Arterial and pulmonary arterial hemodynamics and oxygen delivery/extraction in normal humans exposed to hyperbaric air and oxygen

Lindell K. Weaver,1,2,3 Steve Howe,2 Gregory L. Snow,4 and Kayla Deru2

1Pulmonary/Critical Care Medicine and 2Hyperbaric Medicine, LDS Hospital, Salt Lake City; 3Department of Medicine, University of Utah School of Medicine, Salt Lake City; and 4Statistical Data Center, LDS Hospital, Salt Lake City, Utah

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THOUSANDS OF PATIENTS have been treated with hyperbaric oxygen (HBO2); however, the precise arterial and pulmonary arterial (PA) hemodynamic and gas exchange responses that occur during HBO2 are not clearly known. Determining precise hemodynamic and gas exchange information requires the subject or patient to be instrumented with arterial and PA (Swan-Ganz) catheters, permitting measurement of intravascular pressures and blood gases, and PA catheter data collected in normal humans exposed to HBO2 has been reported only once (24).

It has long been established that heart rate (HR) falls during HBO2 (3). Forty years ago, investigators reported that this reduction in HR was associated with decreased cardiac output (Q) (48), an observation supported by subsequent research Table 1 (21, 24, 27, 29, 48). Generally accepted hemodynamic effects of HBO2 now “include mild bradycardia, leading to a proportional decline in Q and a small increase in systemic vascular resistance” (28).

As Q falls, O2 consumption (V02) may remain constant if O2 extraction increases proportionally. No report of VO2 or O2 extraction under hyperbaric conditions has been published.

HBO2 can precipitate acute pulmonary edema in patients with reduced left ventricular function (43), possibly due to high O2 concentrations reducing myocardial relaxation factor (nitric oxide), thereby making the heart stiffer (23), or by an increase in afterload from increased systemic vascular resistance (48). The systematic recording of intracardiac filling pressures of humans during HBO2 exposure is limited to measurements at 3.0 atmospheres absolute (atm abs; 304 kPa) (24).

A wider alveolar-to-arterial PO2 difference (A-aDO2) than predicted has been observed in normal humans exposed to HBO2 (45). These data suggest an unexplained increase in right-to-left intrapulmonary shunt fraction (Qs/Qt), or venous admixture, due to HBO2, but Qs/Qt measurements during HBO2 have not been published.

A description of the technique of using a PA catheter in patients treated in the monoplace hyperbaric chamber is available (41), and hemodynamic data obtained during HBO2 therapy in critically ill patients have been presented (40), but these data from critically ill patients may not extrapolate to hemodynamic effects due to HBO2 in normal humans.

The purpose of the present study was to measure the hemodynamic and blood gas responses of normal humans instrumented with arterial and PA catheters under hyperbaric air and HBO2 conditions.

METHODS

The Institutional Review Board at the LDS Hospital approved the study protocol. After signing informed consent and completing a prehyperbaric exposure history and physical examination, 10 normal, healthy subjects (5 males and 5 females) between the ages of 18 and 41 yr were selected for participation in this study. None of the subjects had evidence of cardiac or pulmonary disease. None of the subjects smoked or were taking medications, including birth control pills. At least 24 h before undergoing catheter cannulation, each subject was compressed in a monoplace hyperbaric chamber (model 2500B; Schust Industries, Anaheim, CA) to 3.0 atm abs to be confident the
subject could equalize middle ear pressure and could tolerate the confines of the chamber.

The subjects were encouraged to eat breakfast on the day of the experiment. No further nutrition was allowed during the data collection period. Water intake was permitted and was quantified.

The subject was placed supine and had five-lead electrocardiography (ECG) monitoring (GE Healthcare, Little Chalfont, UK). One percent lidocaine without epinephrine (1 ml) was injected as a local anesthetic in the dermis and subcutaneous space of the right subclavian cannulation site. A PA catheter (8 Fr, continuous cardiac output and mixed venous Oximetrix with extra infusion port; Baxter Healthcare, Irvine, CA) was placed through a 9-Fr Introducer sheath (Arrow International, Reading, PA) inserted in the right subclavian vein following standard aseptic techniques. The PA catheter distal port was confirmed with both the arterial and PA catheters before data collection for all subjects (15).

