Bull. Tokyo Med. Dent. Univ., 30: 25–35, 1983

ANALYSIS OF GAS COMPOSITION OF INTRAVASCULAR BUBBLES PRODUCED BY DECOMPRESSION

BY

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ABSTRACT

The gas composition of intravascular bubbles produced by decompression was investigated in rabbits using gas chromatography. The animals were exposed to 8 ATA for 30 min. All samples of bubbles were taken from the animals under 0.2 ATA pressure gradient so that no air could enter the sampling system from the outside.

The percentage of carbon dioxide in the bubbles tended to decrease at first and then increased with post-decompression time. On the other hand, the percentage of oxygen tended to change in the opposite manner.

Actual analysis of bubbles in the living decompressed animals indicates that carbon dioxide may be an outstanding factor in the initiation and ealy growth of bubbles. In view of this, Haldane's classical maximum supersaturation limit for avoiding decompression sickness should be examined and possibly modified for gases other than nitrogen.

Key words: decompression sickness, bubble, gas composition, carbon dioxide, blood gas tension

INTRODUCTION

Decompression sickness (DCS) follows the reduction of the environmental pressure, and various manifestations of this condition are known. These symptoms can be grouped into four categories as follows (Hills [11]):

(I) Limb pain: This is a local pain known as the "bends" and the most common symptom of DCS.

(II) Symptoms related to the central nervous system: These are less common than Type I but are much more serious.

(III) Otologic disorders: These include symptoms involving the dysfunction of the vestibular mechanism and those associated with the cochlear mechanism.

(IV) Dysbaric osteonecrosis: This occurs in both the shaft and the ends of the long bones.

The "chokes": This is a less common symptom leading to death. Different mechanisms have been proposed for these symptoms. The primary cause is generally considered to be the formation and growth of bubbles in the blood and tissues from the gases taken up during exposure (Harvey [1]; Buckles [2]). The principal factors that determine the quantity of gas dissolved in the tissue or blood are pressure and time. The formation of bubbles is determined essentially by the rate of decompression.

Boyle [3] was the first to report on the bubble within the eye of a viper exposed to a high vacuum. On the basis of subsequent animal experiments, this bubble has been believed to be nitrogen that had been stored up in excess in the tissues or blood, following Dalton's law (Bert [4]; Boycott *et al.* [5]).

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Received for publication, February 14, 1983.

Table 1. Data on Bubble Composition Reported to Date

	Animal	Sampling site	Bubble composition (%)				Condition
			N_2	O_2	CO_2		
Bert [4] 1878	Dog	Right heart	79.2 83.0	Traces 1.9	20.8 15.1	Two cases	Hyperbaric, died
	Cat	Right heart	84.1 *	0 *	15.9 17	Two cases	
Armstrong [6] 1939	Goat	Jugular vein	65.0	6.7	28.3	One case (?*)	Hypobaric, (?*) died (?*)
		Right ventricle of the heart	60.3	11.4	28.3		
Harris *et al.* [9] 1945	Frog	Large vein	95	1~2	3.5	Several cases (?*)	Hypobaric, alive (?*)
Smith-Sivertsen [7] 1981	Rat	Aorta	79.3 — 81.3 —	2.60 — 4.2 —	— 22.6 — 16.2	Four cases	Hypobaric, died
Ishiyama *et al.* [8] 1981	Dog	Inferior vena cava	86.26±1.55	2.30±0.88	11.44±1.29	Mean±S.D. n=7	Hyperbaric, died
		Right atrium	82.73±1.28	2.15±0.68	15.12±0.82	Mean±S.D. n=5	

* No description in the paper.

Generally, reports on the bubble composition have been derived from autopsies on decompressed animals (Bert [4]; Armstrong [6]; Smith-Sivertsen [7]; Ishiyama *et al.* [8]) and very little work has been done on the live animals. These reports are summarized in Table 1. It is not expected that the gas composition of bubbles after death is the same as that in the living state, because the gas composition may change with post-decompression time.

