also provided evidence of the complex expressions of multiple cardiac regions which act simultaneously. It was demonstrated specifically that the body surface location of potential maxima and minima cannot always be equated simply with the cardiac location of responsible events when multiple regions are active simultaneously. The body surface location of maxima and minima are, however, only one feature of body surface potential patterns. The contour of isopotential lines, the potential gradients at various locations, and the time sequence of changing potential values, gradients, and isopotential contours also are descriptors whose utility for regional cardiac examination should be examined.

Findings from this study suggest that individual cardiac regions have different effects of body surface potential patterns and support the possibility of regional cardiac examination by electrocardiography. Our findings also demonstrate, however, that simultaneous effects of multiple cardiac regions have complex surface potential manifestations. The use of arithmetic manipulations of maps provided insights concerning the distribution of potentials when more than one dipolar cardiac source was present, and this method is likely to be useful in analysis of maps for clinical diagnosis.* Separation of effects due to individual cardiac areas, when multiple areas have simultaneous effects, is the major problem for development of regional electrocardiographic examination of the heart.

**Reference**


---

**Maintained Stroke Volume but Impaired Arterial Oxygenation in Man at High Altitude with Supplemental CO₂**

ROBERT F. GROVER, M.D., PH.D., JOHN T. REEVES, M.D., JOHN T. MAHER, PH.D., ROBERT E. MCCULLOUGH, JULIO C. CRUZ, M.D., JOSEPH C. DENNISTON, D.V.M., PH.D., AND ALLEN CYMERMAN, PH.D.

**SUMMARY**

Hypobaric hypoxia causes hypocapnia and alkalosis, hemoconcentration and increased hematocrit, and a decreased cardiac stroke volume. To assess the role of the hypocapnic alkalosis in causing these other changes, five men were exposed to hypobaric hypoxia at a barometric pressure (P₀₂) of 440 mm Hg with an alveolar O₂ tension of 55 mm Hg for 5 days with 3.77% CO₂ added to the atmosphere to prevent alkalosis. They did not lose weight, and arterial CO₂ tension, pH, and cardiac stroke volume were unchanged. An unchanged hematocrit implied an unchanged plasma volume. During exercise to maximum, stroke volumes equaled sea level values but arterial hypoxemia was profound, the arterial O₂ tension being 39 mm Hg. By contrast, three men at high altitude without CO₂ supple-

A DECREASED cardiac stroke volume* of unknown cause is largely responsible for the decreased oxygen trans-

From the Cardiovascular Pulmonary Research Laboratory, University of Colorado Medical Center, Denver, Colorado, and the U.S. Army Research Institute of Environmental Medicine, U.S. Army Natick Development Center, Natick, Massachusetts.

---

**Support**

Supported by Grant HL 14985 from the National Institutes of Health, and by the U.S. Army Research Institute of Environmental Medicine.
consistently. Although hypoxia is present from the time of arrival at high altitude, decreased stroke volumes (1) do not occur until the subjects have been at high altitude for 2–3 days. \( ^2 \) \( ^3 \) (2) are not increased to normal by acute oxygen administration, \( ^4 \) and (3) are not accompanied by a decreased coronary sinus blood oxygen tension. \( ^8 \) Therefore, some factor other than the direct effect of hypoxia appears to be responsible for the decrease in stroke volume.

Hypocapnia (alkalosis) which develops in the newcomer at high altitude \( ^9 \) could play a role in causing the decreased stroke volume. Prevention of hypocapnia during acute hypoxia is known to have important effects such as inhibiting forearm vasoconstriction, \( ^10 \) augmenting ventilation, and promoting a sense of well-being. \( ^11 \) Prevention of hypocapnia during several days of hypoxia has not, to our knowledge, been reported previously. In the present investigation we sought to determine whether the maintenance of normocapnia during the first 5 days at high altitude would prevent a decrease in stroke volume. The information obtained appears to provide a better understanding of adaptation to high altitude and circulatory control.