All thermal dilution saline injection Q˙ measurements (10 ml injected with in-line temperature measurements) were performed by one individual with extensive bedside critical care nursing experience using ied normal saline for bolus Q measurements injected through the injection port of the PA catheter, located outside the chamber (41). To verify reproducible Q measurements, we plotted the injection pressure vs. time of injection. A pressure transducer was connected with a four-foot luer-lock neonatal high-pressure monitoring line (Argon Medical Devices, Athens, TX) to a four-way stopcock (Baxter Healthcare), in-line with the Q syringe. A computer displayed a plot in real time of injection pressure vs. time. Successive Q measurements overlaid the previous displays on the computer screen. Five Q injections were performed at each sampling time. The three that had virtually identical pressure vs. time curves were selected for averaging as the thermal dilution Q value. The Baxter monitor displayed a conventional change in temperature vs. time with each of the injections of ied saline, and for selection, these individual Q measures also fell within ±10% of one another.

Collected baseline data included body surface area (BSA), subject core temperature as measured by PA catheter (T), HR, respiratory rate (RR), systemic blood pressure (BP), mean systemic blood pressure (MBP), PA pressure (PAP), mean PA pressure (MPAP), RA pressure (RAP), wedge pressure (balloon occlusion pressure; PAWP), RQ, arterial blood gas data including arterial pH (pHa), arterial partial pressure of CO₂ (Paco₂), PaO₂, arterial O₂ saturation (Sao₂), arterial hemoglobin (Hba), mixed venous pH (pHv), mixed venous partial pressure of CO₂ (PvCO₂), mixed venous partial pressure of O₂ (PvO₂), SvO₂, mixed venous hemoglobin (Hbv), Q by thermal dilution, and

Table 1. Previous cardiac output studies in humans exposed to hyperbaric oxygen

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Technique</th>
<th>No. of Subjects</th>
<th>Pcb, atm abs</th>
<th>FIo₂</th>
<th>HR, beats/min</th>
<th>MBP, Torr</th>
<th>Q, l/min</th>
<th>SVR, dyn·s·cm⁻¹·m⁻⁴</th>
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<tr>
<td>Whalen et al. (48)</td>
<td>1965</td>
<td>Indicator dilution</td>
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<td>−5</td>
<td>1</td>
<td>−5</td>
<td>5</td>
</tr>
<tr>
<td>Kenmure et al. (21)</td>
<td>1972</td>
<td>Indicator dilution</td>
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<td>−1</td>
<td>−7</td>
<td>3</td>
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<tr>
<td>Pisarello et al. (29)</td>
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<td>20</td>
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<td>1.00</td>
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<td>2</td>
<td>−8</td>
<td>12</td>
</tr>
<tr>
<td>Pesala et al. (27)</td>
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<td>Impedance</td>
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<td>McMahon et al. (24)</td>
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<td>Thermal dilution</td>
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<td>3</td>
<td>1.00</td>
<td>−10</td>
<td>−1</td>
<td>−8</td>
<td>8</td>
</tr>
</tbody>
</table>

Percentage changes from breathing air at 1 atm abs.

Values are percent changes from breathing air at 1 atm abs. Pcb, chamber pressure; FlO₂, fraction of inspired O₂; HR, heart rate; MBP, mean systemic blood pressure; Q, cardiac output; SVR, systemic vascular resistance. *P < 0.05, significant difference from breathing air at 1 atm abs.
cardiac index (CI). Calculated baseline data include stroke volume (SV), right-to-left shunt fraction (Qa/Qs) (47), systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) (25). O₂ content by arterial (CaO₂) and mixed venous (CvO₂) measurement, O₂ extraction (CaO₂ - CvO₂), O₂ delivery (QO₂), and VO₂.

