Effects of Acute Hypoxia on the Volume of Blood in the Thorax

By H. W. Fritts, Jr., M.D., J. E. Odell, M.D., P. Harris, M.D., E. W. Braunwald, M.D., and A. P. Fishman, M.D.

The results presented in the first paper of this series confirm the observations of others that acute hypoxia frequently raises the pulmonary arterial pressure in normal man. This pressor effect cannot be solely attributed to an augmented cardiac output, nor can it be ascribed to an elevated left atrial pressure. It seems, therefore, to arise from a change in the dimensions of some portion or portions of the pulmonary vascular bed.

Whether this change involves an alteration in the pulmonary blood volume has not been settled, since experiments in man and in animals have yielded conflicting results. The present study was designed to investigate the relation between volume and pressure by using two dissimilar methods. The first entailed measuring the central blood volume before and during hypoxia; the second involved recording the change in the relative weights of the two ends of the body when hypoxia was induced.

Methods

Measurement of Central Blood Volume

The central blood volume was measured by using the dye-dilution method of Hamilton. For this purpose, a no.-8 cardiac catheter was advanced until its tip lay in the main pulmonary artery and a Cournand needle was inserted into the right brachial artery. The patient was then allowed to rest for 15 minutes before observations were begun.

The experimental protocol comprised 2 20-minute breathing periods, separated by a 10-minute interval of rest. Eight of the 25 patients breathed 21 per cent oxygen during both periods; the remaining 17 breathed 21 per cent oxygen during the first and either 14 per cent or 12 per cent oxygen during the second period.

Pressures were recorded at 2-minute intervals from the pulmonary and brachial arteries. At the eighteenth minute, 4 ml. of Evans blue dye were rapidly injected through the catheter into the pulmonary artery. A dilution curve was inscribed from the brachial artery by withdrawing blood at a constant rate of 0.5 ml. per second through a Colson densitometer. The concentration of dye in plasma was read in a Beckman Model DU spectrophotometer. This value was used to calibrate the dye curve according to the pooled-sample method of McNeely and Gravellese. The calibrated curve, used in conjunction with the formulas of Hamilton, and after allowance was made for the amount of dye retained in the catheter, provided estimates of the cardiac output, the mean circulation time, and the central blood volume.

Determination of Distribution of Weight

For these studies, each subject lay supine on a teeter-board constructed of light-weight pine and plywood. The board was balanced on a fulcrum which could be adjusted to the approximate horizontal level of the center of gravity of the combined mass of the board and the subject (fig. 1). A spring held the board in position; it had a linear coefficient of elasticity over the range of motion involved in the experiments. A dashpot filled with mineral oil damped the rapid oscillations caused by the respiratory movements of the chest and abdomen, and by the beating of the heart. The balance of the board was such that a 50-Gm. weight placed 10 cm. from the fulcrum deflected the kymograph pen approximately 1 cm.

Each subject lay on the board for approximately 2 hours. During the first hour no observations were recorded because experience indicated that this was a minimal period for the 2 ends of the body to attain stable weights. To ensure that stability had been achieved by the end of the hour, 3 records were obtained at 10-minute intervals. The subject then breathed 21 per cent oxygen.
HYPOXIA AND THORACIC BLOOD VOLUME

Figure 1
Schematic drawing of a teeter-board.

Figure 2
Effect of (A) hypoxia and (B) norepinephrine on the relative weights of the 2 ends of the body. Response marked CAL indicates effect of placing a 50-Gm. weight 10 cm. from fulcrum on head-end of the board.

ox oxygen through a mouthpiece for 20 minutes while a continuous tracing of the kymograph pen was recorded and a sample of arterial blood was collected. At the end of this period, the 21 per cent oxygen mixture was replaced by one containing 12 per cent oxygen. The tracing was again recorded and, after 20 minutes of hypoxia, another sample of arterial blood was drawn. In the majority of the subjects the hypoxia period was followed by a second control period. A typical tracing is reproduced in figure 2A.

Subjects
All subjects were either normal laboratory workers or convalescent patients without cardiac or pulmonary disease. Each had fasted for 12 hours before the study. None received premedication.

Results
Subjects in Whom Two Measurements of Central Blood Volume Were Made While They Breathed Ambient Air
The studies in these 8 patients were designed to test the reproducibility of the measurement of the central blood volume in persons lying quietly at rest. Although the average of the volumes measured in the first breathing period was virtually identical with the average of the volumes measured in the second, our data, like those of Doyle, Wilson, Lépine, and Warren,14 demonstrated considerable variation between the 2 measurements in individual patients. When the difference between the volumes measured in each patient was divided by the first volume, the range extended from -11 to +12.6 per cent, with an average difference of -1.9 per cent. With the assumption that these differences had a Gaussian distribution, their standard deviation was 7.33 per cent. Hence, 2.58 standard deviations, the number necessary to include 99 per cent of the observations, was ±18.91 per cent.

Patients in Whom the Central Blood Volume Was Measured before and during Hypoxia
The volumes measured in the 17 patients who were made hypoxic are recorded in table 1. The values obtained while they breathed 21 per cent oxygen gave an average volume of 0.79 L./M.², and a standard deviation of 0.119 L./M.². The volumes measured during hypoxia gave an average value of 0.81, and a standard deviation of 0.566 L./M.². When analyzed by the “t” test of Fisher, the difference between the averages was not significant (p>.10).