**Methods**

**SUBJECTS AND CONDUCT OF THE EXPERIMENT**

The 10 subjects were healthy male volunteers from the United States Army; each man gave informed consent prior to the study. Ages ranged from 18 to 22 years (mean, 20); heights from 170 to 188 cm (mean, 177); weights from 61.4 to 112.3 kg (mean, 75.8); and body surface areas from 1.76 to 2.35 m\(^2\) (mean, 1.91). The experiment was conducted in the hypobaric environmental chamber at the U.S. Army Research Institute of Environmental Medicine (USA-RIEM) at Natick, Massachusetts. During the first 2 weeks, with the chamber open to the ambient sea level pressure, the subjects were familiarized with the procedures, control measurements were made, and the methods were validated. During the mornings, measurements were made of alveolar gas tensions, venous blood was sampled on 2 days for measurement of hematocrit and the oxygen tension at 50% saturation and pH 7.40 \( (P_a = 495 \text{ torr}) \) and forearm plethysmography \( ^{12} \) was performed to measure venous compliance. Urine was collected for 24 hours on 2 consecutive days for measurement of volume and catecholamine excretion. \( ^{13} \) During the afternoons on 2 separate days, measurements were made of the subjects' ventilation, oxygen uptake, and heart rate at rest (sitting on the bicycle ergometer), during bicycle exercise at workloads of 300, 600, and 900 kilogram meters/ min (kg·m/min), and at maximum effort. During the second day of exercise, and for each level of activity, arterial blood was sampled for the measurement of gas tensions and hemoglobin concentration, and cardiac output was measured.

During the third week of the experiment, five subjects (CO\(_2\) group) were exposed to simulated high altitude at a barometric pressure \( (P_b) \) of 465 torr with 3.77% carbon dioxide added to the chamber. The purpose of this was to prevent alkalois and to lower the resting alveolar oxygen tension to a value not lower than 55 torr or higher than 60. To achieve this, on the second day it was necessary to lower the barometric pressure to 440 torr. The alveolar oxygen tensions averaged 56 ± 1 torr and the CO\(_2\) tensions 41 ± 2 torr during the 5 days of exposure to simulated high altitude. Daily measurements included alveolar gas tensions, forearm venous compliance, urinary catecholamine excretion, venous hematocrit, and ventilation during submaximal exercise. On the final day, measurements were made of arterial blood gas tensions, oxygen uptake, and cardiac output at rest and during exercise.

During the fourth week of the experiment, the other subjects (group without CO\(_2\)) were exposed to simulated high altitude \( (P_b = 495 \text{ torr}) \) without carbon dioxide supplementation. The purpose of the protocol for this group was to maintain, throughout the 5 days, the same alveolar oxygen tensions as in the CO\(_2\) group, but allowing the alveolar carbon dioxide tensions to fall. It was necessary on days 3 and 4 to lower the barometric pressure to 475 and 455 torr, respectively. For the 5 days the alveolar oxygen tension averaged 57 ± 5 torr, and the CO\(_2\) tension progressively fell to reach 27 ± 2 torr on the fifth day. Measurements were made at simulated high altitude as in the CO\(_2\) group.

One subject in the group without CO\(_2\) resigned from the study after 24 hours in the altitude chamber, and, on the final day at high altitude, a second subject developed a temperature of 38.5°C, which prevented his participation in the final measurements during exercise. Thus, only three subjects in the group without CO\(_2\) completed the entire protocol. The subjects were cooperative and no ill effects attributable to the study were observed.

**MEASUREMENTS**

The instruments used for ventilatory measurements consisted of a NOVA 1200 computer (Data General Corp.), an oxygen fuel cell, an infrared CO\(_2\) analyzer (Beckman, model LB-1), a thermocouple anemometer for measurement of expired air flow velocity (Technology Inc., model MFG-20H), a high velocity valve (Hans Rudolph), and, on the limb through which expired air was passed a 5-liter mixing chamber with an internal electric fan to ensure adequate mixing. For measurement of oxygen uptake, the oxygen and CO\(_2\) analyzers were used to sample the air in the mixing chamber, and the anemometer to measure the expired air velocity. The outputs from the analyzers and the anemometer were fed into the computer, which printed out the ventilation, gas concentrations, and calculated \( O_2 \) uptake as averaged values for successive 30-second intervals. Prior to measurements on each subject, the oxygen and CO\(_2\) analyzers were calibrated from tanks containing gas of known composition, and inspired air was analyzed for oxygen and CO\(_2\). At each simulated altitude, and usually for each subject, the expired volume measured by the anemometer and computer was compared to that simultaneously collected in a Douglas bag and measured with a Tissot spirometer. Analysis of the expired air within the bag allowed frequent checks on the validity of estimation of oxygen uptake by the computer system. Alveolar air was analyzed by constantly withdrawing air from the dead space of the Rudolph valve at 100 ml/min through the \( O_2 \) and CO\(_2\) analyzers.

