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Air vs. He-O_2 recompression treatment of decompression sickness in guinea pigs

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Lillo RS, MacCallum ME, Pitkin RB. Air vs. He-O_2 recompression treatment of decompression sickness in guinea pigs. Undersea Biomed Res 1988; 15(4):283-300.— Air vs. He-O_2 (20.9% O_2) recompression treatment was examined in a model of severe decompression sickness (DCS) using male albino guinea pigs (*Cavia porcellus*, 500–600 g). Following decompression to the surface from simulated air dives at 200 or 250 fsw, both anesthetized and unanesthetized animals often exhibited responses indicative of a fatal bout of DCS (including hypotension, cardiac arrhythmia, and tachypnea). Upon recompression with air back to depth, good recovery of animals with DCS was observed. Comparison of air vs. He-O_2 recompression responses of unanesthetized animals with recompression back to initial depth (200 fsw) revealed a slower recovery from tachypnea with He-O_2. Recompression partially back to depth following 200-fsw air dives produced significant differences in the breathing recovery vs. recompression depth relationship between air and He-O_2. Treatment effectiveness improved with increasing depth with air, but not with He-O_2. These data indicate potential differences in recompression response to air vs. He-O_2 when using ventilatory recovery as a measure of effectiveness in treatment of DCS in guinea pigs following air dives.

Keywords: gas bubbles; diving; hyperbaric conditions; inert gas; reprints; (KT) counterdiffusion

Standard treatment of decompression sickness (DCS) involves recompression to help resolve bubbles and often the use of O_2 to increase the gradient for inert gas elimination. However, little is known about what constitutes optimal treatment conditions in terms of depth or gas mixture. Treatment procedures are often based more on assumptions, theoretical considerations, and empiricism than on scientific evidence. In many cases, operational convenience is cited as the major reason for selection of the treatment gas. Consequently, recompression with He-O_2 has been suggested for treatment of DCS following air dives (1–3) despite the absence of definitive supporting rationale. In fact, theoretical arguments evolving from the phenomenon of counterdiffusion could be made against performing He-O_2 recompression following dives on air due to different rates of mass transfer of He and N_2 (4, 5). Indeed, a recent study has demonstrated that He-O_2 breathing can exacerbate the

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increase in pulmonary vascular resistance that occurs during DCS following air dives in dogs (6). The present experiments characterize a model of severe DCS in guinea pigs and use it to compare the effectiveness of air vs. He-O_2 treatment for DCS following air dives.

MATERIALS AND METHODS

Male albino guinea pigs (*Cavia porcellus*, Hartley strain), weighing approximately 500–600 g, were obtained from a local supplier and housed locally for at least 2 wk before use.

Animal preparation and physiologic monitoring

Guinea pigs were anesthetized with sodium pentobarbital (30–40 mg/kg), and a catheter for blood pressure measurement was inserted into the common carotid artery and anchored to the surrounding tissue with suture. Three wire leads were inserted s.c. for ECG monitoring, one on the back of the animal and one on each side of the thorax. A tiny thermistor (Thermometrics, Edison, NJ, model AB6B8BR14KAI32J/37C) was implanted into the trachea to allow recording of ventilation rate. For insertion of the thermistor, a needle was used to make a small hole in the ventral side of the trachea, approximately 4 cm distal from the larynx. The thermistor was then inserted into the hole and advanced several millimeters toward the lung so that both the thermistor and its lead rested close to the inside ventral surface of the trachea. A cyanoacrylate-based, fast-drying glue was then used to fix the thermistor to the trachea and seal the small hole in the airway. The lead was then sutured to the muscle at several spots before it was threaded under the skin, along with the catheter, and out via a small incision on the dorsal side of the animal just behind the neck. Catheter, ECG, and thermistor leads were fastened securely to the skin with suture at this location. All incisions were then sutured closed. Experiments began immediately for some animals (anesthetized experiments). No further sodium pentobarbital was required as animals generally remained anesthetized for 6–8 h after initial injection, which was in excess of the total time required for animal preparation and experimentation. Other animals were given until the next day to recover (unanesthetized experiments). Immediately before experiments, a thermistor probe was inserted into the rectum, advanced approximately 5 cm, and secured in place using suture ties that, during surgery, had been stitched into the skin close to the anus. This allowed monitoring of body temperature, which was important during the treatment phase of DCS where thermal stability is usually a problem.

Animals were individually placed into a small wire cage (24 × 12 × 9 cm, length × width × height) which was then put inside a hyperbaric chamber (Bethlehem Corp., Bethlehem, PA, model 615-HP); a piece of wire mesh was adjusted inside the cage to gently restrain the animal. During experiments arterial blood pressure was measured via the carotid cannula using a pressure transducer (Gould Inc., Cleveland, OH, model P50). This transducer was calibrated using pressures generated by known heights of saline. Catheter patency was maintained by period injections of small amounts of heparinized saline (20 IU heparin/ml). Although reports on the effect of heparin on DCS are conflicting (7, 8), care was taken to minimize its potential effects

in these experiments by using small volumes for flushing the catheter and flushing only when absolutely necessary. Total saline infused was generally much less than 2 ml, which is equivalent to a 80 U/kg dose of heparin (i.e., for a 500-g guinea pig), a fairly small amount of heparin compared to what has been used previously.

