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

Lindell K. Weaver, M.D., F.C.C.P.; and Steve Howe, M.A.

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±0.17 (mean ±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_2s of patients 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_2s similar to patients with normal lung function treated with HBO_2.

(Chest 1994; 106:1134-39)

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.[1] Subsequent experiments have shown that similar techniques can be used to measure the arterial O_2 tension (PaO_2) of normal subjects accurately.[2] Measuring arterial blood gases within multiplace chambers is time-consuming and burdensome.[3] Techniques allowing measurement of blood gases at atmospheric pressure generalize the technique to any hyperbaric facility, including monoplace 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[4] 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,[5] the arterial to alveolar O_2 tension ratio (a/A) can be considered a constant.[6] The data of Moon et al[4] 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[4]=[pre-HBO_2 a/A]* [calculated alveolar O_2 tension][4]).

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.[4]

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.[7] 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.[2] 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-

*From the Division of Pulmonary/Critical Care Medicine, Department of Medicine, LDS Hospital, and Division of Respiratory, Critical Care, and Occupational (Pulmonary) Medicine, University of Utah College of Medicine, Salt Lake City.
Manuscript received December 13, 1993; revision accepted February 16, 1994.

Table 1—*Patient Information**

Patient No./Age, yr/Sex	Diagnosis	V_T, ml	RR, BPM	P_{PEAK}, cm H_2O	PEEP, cm H_2O	Intubated	Compliance, ml/cm H_2O	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

*V_T=tidal volume; RR=respiratory rate; P_{PEAK}=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_2 that was recorded was selected according to prior published criteria.[1,2]

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_2 cor-

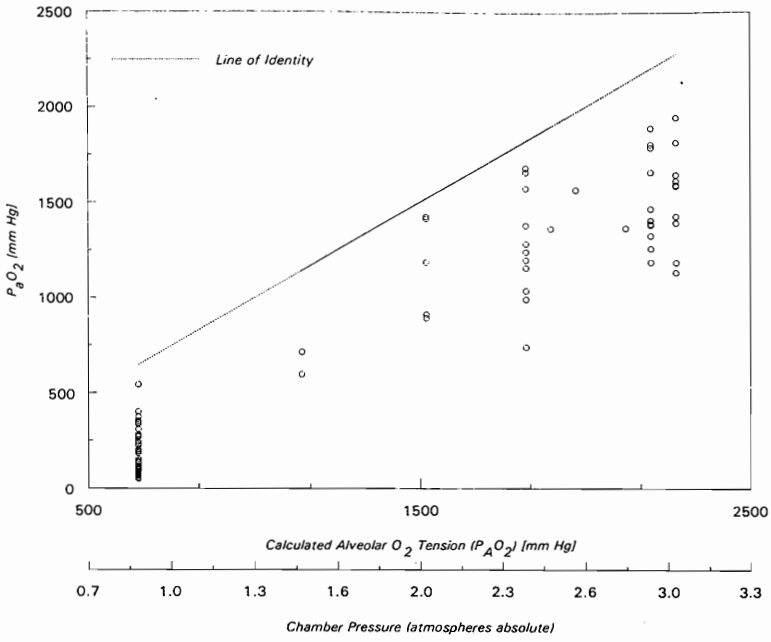

FIGURE 1. PaO_2 vs calculated PaO_2 and chamber pressure of patients with a/A<0.75. Line of identity represents PaO_2.

rected = $(PAO_2-(PAO_2\times0.919)+37.3)+PaO_2$measured; where PAO_2 is the calculated alveolar O_2 tension using the alveolar air equation.[1] All PaO_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 ±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_2 and post-HBO_2 a/As. Significance level was $p\leq0.05$.