In addition, the computer was programmed to accept, simultaneously with oxygen uptake data, the output from a
Lexington Instruments densitometer for the measurement of cardiac output using indocyanine green dye. The dye (5 mg), followed rapidly by 8 ml of saline, was injected through a 24-inch catheter which had been inserted percutaneously into an antecubital vein of one arm. Arterial blood was withdrawn at 20 ml/min by a Harvard withdrawal pump through an 18-gauge Jelco catheter 2½ inches long which had been inserted percutaneously into the brachial artery of the other arm; this blood (mixed with 0.5 ml of heparin) was returned to the subject through the arterial line. Arterial blood was sampled anaerobically with heparinized syringes at the conclusion of each cardiac output measurement. The blood was placed on ice, and was analyzed at 37°C within 30 minutes for oxygen tension, carbon dioxide tension, and pH; an Instrumentation Laboratories microelectrode system was used for this analysis. It was also analyzed for hemoglobin concentration, with a Coleman Jr., spectrophotometer. Venous blood, drawn from supine subjects without a venous occlusion tourniquet was analyzed for hemoglobin concentration and hematocrit, and to determine position of the Hb-O₂ dissociation curve, P₅₀. Forearm venous compliance, expressed as the increase in venous volume at a congesting pressure of 30 torr, VV₃₀, was measured with the subjects supine, using a water-filled plethysmograph.

Mean values and 1 standard error are presented in the tables and in the text. Differences between means were tested by the two-population t-test, and were considered significant when P < 0.05.

Results

BODY WEIGHT AND HEMATOCRIT

All five subjects in the CO₂ group gained weight (increments ranged from 1.3 to 3.3 kg), and all four subjects in the group without CO₂ lost weight (decrements ranged from 1.5 to 4.9 kg) during 5 days at high altitude. The hematocrits measured daily on the venous blood increased more in the group without CO₂ than in the group with CO₂ (Fig. 1). Assuming a constant red cell mass, these hematocrit changes would reflect decreases in plasma volume of 25% and 9%, respectively.

MEASUREMENTS RELATING TO O₂ TRANSPORT

In both groups the heart rate for a given oxygen uptake was greater at high altitude than at sea level. The maximum heart rate for both groups at low and at high altitude was approximately 180 beats/min. Stroke volume increased from rest to exercise (Fig. 2), as would be expected in subjects in the sitting position. Both at rest and during exercise stroke volume in the three subjects without CO₂ was less at high altitude than at sea level in 10 of the 12 paired measurements. Since two-way analysis of variance indicated that these effects of altitude on change in stroke volume were not related to the levels of activity studied, it was deemed permissible to pool these observed changes. Hence, the mean change in stroke volume resulting from exposure to high altitude was -17 ± 4 ml for the group without CO₂; this confirms previous reports. This decrease in stroke volume at high altitude did not occur with CO₂ supplementation. In fact, the values of stroke volume tended to be greater at high altitude than at sea level although the mean change of ±5 ± 4 ml was not significantly different from zero. These findings support the hypothesis upon which this investigation was based, namely, that if hypocapnia is prevented during adaptation to high altitude, then the usual decrease in stroke volume does not occur.