Mean blood pressure was obtained by processing the blood pressure signal using a resistance-capacitance network with a long time constant. Heart rates were measured from a Biotach Preamplifier (Gould Inc., model 13-4615-66) triggered from the ECG signal. Temperature change due to breathing was monitored with a Gould temperature preamplifier (Gould Inc., model 13-4615-54); this allowed ventilation rate to be determined. Recording was done using an 8-channel recorder (Gould Inc., model 2800S). All electrical leads were attached to penetrators inside the chamber, which permitted signals to be recorded outside when the chamber door was closed and the chamber pressurized. The pressure transducer was vented to the chamber pressure by an incision in the insulation of the transducer lead; this allowed the transducer to remain inside the chamber during the dive for blood pressure measurement.

Baseline studies

Two different sets of experiments were performed initially to characterize physiologic responses in guinea pigs to the following: a) recompression with air during a potentially fatal bout of air-dive DCS and b) breathing He-O_2 at depth, no DCS produced.

Recompression response of animals with DCS

The recompression experiments were conducted using only anesthetized animals so that leads could be repositioned if necessary for signal optimization. The animal was placed into the chamber, leads attached for recording, and 15–20 min allowed for animal stabilization. Predive recording of blood pressure, ECG, and heart rate was then performed with the chamber door partially open. The door was then closed, and the chamber compressed with air at a rate of 60 feet sea water (fsw)/min to a depth of 200 fsw gauge (fswg). While at depth, the chamber was vented with air for 1 min every 10 min to maintain O_2 and reduce CO_2 buildup. Levels of these 2 gases were monitored with an infrared CO_2 analyzer and an electrolytic O_2 analyzer (Beckman Instruments, Fullerton, CA, model 865 infrared analyzer and model OM-11 O_2 analyzer). Soda lime was placed on a tray below the cage to absorb CO_2. With only rare exceptions the percentage of O_2 was not found to go below 20.4%, and levels of CO_2 not to rise above 0.15%. Similar fluctuations in gas composition were observed in all subsequent experiments. Chamber temperature was kept at 28.0 ± 0.5°C by means of a temperature-controlling unit (Yellow Springs Instruments, Yellow Springs, OH). This temperature was adequate to allow animals to maintain normal core temperatures during experiments.

After 1 h at depth, the chamber was decompressed to the surface at 60 fsw/min. During the first 10 min at the surface, animals were monitored with the chamber door closed. It was open thereafter to ventilate the chamber. During time at the surface, blood pressure was monitored until one of the following occurred: a) mean arterial blood pressure dropped to at least 25 mmHg, or b) mean arterial blood pressure

dropped and leveled off for several seconds at 35 mmHg or lower. Based on findings from preliminary experiments, either of these two events (denoted as "minimal blood pressure") confirmed that a fatal bout of DCS was developing. Within several seconds after "minimal blood pressure" was reached, recompression of the chamber was begun with air back down to 200 fswg. In nearly all cases, this recompression prevented the animal from dying. After another 60 min at depth, the animal was decompressed to the surface, where it usually died. All data reported here are from recompressions started at the "minimal blood pressure," although treatment initiated either before or after the "minimal" point was also effective in saving the animal. However, the "minimal blood pressure" point was chosen for the majority of recompressions since it allowed recompression at the same relative time during DCS development in each animal.

He-O_2 breathing at depth

The effect of breathing He-O_2 at depth on the physiologic variables being measured was tested by diving 8 animals to 200 fswg for 1 h with He-O_2 (20.9% O_2) at 32°C. This higher chamber temperature avoided potential animal-cooling problems that were possible when using He. Animals were prepared as before, except that He-O_2 was used for compression instead of air. Other dive procedures were the same as in the recompression response experiments. At the end of 1 h, the animals were decompressed to the surface and the experiments ended. These data would be used to determine differences in effect between air and He-O_2 on normal animals due to differences in gas properties (i.e., gas density, thermal conductivity, etc.).

Series I. Two paired treatments for DCS with each animal—recompression back to initial depth (200 fswg)

These experiments were designed to compare the responses of unanesthetized animals with DCS following 200 fsw air dives to recompression with air vs He-O_2. In an attempt to deal with the substantial animal-to-animal variability inherent in decompression studies, a paired design was used for this series where each animal was treated twice for DCS. A control group was treated 2 consecutive times (treatment 1 and 2) with air. The responses of this group allowed quantitation of the variability between the 2 treatments. This variability would be influenced by the stability of the animal preparation over time and failure of the animal to fully recover during treatment 1. The amount of excess inert gas accumulated by the animal at depth also invariably would be different during the 1st compared to the 2nd hyperbaric exposure. These factors are arguably additional sources of error that might be avoided if animals were only treated once. Nevertheless, it was hoped that this design would improve the ability to resolve differences between air and He-O_2 treatment. The difference between consecutive air treatments in the control group could then be used in evaluating the significance of the difference between treatment 1 with air and treatment 2 with He-O_2 (20.9% O_2) in another group of animals (test group).

Animals were prepared as in the previous experiments and allowed a day to recover. Dive procedures were the same as in the earlier recompression studies, except where noted. These experiments, as well as those of the next series (II), examined postdecompression responses relative to predecompression values at depth rather than

relative to predive values. Therefore, no attempt was made to obtain meaningful predive values by waiting a sufficient time for the animal to recover from handling. In these cases, predive recording was done primarily to ensure proper function of the recording system.

The protocol was as follows:

a) compress to 200 fsw with air;
b) leave at depth for 60 min at 28°C;
c) decompress to surface;
d) if DCS developed, recompress (treatment 1) with air back to 200 fsw;
e) leave at depth for 60 min at 28°C;
f) decompress to surface;
g) when second bout of DCS develops, recompress (treatment 2) with air or He-O_2 back to 200 fsw;
h) leave at depth for 60 min, initially at 28°C;
i) decompress to surface where animals generally died and end experiment.