The subjects were compressed on air in the monoplace hyperbaric chamber to 3.0 atm abs (304 kPa), 2.5 atm abs (253 kPa), 2.0 atm abs (203 kPa), 1.3 atm abs (132 kPa), 1.2 atm abs (113 kPa), and then back to 0.85 atm abs (86 kPa) (barometric pressure at our altitude of 1,500 m above sea level) (Fig. 1). Upon completion of the first compression sequence with air and data gathering, the subject breathed 100% O₂ via a 100% O₂ reservoir bag through a one-way flow-directed valve (model 2600; Hans Rudolph, Kansas City, MO) fitted with a SCUBA mouthpiece while wearing a nose clip (chamber hatch slightly open). After the chamber hatch was closed, each subject continued to breathe 100% O₂ by demand regulator (model L451; Life Support Products, St. Louis, MO) supplied with 100% O₂ inside the chamber until we verified that the chamber O₂ concentration was ≥98% O₂. The chamber gas concentration was measured by placing a gas sampling line just above the subject’s face, passing chamber gas out through a pass-through in the chamber hatch while measuring O₂ concentration with an O₂ analyzer, calibrated according to the manufacturer’s recommendations. Once the chamber O₂ concentration measured ≥98%, the subject discontinued use of the demand regulator and breathed chamber O₂. The compression and data collection sequence was repeated in the same fashion on 100% O₂ (Fig. 1).

This compression sequence maximized the hemodynamic and blood gas data obtained while minimizing risk of decompression sickness to the subjects. The air compression was required to separate effects due to hyperbaric pressure from those due to 100% O₂. The decompression stops and times (1.3 and 1.12 atm abs, respectively) for the air compression were derived from the US Navy Dive Manual (9) using cross-corrections for altitude “diving” (1,500 m above sea level) (4).

Hemodynamic data were obtained at all pressure levels except 1.3 atm abs pressure, after 10 min at each pressure exposure and 30 min postcompression for both the air and O₂ exposures (Fig. 1). Arterial and PA mixed venous blood were simultaneously sampled at each data point. The blood gases were measured with an ABL 330 (Radiometer). Data collected included T, HR, RR, BP, MBP, PAP, MPAP, RAP, PAWP, pH, Pao₂, Paco₂, Saco₂, Hba, PvO₂, Pvo₂, SvO₂, Hbh, and Q by bolus injection thermal dilution, CI, and Q and Paco₂ by continuous measurement. SV, Q/Qo, PVR, Cao₂, CvO₂, Cao₂ - CvO₂, Qo₂, and VO₂ were calculated for each data collection point.

Data for each hemodynamic parameter were tallied on a universal flow sheet and subsequently entered into a computerized database, with double checking for accuracy. The chamber T, HR, BP, RAP, and PAP values were continuously measured and stored every 5 min automatically by the HELP system at LDS Hospital (16, 17).

There was an obligate blood loss of ~150–200 ml per subject throughout the entire investigation. The subjects received ~800–1,200 ml of intravenous normal saline due to the number of bolus injection Q measurements (5 injections of 10 ml each at each data-gathering condition) during the experiment. The subjects were weighed before and after the experiment. Urine output was quantified.

After compression with O₂, data were recorded 30 min after atmospheric pressure was reached with the subject breathing 100% O₂ and, finally, after 30 min with the subject breathing air. At this point in time, the experiment was concluded. The PA catheter and the arterial catheters were withdrawn, and firm pressure was held for 10 min with suitable dressings applied. The subjects were encouraged to eat as needed and not to ascend in altitude for at least 24 h. The subjects also were encouraged to notify us if they had complaints referable to the study, especially if they had manifestations of decompression sickness. The subjects were evaluated the following day to ensure adequate hemostasis at the catheter sites and to discuss any worries or concerns.

The data collected by the continuous cardiac output catheter system and intra-arterial continuous O₂ sensor are not presented in this report. Transcutaneous O₂ and CO₂ data collected at this time, compared with PaO₂ and PacO₂, are available elsewhere (42).

For the Q/Qo or venous admixture calculations (47) and for all arterial content of O₂ calculations, we averaged all Hba values. Similarly, for the contents of O₂ in PA blood, all Hbh values were averaged. This averaging was done to minimize possible confounding errors from minor differences in hemoglobin concentrations from across conditions. We did not average hemoglobin when reporting arterial content of O₂ calculations, we averaged all Hba values.

