

# Arterial Oxygen Tension of Patients With Abnormal Lungs Treated With Hyperbaric Oxygen Is Greater Than Predicted\*

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The arterial oxygen ( $O_2$ ) tension ( $PaO_2$ ) of patients with normal gas exchange treated with hyperbaric oxygen ( $HBO_2$ ) can be predicted from their pre- $HBO_2$  arterial to alveolar  $O_2$  tension ratio ( $a/A$ ) which remains constant up to a  $PaO_2$  of 2,000 mm Hg. We observed that the  $a/A$  could not be used to predict the  $PaO_2$  of patients with impaired gas exchange (reduced pre- $HBO_2$   $a/As$ ) treated with  $HBO_2$ . Our study provides information about the  $PaO_2$  of patients with abnormal lungs treated with  $HBO_2$ . For clinical reasons, we measured the  $PaO_2$  of 24 patients treated with  $HBO_2$ . We obtained arterial blood gas values from patients with lung dysfunction ( $a/A < 0.75$ ) prior to, during, and after  $HBO_2$ . The pre- $HBO_2$   $a/A = 0.45 \pm 0.17$  (mean  $\pm 1$  SD). During  $HBO_2$  the  $a/A$  ranged from 0.7 to 0.8 depending on chamber pressure and returned to the pre- $HBO_2$  baseline after  $HBO_2$ . We conclude the following: (1) The hyperbaric  $PaO_2$ s of pa-

tients with  $a/A < 0.75$  is greater than expected. (2) However, the  $PaO_2$  is lower than in patients with normal lung function ( $a/A > 0.75$ ). Possible explanations include improvement in ventilation/perfusion matching, reduction of venous admixture, and/or extra-alveolar uptake of  $O_2$ . (3) Exposures to  $HBO_2$  treatment pressures greater than recommended by existing protocols may be required in patients with impaired transfer of  $O_2$  across the lung to achieve  $PaO_2$ s similar to patients with normal lung function treated with  $HBO_2$ .

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$a/A$ =arterial to alveolar oxygen tension ratio; atm abs=atmospheres absolute;  $HBO_2$ =hyperbaric oxygen; PEEP=positive end-expiratory pressure

Key words: blood gases; hyperbaric oxygen; hyperoxic; oxygen tension

An automated blood gas analyzer (ABL 330, Radiometer, Copenhagen, Denmark) operated at atmospheric pressure can accurately measure the oxygen ( $O_2$ ) tension of saline solution and blood tonometered to 2,000 mm Hg.<sup>1</sup> Subsequent experiments have shown that similar techniques can be used to measure the arterial  $O_2$  tension ( $PaO_2$ ) of normal subjects accurately.<sup>2</sup> Measuring arterial blood gases within multiplace chambers is time-consuming and burdensome.<sup>3</sup> Techniques allowing measurement of blood gases at atmospheric pressure generalize the technique to any hyperbaric facility, including mono-place chambers. Measuring the  $PaO_2$  of patients may be important clinically to titrate the hyperoxic dose or to minimize  $O_2$  toxicity.

Moon et al<sup>4</sup> described a method of predicting the  $PaO_2$  at any given hyperbaric oxygen ( $HBO_2$ ) exposure from the pre- $HBO_2$   $PaO_2$ . Since hemoglobin saturation with  $O_2$  is high (>95 percent) during  $HBO_2$ ,<sup>5</sup> the arterial to alveolar  $O_2$  tension ratio ( $a/A$ ) can be considered a constant.<sup>6</sup> The data of Moon et al<sup>4</sup> agree with the notion that the  $a/A$  remains constant with the patient breathing  $HBO_2$ . Therefore,

the  $PaO_2$  during  $HBO_2$  can be calculated from the pre- $HBO_2$   $a/A$  in patients with normal pulmonary gas exchange ( $a/A > 0.75$ ) the predicted  $PaO_2$  of Moon et al<sup>4</sup>=[pre- $HBO_2$   $a/A$ ]\* [calculated alveolar  $O_2$  tension]<sup>4</sup>.