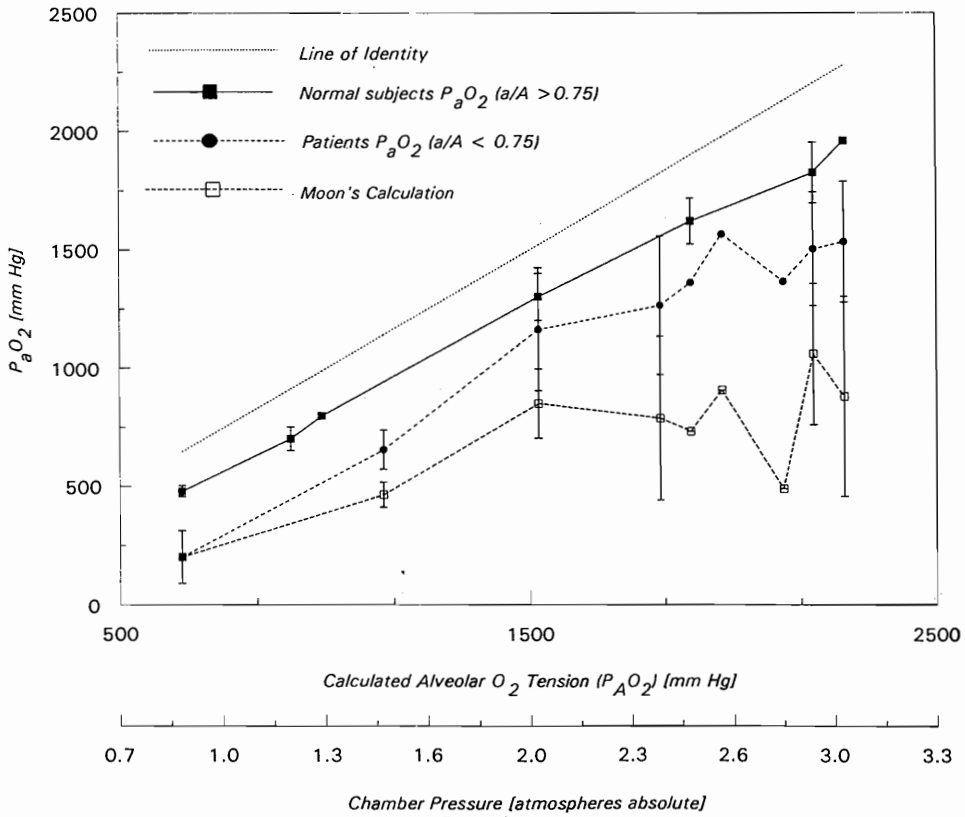

FIGURE 2. PaO_2 vs calculated PaO_2 over range of chamber pressures for normal subjects[2] and patients with pre-HBO_2 a/A<0.75. Predicted PaO_2 of these same patients using the prediction equation of Moon et al[4] is included for comparison. Line of identity represents PaO_2. Vertical bars represent ±1 SD.

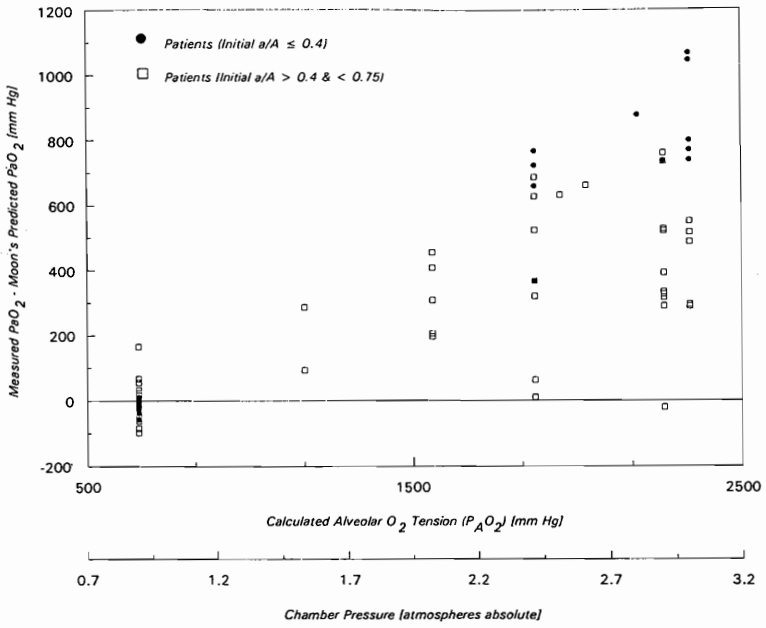

FIGURE 3. PaO_2 minus the predicted PaO_2 of Moon et al[4] vs PaO_2 and chamber pressure.

