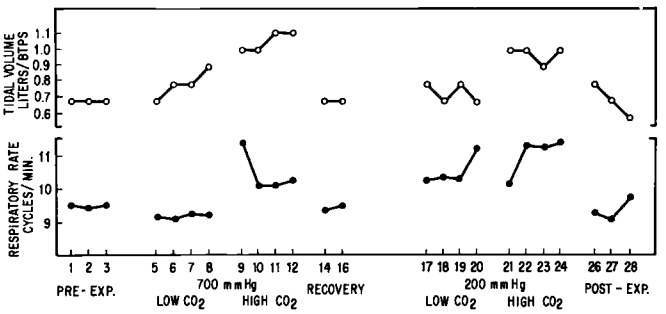

Fig. 3. Tidal volume and respiratory rate. Tidal volume is indicated by open circles and respiratory rate is indicated by solid circles. Each value is the daily average of 8 subjects.

increased during exposures to carbon dioxide ($P < .01$).

It can be seen in Figure 4 that average daily alveolar

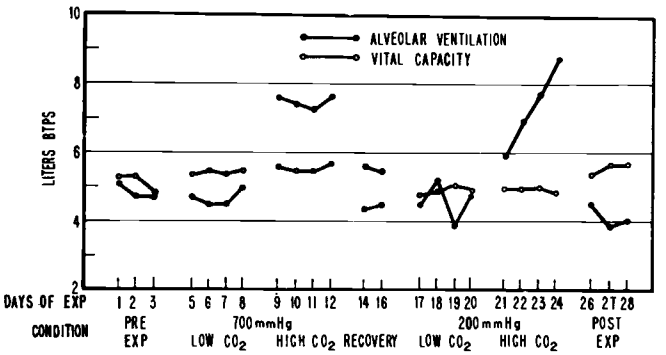

Fig. 4. Vital capacity in liters, BTPS, and alveolar ventilation in liters/minute, BTPS. The open circles are vital capacity. The solid circles are alveolar ventilation. Each value is the daily average of 8 subjects.

ventilation increased upon addition of CO_2 to the atmosphere at 700 mm. Hg and at 200 mm. Hg. These changes paralleled changes in inspiratory minute volume but the average alveolar ventilation at 200 mm. Hg continued to rise throughout the 4 days, reaching borderline significance ($P < .05$). This upward trend is not reflected in a corresponding drop in alveolar P_{CO_2}, and day-to-day fluctuations of this measurement in any given subject were considerable. Thus, the physiologic significance of this upward trend at 200 mm. Hg is not immediately clear.

The daily vital capacity averages are also presented in Figure 4. Though vital capacity was apparently uninfluenced by carbon dioxide exposure, a decrease occurred in all 8 subjects during the exposure to the 200 mm. Hg atmosphere. The average decrease for all 8 subjects for the 8-day period compared to the 8 days in the 700 mm. Hg atmosphere was 10 per cent. This decrement in vital capacity is comparable to those reported previously.[10]

Daily averages of oxygen consumption and carbon dioxide production (Fig. 5) show a gradual downward

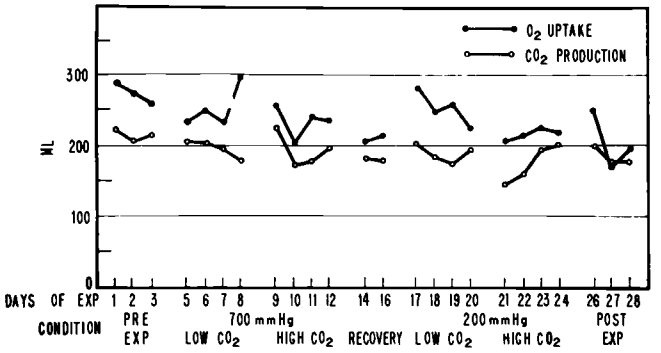

Fig. 5. Oxygen consumption and carbon dioxide production in ml./min. STPD. The solid circles represent oxygen consumption. The open circles represent carbon dioxide production. Each value is the daily average of 8 subjects.

trend throughout the experiment, possibly due to a decreased metabolic rate resulting from the inactivity due to confinement. Oxygen consumption was found to be lower during the exposure to the CO_2-rich atmospheres than during the 4-day control periods. However, those values for the CO_2-rich atmospheres were not lower than the subsequent measurements taken in the recovery and post-experiment phases. Although values for carbon dioxide production paralleled those of oxygen consumption, the greater day-to-day variations preclude any conclusions to significant changes during the carbon dioxide exposure periods.

The daily average alveolar P_{O_2} values are presented (Table V) to indicate that at no time did alveolar

TABLE V. ALVEOLAR P_{O2} (P_{AO2}) mm. Hg

	Days in the Chamber							
	1	2	3	4	5	6	7	8
700 mm. Hg	99.0	99.0	105.2	98.5	128.2	123.4	126.8	124.3
200 mm. Hg	110.4	108.6	108.8	107.7	104.1	103.1	105.3	105.0

Data presented above are the daily averages of 8 subjects. Days 1 to 4 are the low-CO_2 phase, and days 5 to 8 are the high-CO_2 phase.