Recompression treatments were initiated at the "minimum blood pressure"; all compressions and decompressions of the chamber were performed at 60 fsw/min. The chamber temperature was kept at 28°C in all cases except during treatment 2 with He-O_2. For He-O_2 treatment, chamber temperature was increased to 32°C after the first 10 min at depth. This reduced problems of body cooling that were observed toward the end of the 1-h recovery period with He-O_2, but kept the initial treatment period for both gases at the same chamber temperature. In summary, the 2 different groups were treated as follows:

a) Control group—treatment 1 with air
—treatment 2 with air
b) Test group —treatment 1 with air
—treatment 2 with He-O_2 (20.9% O_2)

Series II. Single treatment for DCS with each animal—recompression back to various depths.

These experiments were conducted in a fashion similar to those in series I, but with three important differences:

1) Animals were recompressed following occurrence of DCS to varying depths ranging up to the depth of the preceding dive (200 or 250 fswg, *see* below). This procedure was designed to help accentuate any differences between air and He-O_2 treatments. Differences in treatment may have been masked somewhat in series I because all animals recovered well when recompressed back to depth, regardless of which gas was used. Partial recovery, which would be likely under the partial recompression in this series, would permit finer discrimination between the effect of different gas mixtures. Thus, this series allowed examination of the effect of recompression depth on recovery from DCS separately for air and He-O_2. Results would allow generation of individual dose-response curves describing recovery effectiveness vs. depth. Comparison of individual dose-response curves for the two gas mixtures would increase the statistical power of hypothesis testing in contrast to

comparison of individual recovery data points at one depth. Selection of actual recompression depth for a given animal was done in random fashion.

2) Each animal was subjected to only 1 bout of DCS and 1 subsequent recompression treatment with either air or He-O_2 (20.9% O_2). Unlike series I, these experiments sought to avoid potential problems related to deterioration and instability of the animal over multiple bouts of DCS. Two dive depths were used. If DCS did not develop by 25 min after the first 1 h, 200 fsw dive on air, the animal was recompressed to 250 fswg with air, held there for another hour, and then decompressed to the surface. This procedure generally produced DCS in animals that did not get sick following the first 200 fsw dive.

3) All experiments were conducted with the chamber temperature at 32°C. This allowed core temperature to be more easily maintained, especially toward the end of the 1-h recovery period with He-O_2 treatments. The protocol was, therefore, as follows:

a) compress to 200 fsw with air;
b) leave at depth for 60 min at 32°C;
c) decompress to surface;
d) treatment following 200-fsw air dives:
   i) if DCS developed, recompress with air or He-O_2 to a depth ranging up to 200 fsw,
   ii) leave at depth for 60 min at 32°C, and
   iii) decompress to surface and end experiment;
e) treatment following 250-fsw dives:
   i) if DCS did not develop following the first 200-fsw air dive, recompress to 250 fsw with air,
   ii) leave at depth for 60 min at 32°C,
   iii) decompress to surface,
   iv) in almost all cases, DCS developed and animals were recompressed with air or He-O_2 to a depth ranging up to 220 fsw,
   v) leave at depth for 60 min at 32°C,
   vi) decompress to surface and end experiment.

As in series I, all compressions and decompressions of the chamber were performed at 60 fsw/min. In summary, the protocol resulted in 4 different groups:

a) air treatment to varying depth following 200-fsw air dive;
b) He-O_2 (20.9% O_2) treatment to varying depth following 200-fsw air dive;
c) air treatment to varying depth following 250-fsw air dive;
d) He-O_2 (20.9% O_2) treatment to varying depth following 250-fsw air dive.

Analysis

Changes in mean arterial blood pressure, heart rate, and ventilatory rate that occurred during DCS, and subsequent treatment in series I and II were calculated

relative to predecompression values measured at the end of the 1-h dive immediately before the DCS occurrence. This procedure produced values that represented absolute changes relative to baseline levels (defined to be those measured immediately before decompression). Treatment-response curves based on such values had the advantage in series I of compensating for cases of incomplete recovery following the first 60-min recompression treatment.

A method of calculation of the area under the treatment-response curves in series I and II was developed to quantitate the response of animals to recompression treatment. This permitted statistical comparisons between treatments using a single area number. The assumption here is that deviation from the baseline represents a measure of the response to DCS, and that full recovery has occurred when blood pressure, heart rate, or ventilation rate returns to baseline. Thus, integrating the curve incorporates time into the DCS response, and defines the response to be a function of the magnitude of change in the variable and the amount of time that the change lasts. By definition, a better recovery would be represented by a smaller area.

Area generation from the curves involved calculation of areas under the curve that connected the data points. Area determination was conducted individually for each animal. In the few cases of missing data, the area calculation was based on the curve connecting the available data points. When two successive points were missing, no area was calculated. Areas would be in units of min × mmHg for blood pressure, or dimensionless (min × min^{-1}) for heart rate and ventilation rate.

For purposes of analysis, areas under the response curves were determined starting at 1 min into recompression and ending either after the guinea pig had been at depth for 3 min (series I) or at 9 min into the treatment (series II). Because of the volatility of heart rate and ventilation during the first 60 s of recompression, this time period was ignored in area determination. The 3-min endpoint was chosen for series I because data beyond this point were not available for all animals. This was due to an initial experimental design that called for continuous data recording only up to 3 min at depth. A longer data collection time for series II allowed area determinations that were several minutes greater than before. Venting the chamber at depth at 10-min intervals precluded much longer area calculations, because the venting process disturbed the animal and affected the variables being measured.