We will present  $PaO_2$  data acquired from patients with pulmonary disease ( $a/A < 0.75$ ), many requiring mechanical ventilation and positive end-expiratory pressure (PEEP) treated with  $HBO_2$  therapy. In these patients, the  $PaO_2$  measured during  $HBO_2$  could not be predicted from the equation of Moon et al.<sup>4</sup>

## MATERIALS AND METHODS

Arterial blood gases from 24 patients treated with  $HBO_2$  (Table 1) were obtained for clinical reasons to titrate minute ventilation in mechanically ventilated patients and to inspect the adequacy of arterial oxygenation. Patients were treated with various  $HBO_2$  doses, generally following published guidelines for the particular disorder.<sup>7</sup> Twenty-one patients were intubated and required mechanical ventilation (PEEP range = 0 to 24 cm  $H_2O$ ). Prior to and after  $HBO_2$  treatment, arterial blood was aspirated from radial or femoral arterial catheters using sterile technique following standard blood gas sampling procedures. Arterial blood was aspirated from patients during  $HBO_2$  treatment in the same manner as previously described.<sup>2</sup> Arterial blood was aspirated after at least 20 min at any given  $HBO_2$  pressure and after 10 min when the patients were breathing hyperbaric air. Patients were supine, calm, generally sedated, and paralyzed when the samples were collected. After obtaining the blood sample, the lines and catheters were flushed with sterile saline solution. Arterial blood gas determinations were performed immediately (within 40 s). Samples were not chilled. Each hyperoxic blood sample was an-

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Table 1—Patient Information\*

Patient No./Age, yr/Sex	Diagnosis	VT, ml	RR, BPM	P <sub>PEAK</sub> , cm H <sub>2</sub> O	PEEP, cm H <sub>2</sub> O	Intubated	Compliance, ml/cm H <sub>2</sub> O	Outcome
1/63/F	Venous and arterial gas embolism due to liver resection for cancer	350	12	21	5	Yes	22	L
2/50/M	CO poisoning, aspiration pneumonia	650	14	20	0	Yes	33	L
3/39/M	CO poisoning, aspiration pneumonia	725	15	34	5	Yes	25	L
4/51/M	Necrotizing fasciitis of leg, sepsis, ARDS	590	18	51	24	Yes	22	L
5/32/F	Vincent's angina, anaerobic mediastinitis, ARDS	500	10	30	5	Yes	20	L
6/80/F	CO and cyanide poisoning, acute MI, smoke inhalation, ARDS	700	16	32	8	Yes	29	L
7/45/F	Radiation cardiomyopathy	650	10	30	5	Yes	26	L
8/52/M	Scrotal necrotizing fasciitis, sepsis, basilar atelectasis	800	18	40	10	Yes	27	D
9/20/F	CO poisoning, smoke inhalation, aspiration pneumonia	500	17	34	6	Yes	18	L
10/42/M	Chest wall necrotizing fasciitis, cardiac transplant	825	17	30	4	Yes	32	D
11/76/M	CO poisoning, aspiration pneumonia	700	11	22	7	Yes	47	D
12/20/M	CO poisoning, aspiration pneumonia	620	12	24	0	Yes	26	L
13/67/F	Perineal necrotizing fasciitis	NA	34	NA	NA	No	NA	L
14/45/F	Abdominal and perineal necrotizing fasciitis, sepsis, pneumonia	875	18	30	6	Yes	36	L
15/19/M	CO poisoning, aspiration pneumonia	700	13	27	3	Yes	29	L
16/43/F	Aspergillus abdominal wall infection, sepsis, ARDS	650	18	28	7	Yes	31	D
17/72/F	Abdominal, perineal, buttock necrotizing fasciitis	NA	12	NA	NA	No	NA	L
18/36/M	Gas gangrene left arm, IV drug abuse, basilar atelectasis	740	13	25	8	Yes	44	L
19/3/M	CO poisoning, smoke inhalation	200	18	23	0	Yes	9	L
20/34/M	CO poisoning, aspiration pneumonia	NA	16	NA	NA	No	NA	L
21/56/M	Gas gangrene of leg, sepsis, heart failure, basilar atelectasis	650	12	30	5	Yes	26	L
22/22/F	Perineal necrotizing fasciitis, sepsis, ARDS	550	14	25	7	Yes	31	L
23/27/M	CO poisoning, aspiration pneumonia	650	15	28	10	Yes	36	L
24/71/F	Arterial thrombosis of leg, sepsis, ARDS, carcinoma of colon	600	18	32	8	Yes	25	D