The arterial oxygen tensions at sea level in both groups remained above 90 torr for all levels of exertion. In both groups at high altitude, the arterial oxygen tensions were reduced, and decreased further as the subject went from rest to maximum exercise (Fig. 3). The arterial oxygen tensions tended to be lower for the CO₂ group than in the group without CO₂; for 600 kg-m/min and maximal exercise, the difference was significant. The calculated alveolar oxygen tensions at high altitude were not different between the groups and averaged 60 ± 1.0, 58 ± 1.0, 60 ± 1.0, 62 ± 1.0 torr for rest, 300 kg-m/min, 600 kg-m/min and maximum effort, respectively. The calculated alveolar-arterial oxygen gradients were greater for the CO₂ group than for the group without CO₂ at exercise loads of 600 kg-m/min and maximal exercise. Consequently, in spite of similar calculated alveolar oxygen tensions, arterial hypoxemia was much greater in the group with CO₂ (39 ± 1 torr) than in the group without CO₂ (48 ± 2 torr).

Arterial oxygen saturations were calculated from the values of pH and arterial oxygen tension in Table 1, and a standard oxygen hemoglobin dissociation curve at 37°C and the measured P₅₀ for each group. In both groups for all levels of exertion at low altitude, values of P₅₀ were 26 torr, yielding saturations of 97%. At high altitude, values of P₅₀ were 28 torr in both groups. As the subjects went from rest to maximal exercise, the mean calculated arterial oxygen saturations decreased from 86 ± 1% to 65 ± 2% in the CO₂ group, and from 89 ± 5% to 79 ± 3% in the group without CO₂. The lower pH (Table 1) in the CO₂ group displaced the oxyhemoglobin dissociation curve to the right in relation to the curve for the group without CO₂ and contributed to the lower calculated values of arterial oxygen saturation in subjects in the CO₂ group.

The arterial hemoglobin concentrations were not different between the two groups at sea level (Table 1). At high altitude, all measurements on subjects in the group without CO₂ were higher than any measurement on the CO₂ group subjects. The increased arterial hemoglobin concentrations in the group without CO₂ at high altitude offset the decrease in arterial oxygen saturations, and the calculated arterial...
oxygen content remained near the sea level value for all levels of exertion (Fig. 4). In contrast, the failure of the arterial hemoglobin concentration to increase in the CO₂ group subjects at high altitude, coupled with their lower arterial oxygen saturations, caused a large decrease in calculated arterial oxygen content during exertion (Fig. 4).

FOREARM VENOUS COMPLIANCE

The forearm venous compliance (VVsv) at low altitude of 3.1 ± 0.1 ml/100 ml for both groups, was not different from the value of 3.4 ± 0.1 previously reported for normal subjects.¹¹ The average of four daily measurements at high altitude for the groups with and without CO₂ (respectively, 2.5 ± 0.2 and 2.4 ± 0.2 ml/100 ml) were less than values for the control period. There were no differences between the groups.

**Table 1 Ventilatory, Blood Gas, and Hemodynamic Data at Sea Level and after 4 Days of Exposure to Simulated High Altitude with a CO₂-Enriched Atmosphere (CO₂ Group), or Without Supplemental CO₂ (Group without CO₂).**