Hypotheses testing for series II was performed using a least-squares fitting program with the following model:

$$Y\,(\text{air}) = \text{B0} + \text{B1} \cdot X + \text{B2} \cdot X^2 \qquad (1)$$

$$Y\,(\text{He-O}_2) = Y\,(\text{air}) + \text{B3} \cdot X + \text{B4} \cdot X^2 \qquad (2)$$

The recompression depth was defined to be the independent variable (X); the area under the response curve, the dependent variable (Y), and B0, B1, B2, B3, and B4 parameters in the model estimated by the fitting process. A significant B1 would define a linear relationship between recompression depth and recovery for air treatment, whereas a significant B2 would indicate a curvilinear function. Significant B3 and/or B4 parameters would mean that there were significant effects on the slope or curvilinear function due to $He\text{-}O_2$. Thus, significance of B3 and/or B4 would imply differences in recovery due to treatment gas. This model assumes that the response

area vs. recompression depth curves for both gases have the same B0 or Y intercept, signifying that with no recompression the gas difference drops out.

RESULTS

Baseline studies

Recompression response of animals with DCS

Table 1 presents the data summary from the air recompression experiments following development of DCS after surfacing from an air dive. Comparing the predive (on the surface) and predecompression (at depth, immediately before decompression began) values reveal little change in any of the three variables after being at depth for 1 h. During development of DCS, a 50% or more decline in arterial pressure occurred along with cardiac arrhythmia, resulting in a slight bradycardia at the "minimal blood pressure" defined earlier. These events were accompanied by a doubling of ventilatory frequency. Upon recompression at the "minimal blood pressure," blood pressure quickly rose back toward predecompression levels, although

TABLE 1
RECOMPRESSION OF ANIMALS WITH DCS: DATA SUMMARY DEMONSTRATING ABILITY TO TREAT ANESTHETIZED GUINEA PIGS SUFFERING FROM DCS FOLLOWING A 200-FSW, 60-MIN AIR DIVE

	MABP mmHg	Heart Rate, min^{-1}	Ventilatory Frequency, min^{-1}
Predive, on surface	55 (7)	270 (9)	45 (9)
Predecompression, after 60 min at depth	58 (6)	269 (16)	50 (12)
DCS, at minimum MABP	21 (5)	242 (8)	97 (38)
Recompression, after several seconds at depth	43 (6)	239 (13)	85 (34)
End treatment, after 60 min at depth	59 (9)	271 (36)	59 (16)

Recompression was back to 200 fsw on air for another 60 min.
Values are means from 6 animals; numbers in parentheses are SD; MABP = mean arterial blood pressure. Predive values measured before any dives started. All compressions and decompressions performed at 60 fsw/min. Mean weight (SD) = 528 (17) g.

complete recovery required some time at depth. Breathing and heart rate recovered more slowly, with good if not full recovery in these variables appearing to have occurred by the end of the 60-min dive, as judged by the end treatment values.

He-O_2 *breathing at depth*

Data from the He-O_2 dives examining the effect of breathing He-O_2 at depth on the physiologic variables are presented in Table 2, along with data from series I and II to allow comparison. No differences in the predecompression values (at depth) among the 3 groups could be demonstrated based on confidence limits.

Series I. Two paired treatments for DCS with each animal: recompression back to initial depth (200 fswg)

Treatment response curves during the initial time period are presented in Fig. 1 for both dives of the control and test groups. Responses to DCS are similar to those described before, with blood pressure falling over 50%, ventilatory rate doubling, and heart rate declining slightly. Almost complete recovery of blood pressure occurs very rapidly with all air recompressions, although full recovery back to baseline takes a considerably longer time. Heart rate and breathing recover more slowly, even

TABLE 2
EFFECT OF BREATHING AIR OR HE-O_2 (20.9% O_2) AT DEPTH ON PHYSIOLOGIC VARIABLES

	MABP, mmHg	Heart Rate, min^{-1}	Ventilatory Frequency min^{-1}	Chamber Temperature °C
HE-O_2 dives, baseline studies	73 (5)	301 (23)	94 (14)	32
n	4	8	8	
Air dives, series I	68 (6)	310 (58)	90 (12)	28
n	13	15	15	
Air dives, series II	68 (7)	271 (29)	89 (15)	32
n	65	71	71	

All measurements made on unanesthetized guinea pigs after 1 h at 200 fsw on air or He-O_2 before occurrence of DCS.

Values are means of *n* animals with SD in parentheses. Values from air dives: first dive with all animals. Mean weight (SD): He-O_2 dives: 573 (31), $n = 8$; air dives (series I): 564 (35), $n = 15$; air dives[2] (series II): 574 (28), $n = 71$.