\*VT=tidal volume; RR=respiratory rate; P<sub>PEAK</sub>=peak airway pressure; Outcome: L=lived, D=died; NA=not applicable; ARDS=adult respiratory distress syndrome; MI=myocardial infarction.

alyzed twice with the same automated blood gas analyzer. The PaO<sub>2</sub> that was recorded was selected according to prior published criteria.<sup>1,2</sup>

Tonometry data with fresh whole blood provided a correction equation for our automated blood gas analyzer for chamber pressures above 1.0 atmospheres absolute (atm abs): PaO<sub>2</sub> cor-

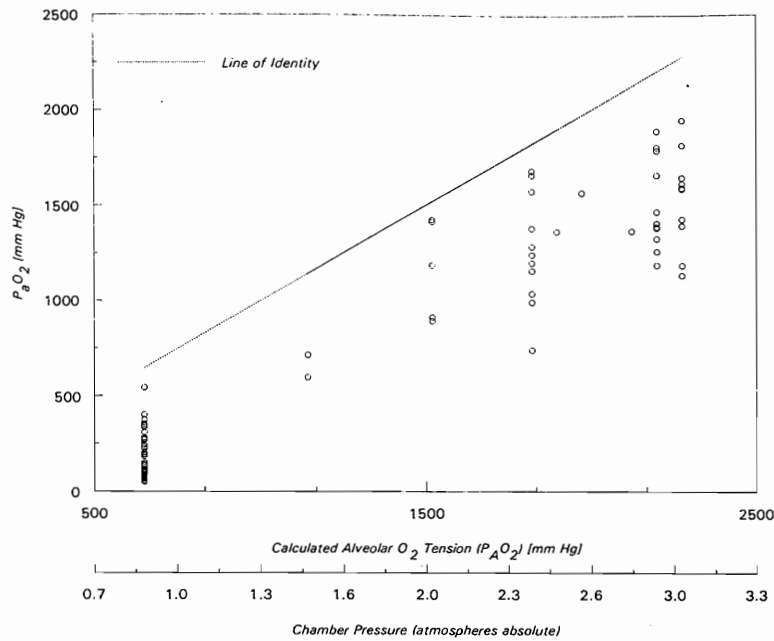


FIGURE 1.  $P_{aO_2}$  vs calculated  $P_{aO_2}$  and chamber pressure of patients with  $a/A < 0.75$ . Line of identity represents  $P_{aO_2}$ .

rected =  $(PAO_2 - (PAO_2 \times 0.919) + 37.3) + P_{aO_2}$  measured; where  $PAO_2$  is the calculated alveolar  $O_2$  tension using the alveolar air equation.<sup>1</sup> All  $P_{aO_2}$  values in this presentation are corrected values (a more thorough discussion is available in reference 2).

The automated blood gas analyzer was two point calibrated every 2 h and single point calibrated every 30 mins.

#### Statistical Analyses

All data are presented as means  $\pm 1$  SD. One-way analysis of variance was used to determine statistical differences between the  $a/A$  at various  $O_2$  partial pressures. Student's  $t$  test was used to compare pre-HBO<sub>2</sub> and post-HBO<sub>2</sub>  $a/A$ s. Significance level was  $p \leq 0.05$ .