<table>
<thead>
<tr>
<th>Exercise Load (kg-m/min)</th>
<th>VO₂ (liters/min STPD)</th>
<th>VO₂ (liters/min STPD)</th>
<th>Arterial PO₂ (torr)</th>
<th>Arterial PCO₂ (torr)</th>
<th>Arterial pH</th>
<th>Hb (g/100 ml)</th>
<th>SV (ml)</th>
<th>HR (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest (Pₘ 760)</td>
<td>10 ± 2.3</td>
<td>0.35 ± 0.05</td>
<td>95 ± 4</td>
<td>7.46 ± 0.01</td>
<td>15.6 ± 0.5</td>
<td>67 ± 5</td>
<td>84 ± 2</td>
<td></td>
</tr>
<tr>
<td>300</td>
<td>21 ± 0.7</td>
<td>0.95 ± 0.03</td>
<td>93 ± 2</td>
<td>7.43 ± 0.02</td>
<td>15.9 ± 0.4</td>
<td>87 ± 7</td>
<td>106 ± 6</td>
<td></td>
</tr>
<tr>
<td>600</td>
<td>35 ± 1.3</td>
<td>1.58 ± 0.06</td>
<td>92 ± 2</td>
<td>7.42 ± 0.01</td>
<td>15.3 ± 0.4</td>
<td>94 ± 15</td>
<td>138 ± 10</td>
<td></td>
</tr>
<tr>
<td>900</td>
<td>58 ± 4.7</td>
<td>2.35 ± 0.09</td>
<td>94 ± 3</td>
<td>7.37 ± 0.01</td>
<td>16.5 ± 0.6</td>
<td>93 ± 12</td>
<td>165 ± 12</td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>90 ± 7.6</td>
<td>3.10 ± 0.29</td>
<td>96 ± 5</td>
<td>7.31 ± 0.02</td>
<td>16.9 ± 0.5</td>
<td>93 ± 9</td>
<td>182 ± 5</td>
<td></td>
</tr>
<tr>
<td>Rest (Pₘ 440)</td>
<td>10 ± 0.3</td>
<td>0.39 ± 0.03</td>
<td>51 ± 1</td>
<td>7.44 ± 0.01</td>
<td>15.2</td>
<td>66 ± 9</td>
<td>106 ± 4</td>
<td></td>
</tr>
<tr>
<td>300</td>
<td>26 ± 1.4</td>
<td>1.05 ± 0.02</td>
<td>46 ± 2</td>
<td>7.43 ± 0.01</td>
<td>16.1</td>
<td>96 ± 13</td>
<td>130 ± 6</td>
<td></td>
</tr>
<tr>
<td>600</td>
<td>46 ± 4.3</td>
<td>1.72 ± 0.04</td>
<td>40 ± 1</td>
<td>7.37 ± 0.01</td>
<td>15.6 ± 0.4</td>
<td>100 ± 10</td>
<td>161 ± 8</td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>67 ± 4.4</td>
<td>2.08 ± 0.08</td>
<td>39 ± 1</td>
<td>7.32 ± 0.02</td>
<td>16.3 ± 0.7</td>
<td>98 ± 4</td>
<td>178 ± 5</td>
<td></td>
</tr>
<tr>
<td>Group without CO₂ (3 subjects)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest (Pₘ 760)</td>
<td>11 ± 1.0</td>
<td>0.32 ± 0.02</td>
<td>93 ± 6</td>
<td>7.45 ± 0.03</td>
<td>16.2 ± 0.4</td>
<td>75 ± 4</td>
<td>70 ± 6</td>
<td></td>
</tr>
<tr>
<td>300</td>
<td>23 ± 2</td>
<td>0.92 ± 0.03</td>
<td>94 ± 2</td>
<td>7.43 ± 0.02</td>
<td>16.8 ± 0.5</td>
<td>96 ± 5</td>
<td>94 ± 7</td>
<td></td>
</tr>
<tr>
<td>600</td>
<td>41 ± 3</td>
<td>1.56 ± 0.05</td>
<td>95 ± 1</td>
<td>7.41 ± 0.01</td>
<td>17.0 ± 0.8</td>
<td>103 ± 5</td>
<td>126 ± 7</td>
<td></td>
</tr>
<tr>
<td>900</td>
<td>62 ± 6</td>
<td>2.30 ± 0.04</td>
<td>96 ± 4</td>
<td>7.38 ± 0.01</td>
<td>17.6 ± 0.6</td>
<td>113 ± 4</td>
<td>162 ± 8</td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>119 ± 11</td>
<td>3.19 ± 0.19</td>
<td>101 ± 3</td>
<td>7.34 ± 0.02</td>
<td>17.2 ± 0.5</td>
<td>105 ± 7</td>
<td>181 ± 2</td>
<td></td>
</tr>
<tr>
<td>Rest (Pₘ 455)</td>
<td>10 ± 2.5</td>
<td>0.35 ± 0.02</td>
<td>56 ± 5</td>
<td>7.50 ± 0.01</td>
<td>18.0 ± 0.1</td>
<td>53 ± 7</td>
<td>95 ± 2</td>
<td></td>
</tr>
<tr>
<td>300</td>
<td>24 ± 4</td>
<td>1.02 ± 0.02</td>
<td>54 ± 2</td>
<td>7.48 ± 0.01</td>
<td>18.3 ± 0.2</td>
<td>88 ± 15</td>
<td>118 ± 7</td>
<td></td>
</tr>
<tr>
<td>600</td>
<td>42 ± 8</td>
<td>1.64 ± 0.04</td>
<td>50 ± 4</td>
<td>7.46 ± 0.02</td>
<td>18.6 ± 0.2</td>
<td>87 ± 7</td>
<td>159 ± 8</td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>70 ± 12</td>
<td>2.26 ± 0.18</td>
<td>48 ± 2</td>
<td>7.38 ± 0.01</td>
<td>19.4 ± 0.4</td>
<td>90 ± 13</td>
<td>179 ± 3</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Pₘ = barometric pressure (in torr); V̇ₑ = minute ventilation; V̇ O₂ = oxygen uptake; Hb = hemoglobin concentration; SV = cardiac stroke volume; HR = heart rate.