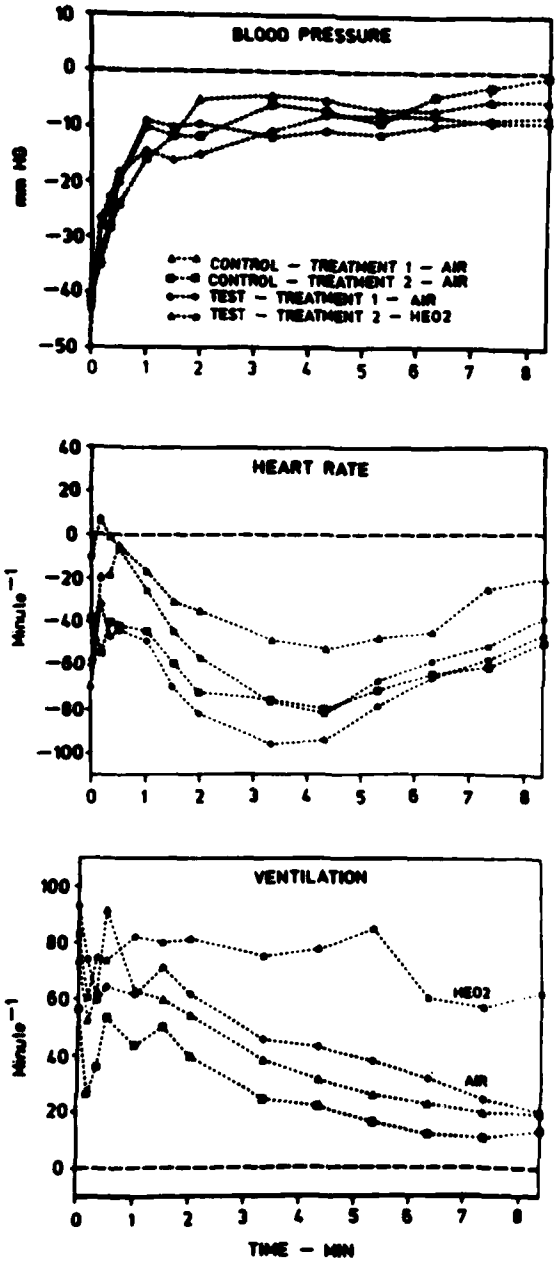

Fig. 1. Changes in MABP, heart rate, and ventilation frequency during DCS and recompression treatment following 200-fsw-air dives. Responses are from unanesthetized guinea pigs to 2 consecutive bouts of DCS and 2 subsequent 60-min recompression treatments back to 200 fsw with each animal. *Curves* represent changes in variables relative to the value at depth immediately before decompression and subsequent DCS. Plotted points are means from 5–9 animals. Values at time of recompression are plotted at time = 0, with subsequent time being time into recompression treatment. Control group: treatment 1 with air, treatment 2 with air; test group: treatment 1 with air, treatment 2 with He-O_2 (20.9% O_2)

though heart rate shows a quick spike toward baseline very early in the treatment phase. With both air and He-O_2 recompression treatments, good recovery of all variables was observed by the end of the treatment period (end-treatment measurements are not presented here). However, it certainly cannot be assumed from this

recovery that complete resolution of bubbles and elimination of the gas phase have occurred by the end of treatment.

Blood pressure responses are remarkably similar for all treatments, whereas the pattern and magnitude of heart rate response are not as consistent among treatments. The breathing recovery curves for the air recompressions appear to agree well, and there appears to be a difference between the effect of air vs. He-O_2 recompression on the ventilatory response. Breathing appears to stay elevated for a longer time when He-O_2 is used for recompression compared to when air is the recompression gas.

In reporting the results from these area determinations, only areas under the breathing rate curves are given in Table 3. Most of the change in blood pressure occurs within the first minute, the initial period of time that is excluded from area calculations. Therefore, blood pressure areas are probably not very meaningful since they only reflect a small proportion of the actual change in blood pressure. The variability in heart rate responses among the 3 air treatments makes comparison difficult between air and He-O_2 treatments. However, the apparent similarity in breathing recovery among the air treatments suggests that examination of areas from this response could be an appropriate method to use in comparing effectiveness of recompression treatments.

Comparison of ventilation rate response areas for the 200-fsw dive control group (*see* Table 3) suggests somewhat better recovery (smaller area) for the second air treatment relative to the first air treatment. Conversely, for the test group, the second treatment (He-O_2) appears to produce a worse recovery relative to the first (air). A least-squares curve fitting program was used to test the significance of the interaction between treatment number (1st and 2nd) and group (control or test). This interaction was found to be significant ($P < 0.01$) and to represent a difference between the responses of the control and test groups to 2 recompression treatments: treatment 2 area being smaller than treatment 1 for the control group and larger than treatment 1 for the test group. Thus, air recompression appears to be more effective in producing recovery in breathing rate following DCS when examined using a paired experimental design such as the one here.

Series II. Single treatment for DCS with each animal: recompression back to various depths

Animals were recompressed with air to depths ranging from 30 to 220 fswg. There were 27 guinea pigs in the 200-fsw-dive group and 11 in the 250-fsw group. Of these,

TABLE 3

AREAS UNDER THE VENTILATORY RATE RESPONSE CURVES (SHOWN IN FIG. 1) FROM SERIES I EXPERIMENTS

	Control	Test
Treatment 1	12,394 (5,096)	15,310 (10,785)
Treatment 2	8,588 (7,068)	24,863 (12,413)
n	5	8

Values are means of *n* animals with SD in parentheses. Control: treatments 1 and 2 are recompressions with air. Test: treatment 1 is recompression with air, treatment 2 is recompression with He-O_2 (20.9% O_2). All recompression treatments are back to the depth of the dive (200 fsw). A significant ($P < 0.01$) interaction exists between group (control or test) and treatment (1 or 2), *see* text.

only 1 animal (from the 200-fsw group) died during treatment before reaching depth (and that was at the most shallow depth, 30 fswg). Two other animals (both also from the 200-fsw group) died at treatment depth before the end of the 1-h recovery period. All other guinea pigs from the 200-fsw-dive group and all from the 250-fsw-dive group survived the DCS and 1-h recompression treatment period. With the exception of the 3 guinea pigs that died and 1 other animal that exhibited a strange hypertensive response during treatment, all animals were used in analysis of recovery patterns. Final analysis was, therefore, performed on data from 23 animals in the 200-fsw group and 11 in the 250-fsw group.