Statistical methods. Data were analyzed using mixed-effects regression models where each subject was allowed to have a different random intercept, but the overall pattern was consistent between subjects. Each response was modeled separately using a guided random intercept, and finally, after 30 min with the subject breathing air. At this point in time, the experiment was concluded. The PA catheter and the arterial catheters were withdrawn, and firm pressure was held for 10 min with suitable dressings applied. The subjects were encouraged to eat as needed and not to ascend in altitude for at least 24 h. The subjects also were encouraged to notify us if they had complaints referable to the study, especially if they had manifestations of decompression sickness. The subjects were evaluated the following day to ensure adequate hemostasis at the catheter sites and to discuss any worries or concerns.

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Statistical methods. Data were analyzed using mixed-effects regression models where each subject was allowed to have a different random intercept, but the overall pattern was consistent between subjects. Each response was modeled separately using a guided stepwise procedure starting with the model that the response is predicted by gas and pressure (with a possibility of different slopes on pressure for air and O₂). Additional models were fit to see whether simpler models fit or if a more complex model was needed to best fit

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**Fig. 1.** Timeline for placing arterial and pulmonary arterial (PA) catheters, when and under what conditions data were collected, while the subject was exposed to hyperbaric pressure in a monoplace hyperbaric chamber. Fio₂, fraction of inspired O₂; CXR, chest radiographs.
the data (curved relation with pressure, individual time points needing an offset from the base model). All tests were done using $\alpha = 0.05$ (2-sided). Descriptive data are expressed as means (SD).

**RESULTS**

Baseline characteristics of individual research subjects are shown in Supplemental Table 1. (Supplemental data for this article is available online at the *Journal of Applied Physiology* website.) One-half of the subjects were male. The subjects had no identified comorbid conditions or influences. All subjects completed the study protocol.

The baseline condition RQ was 0.87 (0.14). Average Hba across all experimental conditions was 14.2 (1.4) mg/dl. The average total blood loss was 185.3 (21.0) ml. The baseline Hba was 14.6 (1.4), and the final Hba was 14.2 (1.5). The baseline weight was 70.4 (13.2) kg, and the final weight was 69.8 (14.0) kg. The normal saline administered was 1,038 (352) ml. The liquid oral intake was 97 (77) ml. The urine output was 630 (299) ml. No complications were noted. The inside chamber temperature increased 3°C with chamber compression and then sloped downward to baseline as the chamber was decompressed (for chamber and subject temperature under experimental conditions, see Supplemental Fig. 1).

Results from this study are depicted in Figs. 2–9. Supplemental Table 2 reports mean change from baseline for each condition. The slopes are shown in Supplemental Table 1. (Supplemental data for this article is available online at the *Journal of Applied Physiology* website.) One-half of the subjects were male. The subjects had no identified comorbid conditions or influences. All subjects completed the study protocol.

Average systolic BP was related to hyperbaric pressure, both on air and on O2 ($P < 0.001$). Systolic PAP dropped 1.52 Torr for each 1 atm abs pressure increase ($P < 0.001$). With the first O2 breathing interval at 0.85 atm abs (*condition 7*) and at the conclusion of the experiment (*condition 13*), breathing air at 0.85 atm abs, systolic PAP was 1.52 Torr lower for *condition 7* and 2.15 Torr higher for *condition 13* than predicted based on pressure measurements alone. Average diastolic PAP was 0.54 Torr lower per 1 atm abs pressure increase while subjects were exposed to air ($P = 0.005$). Average MPAP decreased 0.85 Torr per 1 atm abs increase in pressure ($P < 0.001$) and was 0.9 Torr lower during O2 exposure ($P = 0.002$). Average PAWP increased 0.67 Torr while subjects were breathing HBO2 ($P = 0.005$).

Cardiac output. The thermal dilution Q˙ decreased from baseline 0.19 l/min per 1 atm abs increase in pressure ($P = 0.002$). Q˙ was 0.46 l/min lower while subjects were breathing O2 than while breathing air ($P = 0.001$). The CI dropped 0.11 l·min$^{-1}$·m$^{-2}$ for each 1 atm abs increase in pressure ($P = 0.001$). The CI was 0.25 l·min$^{-1}$·m$^{-2}$ lower while subjects were breathing O2 than while breathing air ($P = 0.002$) (Figs. 4 and 5).