P_{O_2} differ greatly from normal. The changes in themselves are not significant but only reflect the changes in atmospheric P_{O_2}. Hypoxia was not a factor in this experiment.

Venous pH. The summary of pH data for brachial venous blood is presented in Figure 6. Blood pH decreased significantly (P. 01) when measured 24 hours after the beginning of the CO_2 exposure at both the 700 mm. Hg and 200 mm. Hg atmospheres. A further drop occurred after 48 hours exposure, but after 72 hours the pH was essentially normal. At each atmospheric pressure, the pH had climbed to above normal after 96 hours. The initial drop in pH reflects

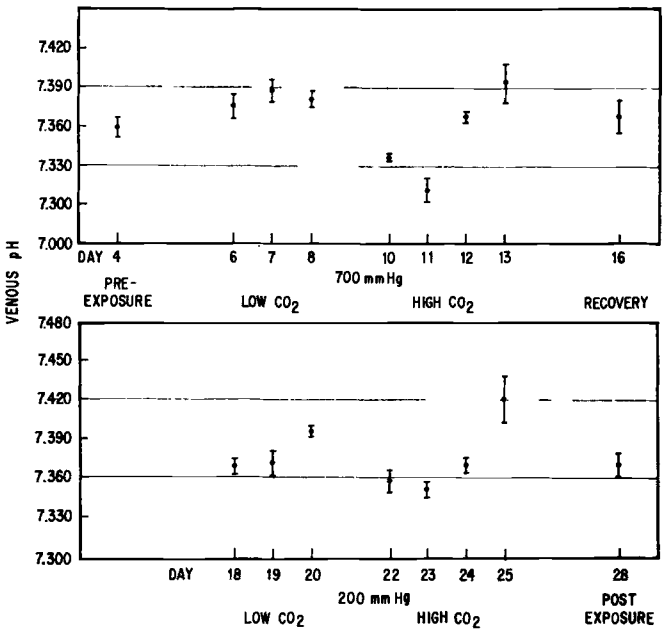

Fig. 6. Blood pH. Each value is the daily average of 8 subjects. The vertical bars represent one standard deviation on either side of the mean.

the level of pulmonary acidosis resulting from the increased P_ACO_2. The average 4 mm. Hg increment in P_ACO_2 (Fig. 2) would be expected to reduce blood pH by approximately 0.06 pH units. The increase in pH on the third and fourth days indicate that some renal (metabolic) compensation occurred. The higher than normal value on the fourth day of each exposure is unexplained.

Electrolyte Excretion. Mean daily chloride excretion for all 8 subjects is shown in Figure 7. All subjects except 26 showed an increased chloride excretion during the CO_2 periods. Of particular interest in the present study is the duration of the elevated chloride excretion. The values did not return to baseline levels during the 4-day high CO_2 periods. This increase in chloride excretion is consistent with the metabolic compensation of respiratory acidosis.

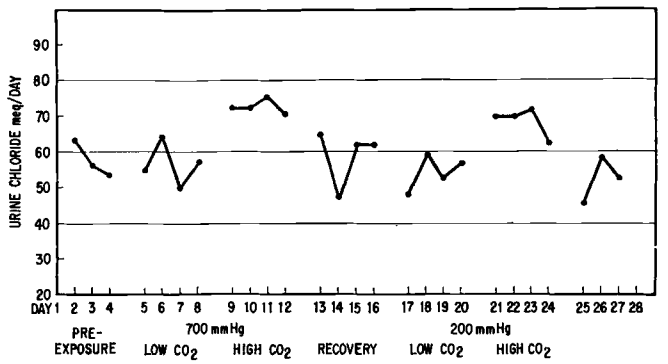

Fig. 7. Mean daily chloride excretion. Each point represents the daily average of 8 subjects.

Analysis of results for sodium, potassium, and phosphate excretion revealed no consistent changes between high and low CO_2 periods or with pressure changes. Bicarbonates were calculated from venous pH and CO_2 values using the Henderson-Hasselbach equation. No significant changes or trends were noted.

Psychomotor Performance Studies. Complete performance data are available for subjects 25, 26, 27, and 28 only. An anitial graphic analysis of the performance measures revealed that in spite of pre-experimental training, there was an apparent continuous improvement in performance for the first 3 days. Day 4 was assumed to represent a period of maximum performance and was used as a control baseline. Since CO_2 was introduced on day 5, it was assumed that if any serious performance effects were produced, they should have been reflected in the scores obtained on day 6. To test this, the scores for each task for the 4 subjects were pooled to yield one score per task for day 4 (normal CO_2), and one for day 6 (elevated CO_2) for both the atmospheres at 700 mm. Hg and at 200 mm. Hg. The results of this analysis are presented in Table VI.