Animals were recompressed with He-O_2 to depths ranging from 60 to 200 fswg. There were 21 animals in the 200-fsw-dive group, and 12 in the 250-fsw-dive group. All lived after recompression treatment and all were used in the analysis. Differences in survival rates between air and He-O_2 treatment are not significant based on binomial confidence limits.

Only areas under breathing recovery response curves will be discussed for this series. Plots of these areas vs. depth of recompression for each animal are presented in Fig. 2. Hypothesis testing using the models described by Eqs. *1* and *2* established the significance of parameters B1 ($P < 0.05$) and B3 ($P < 0.01$) for the 200-fsw dives, and B1 ($P < 0.05$) for the 250-fsw dives. The estimated relationships between response area and treatment were as follows:

$$\begin{aligned}
\text{Dives 200 fsw: Area (air)} &= 34{,}023\,(4229) - 89\,(34)\ \text{recompression depth} \\
\text{Area (He-}O_2\text{)} &= \text{area (air)} + 101\,(22)\ \text{recompression depth} \\
&= 34{,}023\,(4229) + 12\ \text{recompression depth,} \\
\text{Dives 250 fsw: Area (air or He-}O_2\text{)} &= 47{,}802\,(6369) - 99\,(45)\ \text{recompression depth.}
\end{aligned}$$

Standard errors of the estimates are in parentheses. These curves are also included in Fig. 2. The uncertainty associated with parameters B1 and B3 for the 200-fsw dives preclude distinguishing the slope of the curve for He-O_2 treatment from zero. From these results it can be concluded that for the 200-fsw dives treatment effectiveness improves as recompression depth is increased using air, whereas no improvement occurs with depth using He-O_2. In the case of the 250-fsw dives, no difference due to treatment gas could be demonstrated with recovery increasing with recompression depth for both air and He-O_2. The present experiments, therefore, can resolve differences in treatment effectiveness between the two gases for the 200-fsw dives, but not for the 250-fsw dives.

Regardless of differences in effectiveness of the two gases during the treatment phase, by the end of the 60-min treatment period breathing rate on average had nearly returned to predecompression levels for both gases. After 60 min at depth end-treatment breathing rates were on average (all recompression depths averaged together) only 5 and 6 min^{-1} above the predecompression rates for the 200- and 250-fsw air groups, respectively, and only 9 and 11 for the respective He-O_2 groups.

Animal temperature

At the start of the experiments, the rectal temperature of most animals was 39 ± 1°C. This agrees with the normal range of rectal temperatures cited for guinea pigs

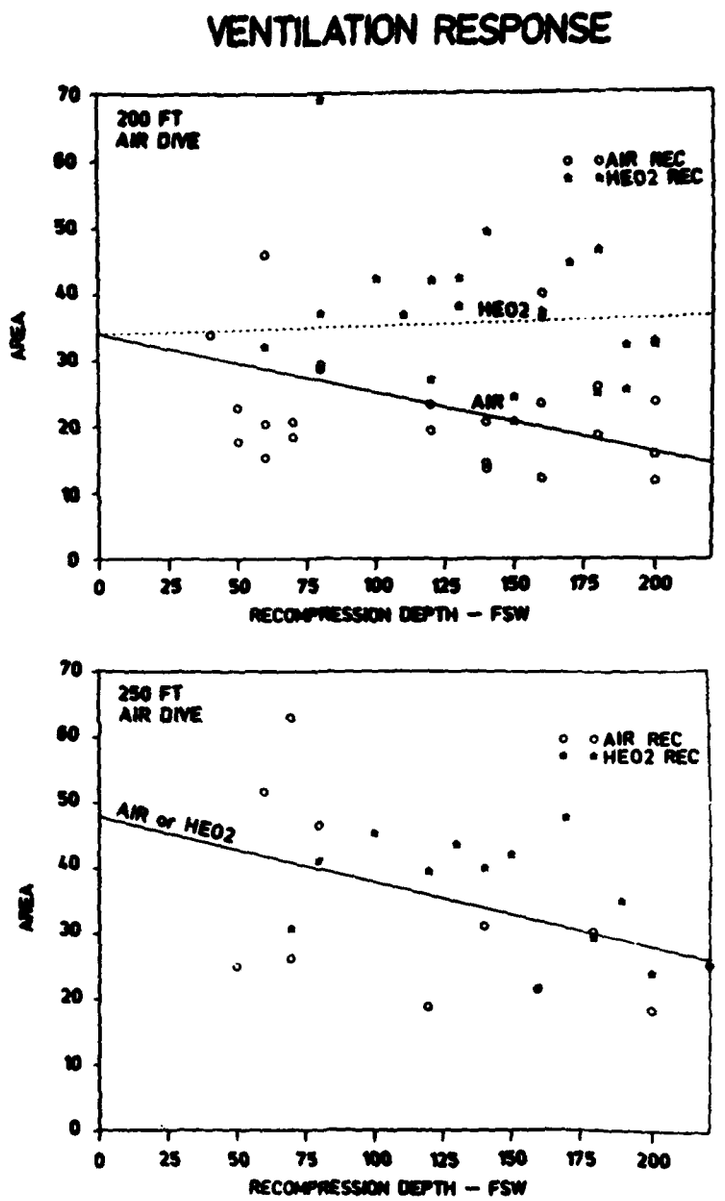

Fig. 2. Recovery in ventilation rate of unanesthetized guinea pigs from DCS vs. recompression depth following 200 or 250-fsw-air dives. Recompression treatment was to various depths with air or He-O_2 (20.9% O_2). Recovery in ventilation rate is quantified by the area under the breathing response curve. Recovery areas measured from 1 to 9 *min into treatment*. Larger areas = smaller recovery. Each point is based on 1 animal. Least-squares-derived curves (as given in text) are included: significant difference between air and He-O_2 treatments following 200-fsw dives, but not following 250-fsw dives.