RESULTS

Eighty-six arterial blood gas determinations (42 during 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 HBO_2.[2]

As expected, the PaO_2 increased as chamber pressure increased (Fig 1). However, the hyperbaric PaO_2s of these patients were higher than predicted from pre-HBO_2 PaO_2 measurements (Figs 2 and 3).[4] During HBO_2, the a/A increased significantly for patients with pre-HBO_2 a/A <0.75, but not in normal subjects[2] (Fig 4). The a/A prior to and immediately following HBO_2 treatments was 0.43 ± 0.03, and 0.43 ± 0.07, respectively. There was no difference between pre-HBO_2 and post-HBO_2 treatment a/A (Fig 4).

During hyperbaric *air* breathing (eight patients), the a/A fell to the pre-HBO_2 baseline (pre-HBO_2 a/A=0.38 ± 0.15; HBO_2 a/A=0.70 ± 0.14; hyperbaric Air a/A=0.35 ± 0.25; next HBO_2 period a/A=0.61 ± 0.16; post-HBO_2 a/A=0.26 ± 0.09).

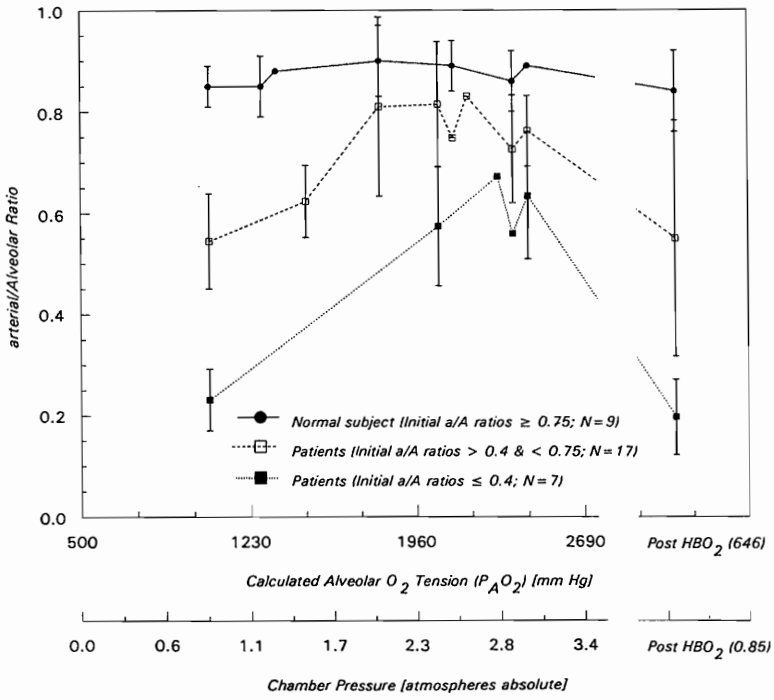

FIGURE 4. a/A vs PAO_2 and chamber pressure for various initial a/As. For patients with a/A<0.75, the HBO_2 a/A is significantly higher than the pre-HBO_2 and post-HBO_2 a/A. There is no difference between pre-HBO_2 and post-HBO_2 a/A.