TABLE VI. "F" RATIOS AND ASSOCIATED SIGNIFICANCE LEVELS OBTAINED FROM ANALYSIS OF VARIANCE OF POOLED TASK SCORES FOR DAYS 4 AND 6 AT 700 mm. Hg, AND AT 200 mm. Hg

Task	Between Groups	CO_2 Effect Between Days (r)	Pressure Effect Between Altitudes (k)	Inter-Actions (rk)
1. Vigilance	N.S.	N.S.	N.S.	N.S.
2. Arithmetic	N.S.	N.S.	N.S.	N.S.
3. Tracking	47.89*	N.S.	41.23**	N.S.
4. Memory	N.S.	N.S.	N.S.	N.S.
5. Problem Solving	1703.69*	N.S.	1350.56**	N.S.

NS = not significant
* = significant at the 5% level
** = significant at the 1% level

There was no significant before-after CO_2 effect upon the type of performance measured, either at 700 mm. Hg or at 200 mm. Hg. The two tasks which do show significant variation yield the same results between 700 mm. Hg and 200 mm. Hg. Another index of performance measurement made possible by the subject-paced nature of the system is that of operator signal rate. This is an important factor to consider because of the possibility that operator proficiency may be maintained at the expense of efficiency. Here operator efficiency is defined as the number of signals processed per hour. An analysis of operator efficiency was made by pooling the number of tasks each operator performed during his work periods for each day at both ground level and altitude. The mean signal processing rate at 700 mm. Hg was 158.76 ± 4.41 signals per hour. At 200 mm. Hg, the mean rate was 165.12 ± 5.29 signals per hour. There were no significant deviations from these processing rates either across days within the 700 mm. Hg and 200 mm. Hg periods, or between the two treatments as a result of increased inspired CO_2. This evaluation shows operator efficiency was maintained at a remarkably even level during the entire experiment.

DISCUSSION

Of the numerous effects which the CO_2-rich atmosphere may have on the body, there are two primary and interrelated changes: hyperventilation and hypercapnia. The hyperventilation will limit the degree of hypercapnia and is itself a consequence of the hypercapnia. The many other consequences such as tissue and blood acidosis, increased blood flow to the brain, and alterations in renal excretion, will be secondary to these two effects. Therefore, we have focused attention upon hyperventilation and hypercapnia in evaluating response to carbon dioxide at 700 mm. Hg and 200 mm. Hg.

One needs to keep in mind the hyperventilation already present in the low CO_2, 200 mm. Hg atmosphere in comparing the nearly identical increases in inspiratory minute ventilation upon addition of CO_2 at each pressure as seen in Table II. This hyperventilation at 200 mm. Hg was not due to hypoxia since alveolar P_{O_2} levels were always above 90 mm. Hg. It has been reported that 100 per cent O_2 at sea level causes hyperventilation and hypocapnia.[3] However, such studies are not comparable to ours since the alveolar P_{O_2} in our experiment was essentially normal during the 8 days at 200 mm. Hg. Another factor is that the 200 mm. Hg atmosphere, being less dense, demands less ventilatory effort.[4] Hence, for an equivalent energy expenditure, the individual would be able to ventilate more. No attempt was made in the present study to quantitate this effect. The experimental data presented here demonstrate the response to CO_2 in the low pressure atmosphere to be substantially the same as for equivalent levels of P_{CO_2} at near sea level.

The ability of individuals to detect subjectively this amount of carbon dioxide was not always reliable, especially after prolonged exposure. Hyperventilation, which was their most sensitive clue, was less noticeable after the first 2 days or when subjects were active and their attention occupied with other matters. Depth of respiration rather than rate showed the greatest change. The fact that when CO_2 was added to the chamber, only one subject developed a headache at 700 mm. Hg, whereas 5 subjects developed headaches at 200 mm. Hg, is of interest. If the headaches were due to hypercapnia, one would have expected from the alveolar P_{CO_2} studies that more headaches would occur in the 700 mm. Hg atmosphere. The variable, unpredictable nature of this symptom precludes firm conclusions in this small series. Moreover, unmeasured peaks of alveolar P_{CO_2} may have occurred throughout the day which could account for headaches.

Aside from the immediate respiratory response to the elevated atmospheric CO_2, there is no apparent evidence in these studies of pulmonary accommodation to CO_2. Hyperventilation became less noticeable to the subjects in the third and fourth days of exposure to the CO_2-rich atmospheres. Inspiratory minute volumes did not diminish and alveolar P_{CO_2} did not increase. There are two indications in this study that a renal (metabolic) compensation occurred. Following the initial drop in venous pH resulting from the respiratory acidosis, the pH increased to a higher than normal value on the fourth day of CO_2 exposure. Chloride excretion remained higher than normal throughout each 4-day CO_2 exposure, but had started to decrease in each case on day 4. At the end of each CO_2 period, venous pH and chloride excretion were still increased, showing that complete adjustment in acid base balance had not occurred. Four days may not be long enough for acclimatization.

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