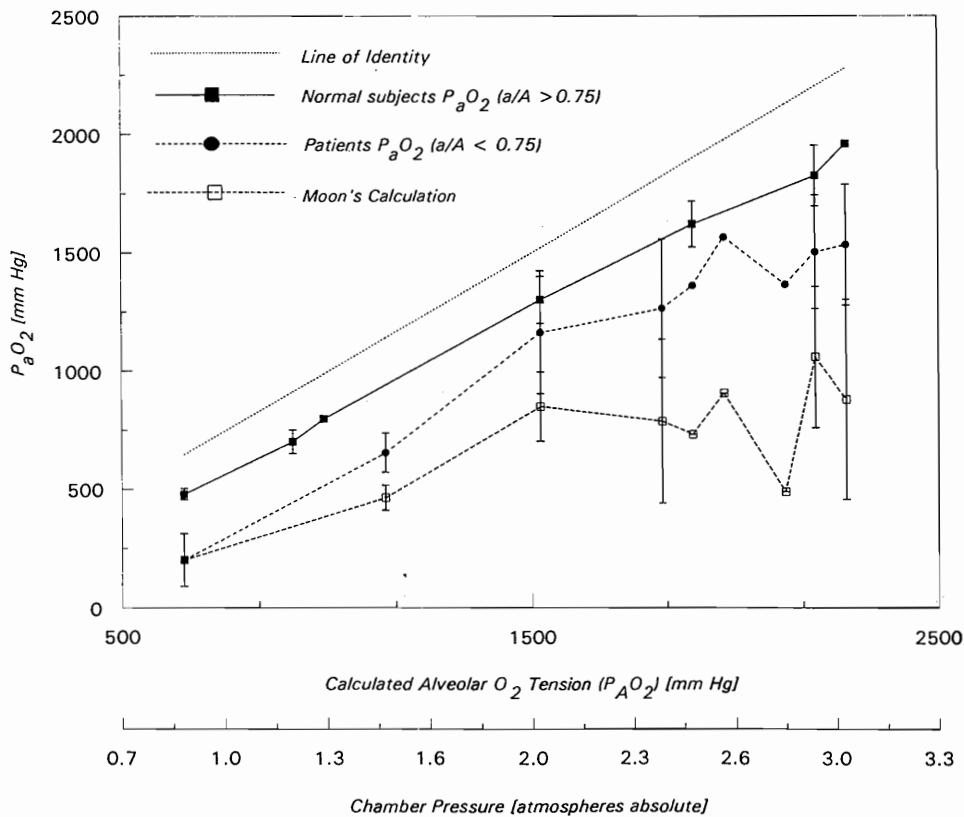


FIGURE 2.  $P_{aO_2}$  vs calculated  $P_{aO_2}$  over range of chamber pressures for normal subjects<sup>2</sup> and patients with pre-HBO<sub>2</sub>  $a/A < 0.75$ . Predicted  $P_{aO_2}$  of these same patients using the prediction equation of Moon et al<sup>4</sup> is included for comparison. Line of identity represents  $P_{aO_2}$ . Vertical bars represent  $\pm 1$  SD.