by Obeck (9). Thus, any temperature below this was assumed to be hypothermic despite recently reported average temperatures for unanesthetized guinea pigs in the laboratory that are as low as 37°C (10). Some animals in the current study started out with temperatures slightly below 38°C; however, most of these animals quickly warmed up above 38°C when initially compressed to depth with air or He-O_2 (in the case of the He-O_2 breathing experiments). Thereafter, rectal temperatures generally remained in the 38–40°C range during all dives and treatments on air with the chamber at 28°C, and during He-O_2 breathing tests with animals without DCS at 32°C. Some cooling problems were evident when He-O_2 was used to compress sick animals. Body temperatures of a few animals fell slightly below 38°C during the latter stages of treatment, even with a chamber temperature of 32°C. These periods of lower temperature, however, were well after data collection for area generation had been completed.

DISCUSSION

This investigation documented a model of severe DCS in guinea pigs that allowed comparison of the effectiveness of recompression treatment using air or He-O_2. The systemic hypotension and tachypnea seen in these animals following decompression are characteristic responses of DCS. In addition to these, pulmonary hypertension, decline in cardiac output, hemoconcentration, and arterial hypoxemia have been reported in animals with severe DCS (11–14).

Pulmonary embolism resulting from DCS or some other insult is know to produce pulmonary hypertension and tachypnea (2, 12, 13). In fact, the first response in anesthetized dogs following experimental venous injection of small amounts of air is an increased respiratory rate (13). From these observations, marked changes in ventilatory rate have been interpreted as evidence that DCS is developing (12, 13). Thus, breathing appears to be an important indicating variable for this disease. Because of its reproducibility and relatively long time course, recovery in ventilatory rate was used as a measure of effectiveness of treatment in the current study.

Comparison of air and He-O_2 recompression responses necessitates separation of the differences in treatment effectiveness of these gases from the differences in levels of the measured variables (i.e., blood pressure, heart rate, and ventilatory frequency) caused by breathing these gases at depth. Physiologic effects due to helium, on the surface and at depth, appear to be secondary effects accompanying body cooling that is promoted by the high thermal conductivity of this gas (15–17). The increases in variables such as breathing and heart rate that have been observed with He-O_2 breathing in other studies appear to occur in conjunction with increasing metabolic rate as body temperature falls. Differences between air and He-O_2 disappear when measurements are made in animals in which normal body temperature is maintained.

Although blood pressures from the current study may seem low (Tables 1 and 2), values agree with previous reports indicating that blood pressures from guinea pigs are unusually low for small mammals (18). Comparison of blood pressure, heart rate, and ventilatory frequency from healthy animals exhibiting normal rectal temperatures (Table 2) agrees with the observations regarding He-O_2 just mentioned. No apparent differences were seen in values between air and He-O_2 breathing at depth. Thus,

observed differences in treatment responses might be assumed to reflect real differences due to the treatment. However, comparisons between air and He-O_2 animals that have not experienced DCS may not be applicable to the situation when animals have DCS and appear to be more susceptible to body cooling. A more appropriate observation probably is the occurrence of almost complete recovery in breathing in animals treated for DCS with either air or He-O_2 after 60 min of treatment (series II). This suggests that both gases will produce nearly complete recovery in breathing rate, but that the rate of recovery may be slower when He-O_2 is used.

Using breathing recovery (as quantitated by the area under the response curve) as an index of treatment effectiveness, air recompression appears more effective than that with He-O_2. The inability to demonstrate a difference between the 2 gas treatments following 250-fsw air dives probably relates to the small number of data points associated with these dives. A paucity of data limits the resolving ability of hypothesis testing. The improved recovery with increased recompression depth that was observed in the present study does not seem particularly surprising at first, assuming that resolution of bubbles is aided by increased hydrostatic pressure. However, P_{O_2} increases directly with depth in these experiments due to use of mixtures with a constant percentage of O_2. Thus, increasing recompression depth would be raising, in tandem, both hydrostatic pressure and P_{O_2}, both of which could be involved in the positive response to depth seen here with air. No previous studies have shown added therapeutic benefit with increasing treatment pressure, although several recent investigations specifically examined this possibility (19, 20). On the other hand, results from experiments that increased the partial pressure of O_2 while keeping depth constant suggested that there was an optimum P_{O_2} at 2.0 bar for treatment of spinal cord DCS in dogs (21). The initial improvement due to P_{O_2} increase was postulated to be due at least partly to increased tissue oxygenation as well as to elevated inert gas clearance. Hyperoxic vasoconstriction was offered as one possible reason for decline in treatment effectiveness with P_{O_2} higher than 2.0 bar. In this case, although bubble resolution would be hastened by an increased inert gas gradient, vasoconstriction would reduce blood flow thereby slowing shrinkage of bubbles.