No patient exhibited manifestations of pulmonary or central nervous O_2 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_2 tension of saline solution and blood tonometered to 2,000 mm Hg.[1] We have also presented a technique of obtaining arterial blood samples from subjects compressed within the monoplace hyperbaric chamber.[2] The PaO_2 data from that study demonstrated results in agreement with studies in which the PaO_2 was measured by blood gas analyzers calibrated inside multiplace chambers.[2-4]

This study shows that patients with abnormal pulmonary function have considerably higher PaO_2s during HBO_2 exposures than predicted by Moon et al[4] (Figs 2 and 3). Our data suggest that in patients with pulmonary disease ($a/A < 0.75$) requiring HBO_2 therapy, the PaO_2 can be determined only by actual measurement.

The PaO_2s in our patients are lower than in patients with normal pulmonary function treated at analogous chamber pressures (Fig 2).[2,3] For example, a patient with normal pulmonary function, breathing 100 percent O_2, would be expected to have a PaO_2 of approximately 2,000 mm Hg at 3.0 atm abs. Our patients had a mean PaO_2 of 1,500 mm Hg at 3.0 atm abs. For patients with pre-HBO_2 $a/A < 0.4$, the mean PaO_2 at 3.0 atm abs was 1,400 mm Hg. Several patients treated between 2 and 3 atm abs had PaO_2s less than 1,000 mm Hg (Fig 1). Based on our observations, for patients with $a/A = 0.48$ to have an $PaO_2 = 2{,}000$ mm Hg may require hyperbaric O_2 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.[7]

Why would the a/A increase in patients with ventilation-perfusion inequalities when exposed to HBO_2 (Fig 2)? There are several possible explanations. With such high partial pressures of O_2 (>1,000 mm Hg), is it possible that O_2 transfer occurs across nonalveolar surfaces? Studies have demonstrated that skin is an effective barrier to O_2 transport.[8] Also, the patient's HBO_2 a/A falls to the pre-HBO_2 baseline when breathing hyperbaric air but compressed with O_2 suggesting that skin transport of O_2 is not the explanation. Therefore, one can postulate that the abnormal lung must increase its gas exchange efficiency during HBO_2 exposure. This could occur by bronchial capillary uptake of O_2 or by alteration in ventilation-perfusion relationships.

The physiologic shunt represents approximately 2 to 5 percent of the cardiac output.[9,10] This shunt is due to the bronchial circulation, the venae cordis minimae (thebesian), and any other shunt bypassing alveoli.[9,11] Our findings might be explained by O_2 uptake by these circulations. However, we discount this possibility. If O_2 uptake during HBO_2 were to occur in these circulations that generally bypass the lung, one would expect that the A-a gradient would not increase during HBO_2 which is contrary to what is observed in normal human subjects.[3] Furthermore, the magnitude of the increase in arterial O_2 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.[12] If the cardiac output falls during HBO_2, shunt would decrease, and the PaO_2 would increase. During HBO_2 in normal subjects the cardiac output falls by approximately 20 percent.[13] However, in patients with sepsis syndrome, there is no change in cardiac output with HBO_2.[14] 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_2 in patients with these disorders. Data from pulmonary arterial catheters in patients treated with HBO_2[5] could aid in explaining if our findings might be explained by a reduction in cardiac output.

Pulmonary O_2 toxicity is caused by HBO_2.[15,16] Most of these patients required supplemental O_2 prior to and after HBO_2 therapy to maintain adequate arterial O_2 saturation. In this study, the pre-HBO_2 and post-HBO_2 treatment mean a/A ratios were the same (Fig 4), suggesting that HBO_2 did not worsen pulmonary function acutely. However, individual patients occasionally required higher FIO_2s following HBO_2. This observation was more frequent in patients with sepsis syndrome. One- to 2-h post-HBO_2, the FIO_2 was the same as prior to HBO_2.

In patients exhibiting abnormal pulmonary function (reduced a/A) requiring HBO_2, it may be reasonable to treat the patient at chamber pressures greater than standard protocols recommend.[7] Since individual PaO_2 responses with HBO_2 exposure are unpredictable, performing PaO_2 measurements in patients with abnormal pulmonary function treated with HBO_2 may be necessary. Generally, increased tissue oxygenation is the goal of HBO_2 treatment.[7] It is not known if the PaO_2 can accurately reflect tissue O_2 tension. Further studies could be performed to try to correlate PaO_2 with tissue oxygenation.