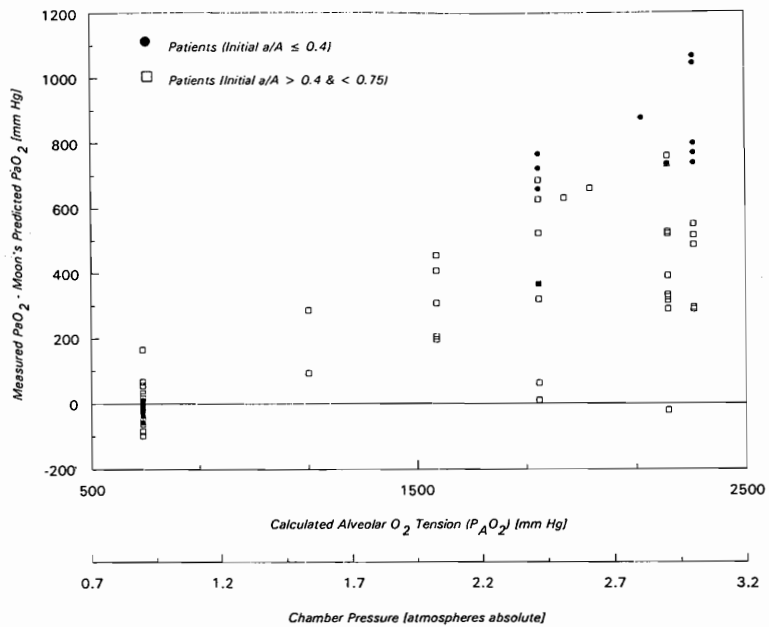


FIGURE 3.  $\text{PaO}_2$  minus the predicted  $\text{PaO}_2$  of Moon et al<sup>4</sup> vs  $\text{PaO}_2$  and chamber pressure.

### RESULTS

Eighty-six arterial blood gas determinations (42 during  $\text{HBO}_2$ ) were measured on 24 patients with  $a/A < 0.75$ . Table 1 provides clinical information regarding these patients. For comparison, we used previously published data from nine normal subjects exposed to  $\text{HBO}_2$ .<sup>2</sup>

As expected, the  $\text{PaO}_2$  increased as chamber pressure increased (Fig 1). However, the hyperbaric  $\text{PaO}_2$ s of these patients were higher than predicted from pre- $\text{HBO}_2$   $\text{PaO}_2$  measurements (Figs 2 and 3).<sup>4</sup>

During  $\text{HBO}_2$ , the  $a/A$  increased significantly for patients with pre- $\text{HBO}_2$   $a/A < 0.75$ , but not in normal subjects<sup>2</sup> (Fig 4). The  $a/A$  prior to and immediately following  $\text{HBO}_2$  treatments was  $0.43 \pm 0.03$ , and  $0.43 \pm 0.07$ , respectively. There was no difference between pre- $\text{HBO}_2$  and post- $\text{HBO}_2$  treatment  $a/A$  (Fig 4).

During hyperbaric air breathing (eight patients), the  $a/A$  fell to the pre- $\text{HBO}_2$  baseline (pre- $\text{HBO}_2$   $a/A = 0.38 \pm 0.15$ ;  $\text{HBO}_2$   $a/A = 0.70 \pm 0.14$ ; hyperbaric Air  $a/A = 0.35 \pm 0.25$ ; next  $\text{HBO}_2$  period  $a/A = 0.61 \pm 0.16$ ; post- $\text{HBO}_2$   $a/A = 0.26 \pm 0.09$ ).