**Discussion**

Increased hematocrit,²⁶ negative water balance, and weight loss³⁶ are known to occur during the first week at high altitude, and total red cell mass is unchanged.² ¹ Thus, the increased hematocrits in our subjects not supplemented with CO₂ probably occurred because of intravascular water loss and contraction of the plasma volume which resulted in hemoconcentration and a decreased total blood volume. Dill

**Figure 2** Mean cardiac stroke volume (± SEM) at rest and during increased oxygen uptake with exercise. The five subjects in the group with CO₂ are shown on the left (solid circles), compared with the three subjects without CO₂ on the right (open circles). Resting and exercise measurements at sea level (Pₘ = 760 torr) and on the fifth day at high altitude (Pₘ = 440 or 455 torr) are indicated.

**Figure 3** Mean arterial oxygen tensions (± SEM) at rest and during exercise at high altitude in the five subjects in the group with CO₂ (solid circles) and the three subjects in the group without CO₂ (open circles).
decrease in blood volume. Alexander et al. found that at an altitude of 3,800 m also failed to show a decrease in stroke volume at an altitude of 3,100 m "a reduced blood volume was accompanied by a decrement in ventricular filling pressures at rest." Expansion of plasma volume by the administration of 500 ml of dextran to two subjects increased their right atrial volumes were not measured directly, presumably they were maintained near sea level values in the subjects given CO 2 at high altitude. However, prevention of alkalosis did not ameliorate venoconstriction during 5 days at high altitude. Thus, venoconstriction and hemoconcentration were dissociated in the subjects given supplemental CO 2. Possibly the forearm venous bed is not representative of veins in other parts of the body, or perhaps plasma volume changes at high altitude are mediated by other mechanisms, such as a decrease in renin and aldosterone secretion or in antidiuretic hormone.

The relationship between a decrease in plasma or blood volume at high altitude and the decreased stroke volume is uncertain. Although Asmussen and Consolazio found the initial decrease in plasma volume on Mount Evans (4,300 m) to be accompanied by an increased cardiac output, their rebreathing method may have overestimated cardiac output at high altitude. Klausen considered that the early decrease in blood volume at high altitude played an important role in causing the decrease of cardiac output, because the only subject of three who failed to show a decrease in stroke volume at an altitude of 3,800 m also failed to show a decrease in blood volume. Alexander et al. found that at an altitude of 3,100 m "a reduced blood volume was accompanied by a decrement in ventricular filling pressures at rest." Expansion of plasma volume by the administration of 500 ml of dextran to two subjects increased their right atrial pressures. However, in only one of the subjects did the stroke volume approach sea level values. Interpretation of these results is difficult because of the sequential influence of multiple bouts of exercise which tends to decrease stroke volume. Therefore, they concluded tentatively that decreased filling pressures at high altitude did not entirely explain the decreased stroke volume.