Arterial blood gases. Results are depicted in Fig. 6. pH dropped during hyperbaric air and was higher than baseline during HBO2 exposure. $P_{CO2}$ was lower during HBO2 expo-

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**Fig. 2.** Heart rates (HR; A), respiratory rates (RR; A), and mean arterial blood pressures (MBP; B) of subjects exposed to hyperbaric air and hyperbaric oxygen (HBO2). Values are means ± SE. HR dropped with both hyperbaric air and HBO2 exposures compared with baseline, with a larger reduction during HBO2 exposure. RR trended downward from baseline with hyperbaric air exposure and was lower than baseline during HBO2 exposure at 3.0 and 2.5 atm abs. Systolic BP was higher with O2 than air breathing. Diastolic BP and MBP did not change across the hyperbaric air and HBO2 conditions. Systolic and diastolic systemic BP values are shown in Supplemental Fig. 2.
Fig. 3. Right atrial pressures (RAP), mean pulmonary arterial pressures (MPAP), and PA catheter balloon occlusion pressures, or PA wedge pressures (PAWP), of subjects exposed to hyperbaric air and HBO2. Values are means ± SE. The RAP elevation under condition 11 (100% O2 at 1.12 atm abs) is explained by 2 subjects. The systolic PAP and MPAP values were lower than baseline during hyperbaric air and HBO2 exposures. The PAWP value increased compared with baseline during HBO2 exposure. Systolic and diastolic PaCO2 occurred at 100% O2 at 3 atm abs and increased as HBO2 pressure decreased. The PaO2 measurements were in the range predicted based on the subjects’ inhaled partial O2 pressures.

Pulmonary arterial (mixed venous) blood gases. Results are depicted in Fig. 7. pHV was essentially constant across test conditions. PVCCO2 was lower during HBO2 exposure at 3.0 and 2.0 atm abs (P = 0.02). PVCO2 and SVCO2 were elevated during hyperbaric air and O2 exposures.

Calculations from arterial and pulmonary arterial measurements. CaO2 and CVo2 increased as the partial pressures of inhaled O2 increased, during both hyperbaric air and HBO2 exposures (Fig. 8). From the mixed-effects model, CaO2 – CVo2 increased 0.18 Torr with each 1 atm abs increase in air pressure (P = 0.006). CaO2 – CVo2 increased 0.61 Torr for each 1 atm abs pressure increase with O2 breathing (P < 0.001). CaO2 – CVo2 was higher during HBO2 breathing at 3.0, 2.5, and 2.0 atm abs (Fig. 8). The QO2 delivery (Q x PAO2) and VO2 [Q x (CAO2 – CVo2)] were relatively constant across test conditions (Fig. 8).

There was no significant change in SV across conditions (Fig. 9). From the mixed-effects model, SVR increased 38.7 dyn·s·cm⁻⁵ with each 1 atm abs increase in air pressure (P = 0.003). SVR was higher during HBO2 breathing at 2.5 and 2.0 atm abs compared with baseline (Fig. 9). From the mixed-effects model, PVR decreased 15 dyn·s·cm⁻⁵ with each 1 atm abs increase in pressure (P < 0.001) and was 39.4 dyn·s·cm⁻⁵ lower with HBO2 than air exposure (P < 0.001). Q/QI was 15% during all air breathing periods at 0.85 atm abs. During both hyperbaric air and HBO2 breathing, Q/QI decreased. This change was greater during HBO2 than hyperbaric air breathing (Fig. 9).