In conclusion, we have demonstrated that the PaO_2s of patients with pulmonary dysfunction (reduced a/A ratios) are higher than predicted when treated with HBO_2, but lower than would be ex-

pected in patients with normal pulmonary function. Pulmonary function does not seem to be altered by clinical HBO_2 exposures. It may be reasonable to measure the PaO_2 of patients with reduced a/A ratios to titrate the specific PaO_2 treatment protocol.

ACKNOWLEDGMENTS: We would like to thank the hyperbaric therapists and the blood gas laboratory at the LDS Hospital for assisting with collection and measurement of the arterial blood samples. We appreciate the critical reviews of this work by G. Michael Vincent, M.D., Terry Clemmer, M.D., C. Gregory Elliott, M.D., and Valerie Larson-Lohr, M.S., C.C.R.N.

References

1 Weaver LK, Howe S, Berlin SL. Normobaric measurement of O_2 tension of blood and saline tonometered under hyperbaric O_2 conditions. J Hyperbaric Med 1990; 5:29-38
2 Weaver LK, Howe S. Normobaric measurement of arterial oxygen tension of subjects exposed to hyperbaric oxygen. Chest 1992; 102:1175-81
3 Clark JM, Lambertsen CJ. Alveolar-arterial O_2 differences in man at 0.2, 1.0, 2.0, and 3.5 Ata inspired PO_2. J Appl Physiol 1971; 30:753-63
4 Moon RE, Camporesi EM, Shelton DL. Prediction of arterial PO_2 during hyperbaric treatments. In: Bove AA, Bachrach AJ, Greenbaum LJ Jr, eds. Proceedings of the ninth international symposium on underwater and hyperbaric physiology. Bethesda, Md: Undersea and Hyperbaric Medical Society, 1987; 1125-31
5 Weaver LK. Technique of Swan-Ganz catheter monitoring in patients treated in the monoplace hyperbaric chamber. J Hyperbaric Med 1992; 7:1-18
6 Gilbert R, Keighley JF. The arterial/alveolar oxygen tension ratio: an index of gas exchange applicable to varying inspired oxygen concentrations. Am Rev Respir Dis 1974; 109:142-45
7 Thom SR. Hyperbaric oxygen therapy—a committee report. Bethesda, Md: Undersea and Hyperbaric Medical Society, 1992
8 Gruber RP, Heitkamp DH, Billy LJ, Amato JJ. Skin permeability to oxygen and hyperbaric oxygen. Arch Surg 1970; 101:69-70
9 Lambertsen CJ. Gas exchanges of the atmosphere with the lungs and blood. In: Mountcastle VB, ed. Medical physiology. St. Louis: CV Mosby, 1980; 1691-720
10 Morris AH, Kanner RE, Crapo RO, Gardner RM. Clinical pulmonary function testing. 2nd ed. Salt Lake City, Utah: Intermountain Thoracic Society, 1984; 56-7
11 Nunn JF. Applied respiratory physiology. 2nd ed. Boston: Butterworths, 1981; 291-92
12 Nunn JF. Applied respiratory physiology. 2nd ed. Boston: Butterworths, 1981; 388-95
13 Whalen RE, Saltzman HA, Holloway DH, et al. Cardiovascular and blood gas responses to hyperbaric oxygen. Am J Cardiol 1965; 15:638-46
14 Weaver LK. Pulmonary artery catheter use in critically ill patients treated in the monoplace hyperbaric chamber [abstract]. Undersea Biomed Res 1990; 17(suppl):132
15 Balentine JD. Pathology of oxygen toxicity. Charleston, SC: Academic Press, 1982; 82-147
16 Hendricks PL, Hall DA, Hunter WH Jr, Haley PJ. Extension of pulmonary oxygen tolerance in man at 2 ATA by intermittent oxygen exposure. J Appl Physiol 1977; 42:593-99