Our present study at high altitude indicated that the stroke volumes at rest and during exercise were maintained at sea level values in the normocapnic subjects. The maintenance of plasma volumes, acting through the Frank-Starling mechanism, may have maintained filling pressure (not measured) and therefore stroke volume. In addition, urinary catecholamine excretion was greater in the CO 2 group than in the group without CO 2. Higher levels of circulating catecholamines could serve to increase myocardial contractility which, at a constant filling pressure, would increase stroke volume. Indeed, sympathetic stimulation is important in maintaining myocardial contractility in goats at an altitude of 4,300 m. Perhaps the level of sympathetic activity affecting both contractility and stroke volume at high altitude is the additional factor postulated by Alexander et al.

Despite the greater catecholamine excretion and maintenance of blood volume and stroke volume, maximum oxygen uptake at high altitude was not higher in the CO 2 group than in the group without CO 2. In the groups with and without CO 2, respectively, the maximum oxygen uptake at high altitude were 67% and 72% of the sea level value, compared to the 70% predicted for the altitude of 4,300 m. The CO 2 group during heavy exercise had a large decrement in calculated arterial oxygen content, which was the compound result of an acid pH, a low arterial oxygen capacity, and a lowered arterial oxygen tension. Thus, in the CO 2 group the "advantage" of maintained blood volume and stroke volume was offset by a reduced arterial O 2 content during heavy exercise. The more acid pH resulted from the addition of carbon dioxide to the environment in keeping with the experimental design. The low arterial oxygen capacity resulted from the failure of hemoconcentration, presumably as a consequence of the maintained plasma volume. Least expected, and least well understood, was the low arterial oxygen tension during maximal and submaximal exercise. The calculated alveolar oxygen tension was not lower in the CO 2 group and the values of approximately 60 torr for both groups is close to those found in acclimatized subjects at 4,300 m. Furthermore, the presence of a carbon dioxide tension normal for sea level per se, would not impede oxygen diffusion from alveolus to blood.

The pulmonary capillary blood volume, membrane diffusing capacity, and ventilation to perfusion ratios all affect the gradient for oxygen transport across the lung but were not evaluated in this study. However, the addition of CO 2 to the inspired air at sea level causes the measured end-tidal (and mixed expired) PCO 2 to exceed that in the arterial blood. Either pulmonary capillary PCO 2 is higher than that measured in arterial blood, or CO 2 excretion proceeds against a CO 2 gradient. Were the effect present at high altitude at an alveolar PCO 2 of 40 torr, the alveolar PCO 2 would exceed arterial PCO 2, invalidating our use of the alveolar air...
equation. The true alveolar $O_2$ tensions then would be less than those calculated and contribute to the exaggerated hypoxemia observed in the $CO_2$ group.

The present investigation has confirmed previous reports\(^3\)\(^-\)\(^9\) that, in the usual high altitude environment, the body "elects" to transport oxygen by using a lower blood volume, a lower cardiac output, and a higher hemoglobin concentration than at sea level. Addition of carbon dioxide to the high altitude environment, through mechanisms yet undefined, prevents the early increase in hemoglobin concentration and exaggerates the arterial hypoxemia. Consequently, transport of the same quantity of oxygen occurs at a somewhat higher stroke volume and a reduced arterial oxygen content.

Acknowledgments

We gratefully acknowledge the valuable assistance of the chamber operators, James A. Devine, Joseph F. Gardella, and Edward J. Powers, and observers, A.G. Bagtas, M.J. Bharmal, J.T. Crepeau, L.M. Dong, J.M. Foster, and J.C. Howell, and the technical research support of Robert Mello, Charles Bravo, and William Clifford. We also thank Eleanor Register for editing and Diann Smith for preparing the manuscript. We are grateful to Drs. F. G. Heineken and Giles F. Filley for the hours spent in analyzing and discussing our data.

References

2. Klausen K: Cardiac output in man in rest and work during and after acclimatization to 3800 m. J Appl Physiol 21: 609-616, 1966
Maintained stroke volume but impaired arterial oxygenation in man at high altitude with supplemental CO2.

R F Grover, J T Reeves, J T Maher, R E McCullough, J C Cruz, J C Denniston and A Cymerman

*Circ Res.* 1976;38:391-396
doi: 10.1161/01.RES.38.5.391

*Circulation Research* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1976 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/38/5/391

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation Research* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation Research* is online at:
http://circres.ahajournals.org/subscriptions/