DISCUSSION

This is the only study that reports arterial and PA hemodynamic measurements with blood gases of healthy volunteers exposed to both hyperbaric air and HBO2. Limited observations in prior human studies measuring Q suggest that HR and Q decrease ~20% during HBO2 exposure (21, 24, 27, 29, 48). In our subjects, we noted a decrease in HR with exposure to hyperbaric air and HBO2. The Q value also dropped with HBO2 exposure, but the magnitude of change was <20% and could have been influenced by noise in thermal dilution measurements (34), despite making these measurements carefully. Although not using HBO2 in their experimental protocol, some studies noted a decrease in Q on exposure to hyperoxia (1, 30). However, other studies found that Q did not change with exposure to hyperoxia (2, 23). Only a few studies have measured cardiac output during HBO2 exposure (Table 1). In a prior report (24), investigators used flow-directed PA catheters in 11–12 healthy volunteers exposed to air at 0.56 atm abs, then air at 1 atm abs, and then 100% O2 at 3 atm abs and found that exposure to HBO2 resulted in decreases in Q, PAP, and PVR. The fall in HR and Q during HBO2 exposure may be due to increased vagal stimulation, since atropine administration reverses the fall in HR and Q with 100% O2 at 1 atm abs (14). However, in an animal study, dogs pretreated with propranolol, phentolamine, and atropine demonstrated decreased Q during HBO2 exposure (35), presumably due to physiological autoregulation of the myocardium (35) and vasculature (5) due to increased PAO2.

Hyperoxic breathing at 1 atm abs may increase left ventricular end-diastolic pressure (LVEDP) (23). Explanations for this finding are reductions in nitric oxide myocardial relaxant factor attributable to increased PAO2 (28, 33). LVEDP was not measured in this study, but PAWP approximates LVEDP closely in normal individuals (11, 19). The PAWP values in this study were slightly lower than baseline with inhalation of...
100% O₂ at 0.85 atm abs, and LVEDP should have been similarly reduced from baseline under these conditions. During HBO₂ exposure, the PAWP was higher than baseline or air breathing values, and therefore the LVEDP should have been higher. This finding supports other evidence that HBO₂ may increase left ventricular wall stiffness (23, 43). Hyperoxia may reduce myocardial relaxant factor and increase left ventricular myocardial stiffness, resulting in increases in LVEDP, which could contribute to acute lung edema in heart failure patients treated with HBO₂ (43). However, during HBO₂ exposure, RAP and PAP did not increase compared with baseline values: their values were lower than baseline. It is possible that only the left ventricle increases filling pressures during HBO₂ exposure. It also is possible that the hyperbaric air exposure before HBO₂ exposure modified the RAP and PAP responses to HBO₂ with the increased partial pressures of nitrogen modulating a subsequent HBO₂ effect. It also is possible that the duration of O₂ inhalation was insufficient to alter RAP or PAP. Differences in intracardiac pressure measurement results also may be accounted for by different dosing of O₂ inhalation [P₂O₂ ~ 0.7 atm abs (23) compared with 0.85 to 3.0 atm abs in this study].

The pHa increased and PaCO₂ decreased during HBO₂ exposure, a confirmatory finding (22). A previous study reported hypocapnea during hyperbaric oxygen inhalation caused by a central accumulation of CO₂, contributing to hyperventilation (22).

Whalen et al. (48) demonstrated that in 10 healthy volunteers breathing 100% O₂ at 3.04 atm abs, PaCO₂ did not change compared with baseline, whereas PvcO₂ increased 4 Torr from baseline. However, we observed that PvcO₂ was slightly lower during HBO₂ exposure. Explanations these conflicting data include the following. 1) Whalen et al. did not measure true mixed venous blood, since the sampling catheter was located near the RA, not the PA. 2) A reduction in VO₂ and CO₂ production during HBO₂ exposure could contribute to reduced PvcO₂. In our study, VO₂ did not change during the experiment, so this explanation is not supported by the data. 3) If PaCO₂ fell sufficiently during HBO₂ exposure, PvcO₂ might not elevate as expected, since the arterial capillary values were lower. 4) There may be ventilatory effects such as hyperventilation (22) acting independently regarding the reduction seen in PaCO₂. 5) It is possible the prior hyperbaric air exposure influenced the CO₂ measurements during subsequent HBO₂ exposure, although we do not have an explanation based on physiological principles. 6) The time course from the baseline value to those obtained during HBO₂ exposure in our study was several hours, whereas was likely a shorter interval in research conducted by Whalen et al. 7) Finally, it is possible a difference in measurement technique of CO₂ in 1965 compared with that used now has contributed to small differences in observed results.