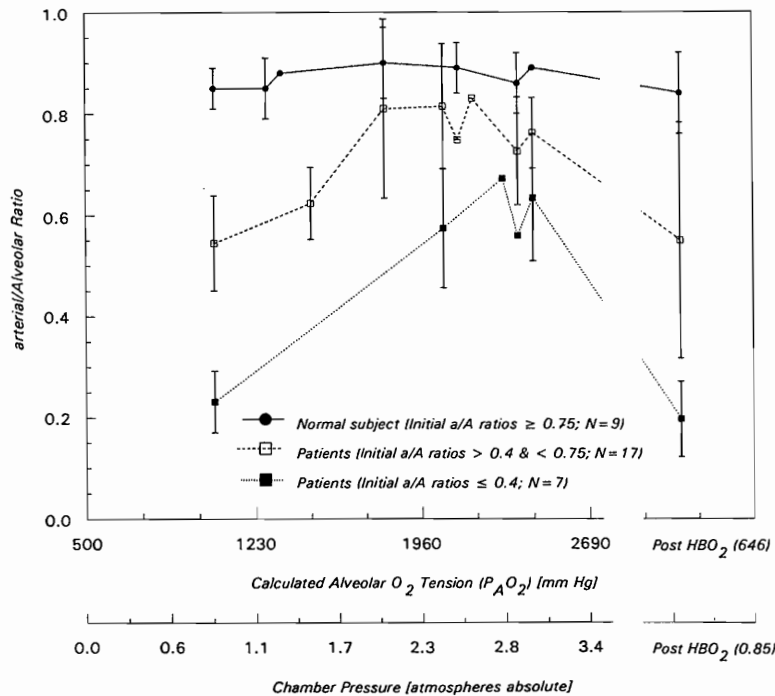


FIGURE 4.  $a/A$  vs  $\text{PAO}_2$  and chamber pressure for various initial  $a/A$ s. For patients with  $a/A < 0.75$ , the  $\text{HBO}_2$   $a/A$  is significantly higher than the pre- $\text{HBO}_2$  and post- $\text{HBO}_2$   $a/A$ . There is no difference between pre- $\text{HBO}_2$  and post- $\text{HBO}_2$   $a/A$ .

No patient exhibited manifestations of pulmonary or central nervous O<sub>2</sub> toxicity. There were no complications related to the arterial catheters.

#### DISCUSSION

The automated blood gas analyzer operated at atmospheric pressure can accurately and reproducibly measure O<sub>2</sub> tension of saline solution and blood tonometered to 2,000 mm Hg.<sup>1</sup> We have also presented a technique of obtaining arterial blood samples from subjects compressed within the monoplace hyperbaric chamber.<sup>2</sup> The PaO<sub>2</sub> data from that study demonstrated results in agreement with studies in which the PaO<sub>2</sub> was measured by blood gas analyzers calibrated inside multiplace chambers.<sup>2-4</sup>

This study shows that patients with abnormal pulmonary function have considerably higher PaO<sub>2</sub>s during HBO<sub>2</sub> exposures than predicted by Moon et al<sup>4</sup> (Figs 2 and 3). Our data suggest that in patients with pulmonary disease ( $a/A < 0.75$ ) requiring HBO<sub>2</sub> therapy, the PaO<sub>2</sub> can be determined only by actual measurement.

The PaO<sub>2</sub>s in our patients are lower than in patients with normal pulmonary function treated at analogous chamber pressures (Fig 2).<sup>2,3</sup> For example, a patient with normal pulmonary function, breathing 100 percent O<sub>2</sub>, would be expected to have a PaO<sub>2</sub> of approximately 2,000 mm Hg at 3.0 atm abs. Our patients had a mean PaO<sub>2</sub> of 1,500 mm Hg at 3.0 atm abs. For patients with pre-HBO<sub>2</sub>  $a/A < 0.4$ , the mean PaO<sub>2</sub> at 3.0 atm abs was 1,400 mm Hg. Several patients treated between 2 and 3 atm abs had PaO<sub>2</sub>s less than 1,000 mm Hg (Fig 1). Based on our observations, for patients with  $a/A = 0.48$  to have an PaO<sub>2</sub> = 2,000 mm Hg may require hyperbaric O<sub>2</sub> pressures greater than 3.0 atm abs. This information may be clinically relevant since hyperbaric treatment protocols generally recommend treatment pressures ranging from 2 to 2.5 atm abs.<sup>7</sup>

Why would the  $a/A$  increase in patients with ventilation-perfusion inequalities when exposed to HBO<sub>2</sub> (Fig 2)? There are several possible explanations. With such high partial pressures of O<sub>2</sub> (>1,000 mm Hg), is it possible that O<sub>2</sub> transfer occurs across nonalveolar surfaces? Studies have demonstrated that skin is an effective barrier to O<sub>2</sub> transport.<sup>8</sup> Also, the patient's HBO<sub>2</sub>  $a/A$  falls to the pre-HBO<sub>2</sub> baseline when breathing hyperbaric air but compressed with O<sub>2</sub> suggesting that skin transport of O<sub>2</sub> is not the explanation. Therefore, one can postulate that the abnormal lung must increase its gas exchange efficiency during HBO<sub>2</sub> exposure. This could occur by bronchial capillary uptake of O<sub>2</sub> or by alteration in ventilation-perfusion relationships.