The changes in volume are depicted graphically in figure 3. Each bar represents a single patient. The length of the bar represents the percentage change in volume calculated as the difference between the ambient air and hypoxic values divided by the ambient air value. In only 2 patients (J.O'C. and J.H.) did the percentage change exceed the limits

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of ±18.91 per cent calculated for all 8 subjects.

Despite the lack of change in the central blood volume, hypoxia exhibited its usual pressor effect on the pulmonary arterial pressure. Thus, the average value during the control period was 13.7 mm Hg and during the period of hypoxia it rose to 18.7 mm Hg. This difference would have arisen by chance less frequently than 1 in 100 times (p. < .01).

**Patients Studied on the Teeter-Board**

None of the 9 patients studied on the teeter-board demonstrated any change in the position of the center of gravity during hypoxia, despite the fact that arterial saturations as low as 62 per cent were induced. A typical record is shown in figure 2A, and is contrasted with a tracing recorded during an infusion of norepinephrine (fig. 2B). In the latter instance, the center of gravity shifted toward the head-end of the body.

**Discussion**

In the studies reported in the preceding paper, the cardiac output was measured by the Fick principle and the importance of the steady-state was emphasized. In the present studies, the cardiac output was measured by the dilution principle and safeguards of the same sort were applied. The most frequent difficulty was imposed by an unstable densitometer baseline during the hypoxic period. This unsteadiness was caused by variations in the oxygen saturation of the blood in the systemic arteries, and in 12 patients the fluctuations were so large that the data were discarded. In the patients included in this report, baselines recorded over a period of 20 seconds showed variations that were less than 5 per cent of the maximum height of the curve.

The central blood volume as measured in these studies included not only the blood in

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**Table 1**

**Changes in Arterial Blood Oxyhemoglobin Saturation, Pulmonary Arterial Pressure, Cardiac Index, Mean Circulation Time, and Central Blood Volume during Acute Hypoxia in Seventeen Normal Subjects**

<table>
<thead>
<tr>
<th>Breathing mixture: Ambient air</th>
<th>Breathing mixture: 12-14% O₂ in N₂</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subject</strong></td>
<td><strong>Arterial blood O₂ sat. %</strong></td>
</tr>
<tr>
<td>J.O.</td>
<td>98</td>
</tr>
<tr>
<td>C.D.</td>
<td>93</td>
</tr>
<tr>
<td>J.O.C.</td>
<td>91</td>
</tr>
<tr>
<td>P.M.</td>
<td>95</td>
</tr>
<tr>
<td>M.B.</td>
<td>94</td>
</tr>
<tr>
<td>E.J.</td>
<td>98</td>
</tr>
<tr>
<td>A.O.</td>
<td>95</td>
</tr>
<tr>
<td>C.G.</td>
<td>98</td>
</tr>
<tr>
<td>J.L.</td>
<td>94</td>
</tr>
<tr>
<td>W.M.</td>
<td>96</td>
</tr>
<tr>
<td>V.P.</td>
<td>95</td>
</tr>
<tr>
<td>H.C.</td>
<td>95</td>
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<tr>
<td>J.H.</td>
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<td>A.P.</td>
<td>93</td>
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<tr>
<td>A.C.</td>
<td>96</td>
</tr>
<tr>
<td>O.S.</td>
<td>97</td>
</tr>
<tr>
<td>G.Y.</td>
<td>96</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>95</td>
</tr>
</tbody>
</table>
the pulmonary vessels, but that contained in
the chambers of the left heart and that seg-
ment of the aorta and its branches that lay
at points temporally equidistant from the
aortic valve. In keeping with the observa-
tions of Doyle, Wilson, and Warren, our
results indicated that hypoxia did not alter
this volume of blood.

Furthermore, no shift in the center of grav-
ity could be demonstrated when hypoxia was
induced in patients lying on the teeter-board.
These results confirm and extend earlier ob-
servations from this laboratory and agree
with those published by Honig and Tenney.
According to the calibration, the teeter-board
would have disclosed a change in the pul-
monary blood volume of 50 ml or less, if the
blood moved through a distance of 10 cm
along the length of the body. These observa-
tions support the measurements of the cen-
tral blood volume in indicating that the
volume of blood in the thorax does not change
appreciably during hypoxia.

Summary

Two different methods were used to study
the effect of acute hypoxia on the volume of
blood in the thorax. The first method entailed
estimating the central blood volume by the
Stewart-Hamilton dye-dilution technic; the
second involved the use of a teeter-board. The
2 methods gave comparable results. Both in-
dicated that the volume of blood in the thorax
is not appreciably altered by hypoxia.

Summarro in Interlingua

Duo differente methodos esseva usate pro studiar le
effecto de hypoxia acute super le volumine del san-
guine in le thorace. Le prime del duo methodos con-
sisteva in estimar le volumine de sanguine central
per medio del technica a dilution de colorante se-
cundo Stewart-Hamilton; le secundo utilissiava un
plana basculante. Le resultatos obtinente per le duo
methodos esseva comparabile. Ambes indicava que le
volumine de sanguine in le thorace non es alterate
appreciabilemente le effectos de hypoxia.

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