As expected, PaO₂, PvoO₂, SvoO₂, and SvoO₂ were elevated during exposure to hyperbaric air and HBO₂, within predicted

Fig. 5. Predictions from the mixed-effects model for arterial carbon dioxide tension (PaCO₂; A), Q (B), and CI (C). Plots at the top of each panel represent data for 1 subject with circles showing the actual data values, solid lines showing the predicted values from the model for that specific subject, and dotted lines showing the average predicted values (the prediction for a new subject). Bar graphs at the bottom of each panel show the air and oxygen pressure exposures for that subject (see Fig. 1).
ranges (6, 8, 24, 41, 45). The SV was constant across the experimental conditions. This finding is expected, since the reduction in Q seems to be proportional to the reduction in HR.

Although QO₂ and VO₂, as determined using PaO₂, P vO₂, and Q by thermal dilution, did not change across conditions, Cao₂ − CVO₂ increased during HBO₂ exposure. If VO₂ remains constant (as expected in a normal volunteer while at rest) and if Q falls, Cao₂ − CVO₂ must increase because VO₂ is proportional to Q × (Cao₂ − CVO₂).

As expected, SVR increased during HBO₂ exposure. Since SVR is calculated as (MPAP − RAP)/Q, if the pressures in the numerator remain constant and Q falls, then SVR must increase. Since vascular tone was not actually measured in our study, we cannot determine whether the actual caliber of arterial blood vessels was reduced during HBO₂ exposure.

PVR fell while subjects breathed increased partial pressures of O₂, during both hyperbaric air and HBO₂ exposures. It is well accepted that increased partial pressures of O₂ reduce pulmonary pressures in patients with chronic pulmonary disease or in patients with hypoxic vasoconstriction, but normobaric hyperoxia has no significant effect on PAP (10). However, in our study, hyperbaric oxygen pressures were used. Our findings are in agreement with the limited data presented by McMahon et al. (24).

Fig. 6. Arterial pH (pHa; A), PaCO₂ (A), and arterial oxygen tension (PaO₂; B) values of subjects exposed to hyperbaric air and HBO₂. Values are means ± SE. The pHa was lower than baseline during hyperbaric air exposure and greater than baseline during HBO₂ exposure. PaCO₂ was lower than baseline during HBO₂ exposure. PaO₂ increased as the alveolar partial pressure of O₂ increased during hyperbaric air and HBO₂ exposures.

Fig. 7. Pulmonary arterial pH (pHV; A), pulmonary arterial carbon dioxide tension (PvCO₂; A), pulmonary arterial oxygen tension (PvO₂; B), and pulmonary arterial oxyhemoglobin saturation (SvO₂; B) of subjects exposed to hyperbaric air and HBO₂. Values are means ± SE. The pHV did not change from baseline across conditions. PvCO₂ was lower than baseline during HBO₂ exposure at 3.0 and 2.0 atm abs. PvO₂ and SvO₂ increased as the alveolar partial pressure of O₂ increased during hyperbaric air and HBO₂ exposures.
Q˙s/Q˙t was higher than expected while subjects breathed air at 0.85 atm abs. One explanation for this elevation is the fact that this research took place at 1,500 m above sea level, where the resting baseline PaO₂ was 75–80 Torr. In one study, intubated patients with pulmonary problems breathing supplemental oxygen also had increased Q˙s/Q˙t (10), but we could find no other experiment in normal human subjects where Q˙s/Q˙t was measured by incorporating data from PA catheters at increased altitude. Other investigators have demonstrated that ventilation-perfusion (V˙A/Q˙) mismatch does not increase while breathing at increased altitude at rest (13, 18, 37). If V˙A/Q˙ does not change, it is reasonable to assume that Q˙s/Q˙t will not change. An increased Q˙t due to stress or exercise could increase Q˙s/Q˙t while breathing air at our altitude, but all subjects were at rest and simultaneous measurements of Q˙t were normal. Atelectasis could contribute to an increased Q˙s/Q˙t value. All subjects in this study were normal, and a chest radiograph taken only a short period before measurement of the initial Q˙s/Q˙t value was normal in all 10 subjects, without evidence of atelectasis. However, subjects were supine for up to 2 h before initial Q˙s/Q˙t measurement, so it is possible undiscovered atelectasis played a role in increasing Q˙s/Q˙t in these subjects.