The physiologic shunt represents approximately 2 to 5 percent of the cardiac output.<sup>9,10</sup> This shunt is

due to the bronchial circulation, the venae cordis minimae (thebesian), and any other shunt bypassing alveoli.<sup>9,11</sup> Our findings might be explained by O<sub>2</sub> uptake by these circulations. However, we discount this possibility. If O<sub>2</sub> uptake during HBO<sub>2</sub> were to occur in these circulations that generally bypass the lung, one would expect that the A-a gradient would not increase during HBO<sub>2</sub> which is contrary to what is observed in normal human subjects.<sup>3</sup> Furthermore, the magnitude of the increase in arterial O<sub>2</sub> content in patients with  $a/A < 0.4$  is approximately 15 percent. This amount of change is not solely explained by a reduction of the physiologic shunt.

The shunt fraction is directly proportional to the cardiac output.<sup>12</sup> If the cardiac output falls during HBO<sub>2</sub>, shunt would decrease, and the PaO<sub>2</sub> would increase. During HBO<sub>2</sub> in normal subjects the cardiac output falls by approximately 20 percent.<sup>13</sup> However, in patients with sepsis syndrome, there is no change in cardiac output with HBO<sub>2</sub>.<sup>14</sup> The patients treated in the present study had acute carbon monoxide poisoning with concomitant aspiration, necrotizing fasciitis, gas gangrene, gas embolism, and acute arterial thrombosis (Table 1). It is not known if the cardiac output changes due to HBO<sub>2</sub> in patients with these disorders. Data from pulmonary arterial catheters in patients treated with HBO<sub>2</sub><sup>5</sup> could aid in explaining if our findings might be explained by a reduction in cardiac output.

Pulmonary O<sub>2</sub> toxicity is caused by HBO<sub>2</sub>.<sup>15,16</sup> Most of these patients required supplemental O<sub>2</sub> prior to and after HBO<sub>2</sub> therapy to maintain adequate arterial O<sub>2</sub> saturation. In this study, the pre-HBO<sub>2</sub> and post-HBO<sub>2</sub> treatment mean  $a/A$  ratios were the same (Fig 4), suggesting that HBO<sub>2</sub> did not worsen pulmonary function acutely. However, individual patients occasionally required higher FIO<sub>2</sub>s following HBO<sub>2</sub>. This observation was more frequent in patients with sepsis syndrome. One- to 2-h post-HBO<sub>2</sub>, the FIO<sub>2</sub> was the same as prior to HBO<sub>2</sub>.

In patients exhibiting abnormal pulmonary function (reduced  $a/A$ ) requiring HBO<sub>2</sub>, it may be reasonable to treat the patient at chamber pressures greater than standard protocols recommend.<sup>7</sup> Since individual PaO<sub>2</sub> responses with HBO<sub>2</sub> exposure are unpredictable, performing PaO<sub>2</sub> measurements in patients with abnormal pulmonary function treated with HBO<sub>2</sub> may be necessary. Generally, increased tissue oxygenation is the goal of HBO<sub>2</sub> treatment.<sup>7</sup> It is not known if the PaO<sub>2</sub> can accurately reflect tissue O<sub>2</sub> tension. Further studies could be performed to try to correlate PaO<sub>2</sub> with tissue oxygenation.

In conclusion, we have demonstrated that the PaO<sub>2</sub>s of patients with pulmonary dysfunction (reduced  $a/A$  ratios) are higher than predicted when treated with HBO<sub>2</sub>, but lower than would be ex-

pected in patients with normal pulmonary function. Pulmonary function does not seem to be altered by clinical HBO<sub>2</sub> exposures. It may be reasonable to measure the PaO<sub>2</sub> of patients with reduced a/A ratios to titrate the specific PaO<sub>2</sub> treatment protocol.

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