Explanation of differences in treatment response between air and He-O_2 may reside in differences in mass transfer rates of the two gases. These rate differences depend on solubility and diffusion coefficients and partial pressure gradients. Because the O_2 fraction is identical in both instances, the slower recovery with He-O_2 recompression could be due to hindrance of bubble resolution by a counterdiffusion phenomenon (4, 5). Recompression with He-O_2 would not only increase hydrostatic pressure and P_{O_2}, but also ambient P_{He}. Relative rates of uptake or elimination of gas from intravascular bubbles should partially depend on the ratio of the products of solubility and diffusion coefficients in blood (6). These bubbles might be expected to grow, at least temporarily, under certain circumstances based on reported values of these coefficients (22). Prediction of gas-switching effects on bubbles in other situations, such as in poorly perfused tissues, are probably more complex (23) and might depend on gas coefficients for the particular tissues as well as limiting perfusion rates. In these experiments a negative effect of increased P_{He} may be reversing the beneficial effect of recompression following air dives. Experiments switching from N_2 to He both in vitro (24) and in animals (4, 6, 25) support this possibility. Recently, recompression with He-O_2 was demonstrated to be less effective than with air for treatment of spinal cord DCS in dogs (Sykes, Hallenbeck, Flynn, unpublished data).

Blood pressure was observed here to recover rapidly, with most of the recovery occurring before reaching full recompression depth (*see* Fig. 1 for series I responses). Although blood pressure recovery data were not presented from series II with variable recompression depth, blood pressure also recovered quickly in the series, even with shallow recompression treatments. Apparently only a relatively small amount of recompression pressure is needed to quickly reverse the hypotensive response to DCS. This agrees with previous reports that small increases in ambient pressure are sometimes very effective in treating severe DCS (12, 26). Neither heart rate nor breathing respond in this manner; their recoveries require considerably more time.

The applicability of results reported here to human diving may be limited because guinea pigs and a very severe model of DCS were used. However, these findings suggest that there is a potential for interference with normal bubble resolution when $He-O_2$ is used to treat air dive DCS. This possibility should be considered when a treatment protocol is selected for cases of DCS following air dives.

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The experiments reported herein were conducted according to the principles set forth in the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council, DHHS, Publication Number (NIH)85-23.

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Lillo RS, MacCallum ME, Pitkin RB. Recompression à l'air vs. $He-O_2$ pour le traitement de la maladie de décompression chez le cobaye. Undersea Biomed Res 1988; 15(4):283–300.—Le traitement par recompression avec un mélange gazeux d'air vs. hélium-oxygène (79.1% He:20.9% O_2) fut examiné dans un modèle de maladie de décompression (MDC) sévère avec des cobayes albinos mâles (*Cavia porcellus*, 500–600 g). Après la décompression à la surface de plongées simulée à l'air à 200 ou 250 pes, les animaux anesthésiés et non anesthésiés montrèrent souvent des réponses indicatrices d'une attaque fatale de MDC (incluant hypotension, arhythmie cardiaque et tachypnée). Dès la recompression en profondeur à l'air, un recouvrement satisfaisant fut observé chez les animaux souffrant de MDC. La comparaison des réponses de la recompression à l'air vs. $He-O_2$ des animaux non anesthésiés avec recompression à la profondeur initiale (200 pes) révéla un recouvrement plus lent de la tachypnée avec $He-O_2$. La recompression à une profondeur intermédiaire après des plongées à l'air à 200 pes produisit des différences significatives dans le recouvrement selon la relation entre la profondeur de recompression avec l'air et $He-O_2$. L'efficacité du traitement augmenta avec la profondeur pour l'air, mais non pour l'$He-O_2$. Ces résultats indiquent la possibilité de différences dans la réponse à la recompression avec l'air vs. $He-O_2$ lorsque le recouvrement de la ventilation est employé comme mesure de l'efficacité pour le traitement de la MDC chez les cobayes après des plongées à l'air.

Lillo RS, MacCallum ME, Pitkin RB. Tratamiento de recompresion con aire vs. $He-O_2$ para enfermedad por descompresion en conejillos de indias. Undersea Biomed Res 1988; 15(4):283–300.—Se estudio el tratamiento de recompresion con aire vs. $He-O_2$ (20.9% O_2) en un modelo de enfermedad por descompresion severa (EPD), empleando conejillos de indias albinos machos (*Cavia parcellus*, 500–600 g). Los animales anestesiados, como los que no lo estaban, mostraban con frecuencia, respuestas indicativas de un ataque fatal de EPD (incluyendo hipotension, arritmias cardiacas, y taquipnea), posterior a la descompresion a superficie en simulacros de inmersiones con aire a 200 o 250 pies de agua salada (pas). Se observo una

recuperacion buena en los animales con EPD al recomprimirlos con aire a la profundidad. Al comparar la respuesta de la recompresion a la profundidad inicial (200 pas) con aire vs. He-O_2 en los animales no anestesiados, se encontro una recuperacion mas lenta a la taquipnea con He-O_2. La recompresion a una profundidad parcial, posterior a inmersiones con aire a 200 pas, produjo diferencias significativas en la recuperacion vs. relación de la profundidad de recompresion entre aire y He-O_2. La eficacia del tratamiento mejoro con profundidades mayores con aire, pero no con He-O_2. Estos datos indican las diferencias potenciales en la respuesta a la recompresion con aire vs. He-O_2, cuando se emplea la recuperacion ventilatoria para medir la efectividad del tratamiento de EPD en conejillos de indias posterior a inmersiones con aire.

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