During breathing of 100% O₂ at 1.12 atm abs, a pressure slightly greater than sea level, Q˙s/Q˙t was 7%, a value that is within the expected range. With exposure to HBO₂, Q˙s/Q˙t dropped to zero. It is reasonable to assume that this low Q˙s/Q˙t value is attributable to high O₂ concentrations in mixed venous blood and in other circulations that contribute to venous admixture (e.g., Thesian and bronchial circulation) such that venous admixture (physiological shunt) do not significantly contribute to increasing the shunt fraction.

In addition, intrapulmonary shunts may contribute to Q˙s/Q˙t (20). With high alveolar oxygen tensions during hyperbaric oxygen exposure, these intrapulmonary shunts may participate in gas exchange because of high oxygen diffusion gradients. In patients with abnormal lung function, PaO₂ was greater than predicted during HBO₂ compared with 1.0 atm abs measurements, suggesting their Q˙s/Q˙t fell during HBO₂ exposure (44). Mathematical modeling demonstrates that Q˙s/Q˙t falls as the ratio of PaO₂ to FIO₂ (fraction of inspired O₂) increases (31), such as during hyperbaric air and HBO₂ breathing, which our data support. This is the first published report measuring Q˙s/Q˙t of humans exposed to HBO₂, so these results cannot be compared with other work.

In prior research, we found subjects exposed to HBO₂ had a wider A-aDO₂ (45) compared with those in a prior study (7), similar to a finding in patients following open-heart surgery (32). These findings raise the question of whether the increased A-aDO₂ might be due to a worsening Q˙s/Q˙t in association with HBO₂. On the contrary, in this present study, we found Q˙s/Q˙t fell below baseline and did not increase.

Study limitations. Our study is limited due to the relatively small sample size of 10 subjects and individual variability. Other limitations include confounding covariables such as the stress of catheter insertion and variation in ambient chamber temperature. The contribution to hemodynamic variables of a change in chamber temperature up to 3°C is unknown but is probably of little significance.

Measurements of V˙O₂ in this study may be limited by measurement of V˙O₂ by PA catheter. Because of the technical challenges of measuring V˙O₂ when a subject breathes 100% O₂, compounded by the difficulty performing V˙O₂ measurements inside a monoplace hyperbaric chamber, we were not able to overcome this limitation.

The apparent reduction in calculated Q˙s/Q˙t may not reflect an actual reduction in Q˙s/Q˙t because of limitation in the calculations when applied to HBO₂ conditions. Inaccuracy can occur in this calculation when very high PaO₂ and PVO₂ values are present, as well as by low effective solubility of oxygen during HBO₂ (36).
It is possible the hyperbaric air exposure modified the subjects’ hemodynamic response to 100% O₂ inhalation, including HBO₂. To maximize the information obtained from each subject, they were compressed with analogous hyperbaric profiles, differing only in the F(IO₂). Subjects underwent the hyperbaric air profile before the HBO₂ profile to reduce the risk of decompression sickness. The study design could have been improved by randomly allocating subjects to receive either hyperbaric air or HBO₂ initially, but we did not have a sufficient number of subjects to gain useful information by randomization. Hyperbaric air compression could have been omitted but would have limited the conclusions that could be drawn regarding the effect of hyperbaric pressure vs. the effect of HBO₂.

**Conclusion.** This study examined the effect of hyperbaric air and HBO₂ on arterial and PA hemodynamics and blood gas measures. The data presented are in agreement with others that HR and Q fall with HBO₂ exposure. The PaO₂, PₐVCO₂, SvO₂, and PaCO₂ values were within expected ranges during hyperbaric air and HBO₂ exposures. PVR and PₐVCO₂ decreased during HBO₂ exposure. Finally, Q/s/Qt was higher than expected with subjects breathing air at atmospheric pressure and fell to zero during HBO₂ exposure.

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Present address of S. Howe: Medical Informatics, LDS Hospital, Salt Lake City, UT 84143.
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