This study is designed to determine the bubble composition by the analysis of bubble and blood samples taken from the vessels of live rabbits at various intervals following decompression. It is very important to ascertain the gas composition of the intravascular bubbles and their changes with post-decompression time, since this may give some insight into their origin and lead to the prevention of DCS.

Materials and Methods

The methods adopted here are modified from those that Hills *et al.* [10] have introduced.

I. Surgical and compression procedures

Healthy male adult Japanese white rabbits weighing 2.5~3.5 kg were used in this study. The animals were anesthetized with intravenous sodium pentobarbital (25 mg/kg) and catheters (Fr. No. 5) were placed in the inferior vena cava and aorta from the left femoral vein and artery (Fig. 1). After the animals were heparinized (1000 U/kg sodium heparin), the surgical cradle was placed inside the pressure chamber. The venous catheter was passed through and

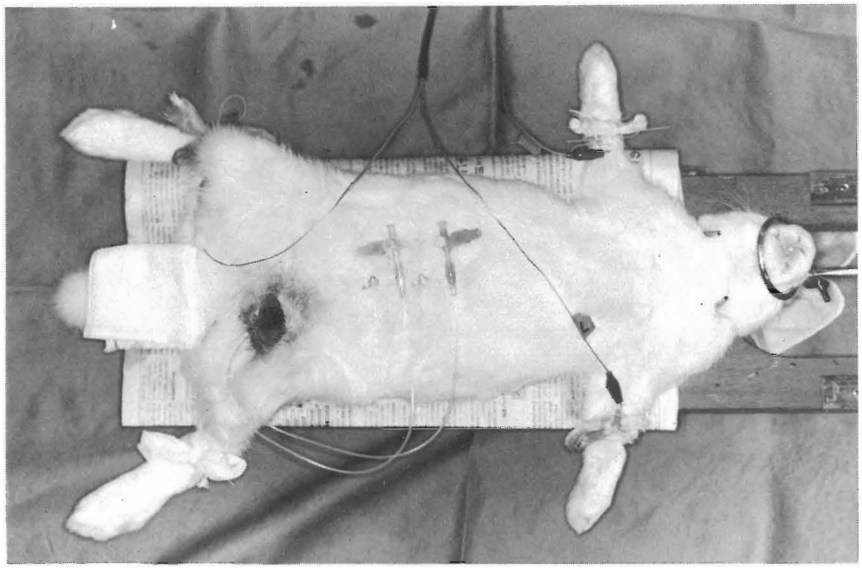

Fig. 1. Intravascular Catheterization and E.C.G. Monitoring.

the arterial catheter was connected to the high pressure stopcock valve located on the external wall of the chamber, which allowed the withdrawal of the blood at depth while the animal remained within the chamber (Fig. 2).

The chamber was pressurized with air at a rate of 10 ATA/min. Following 30 min of exposure at 8 ATA, the animals were decompressed at a rate of 3.4 ATA/min to a sampling pressure of 1.2 ATA (Fig. 3). This decompression rate was so severe that the bubbles in the vessel could be taken from almost all animals. The 1.2 ATA sampling pressure was selected to allow blood to flow freely from the sampling catheters. Electrocardiograms (E.C.G.) were also taken simultaneously.

II. Sampling of bubbles and blood

After decompression, the bubbles and blood were passively withdrawn into the 3-ml syringe via the venous catheter at various intervals (1~3 min). The plunger of the sampling syringe had been dipped in octyl alcohol and wiped lightly, and then the dead space of the syringe had been filled with heparin sodium. Under the pressure gradient, no air was admitted into the sampling system from the outside.

III. Analysis of samples

Immediately after taking the samples, the bubbles were transfered into the 25-μl S.G.E. Microlitre Gas/High Pressure Liquid Syringe Type A (Scientific Glass Engineering Pty. Ltd., North Melbourne, Australia). Samples of gas were then analyzed by gas chromatograph (GC-3BT, Schimadzu Corporation, Kyoto, Japan) for nitrogen, oxygen and carbon dioxide contents. The flow line system is illustrated in Fig. 4. In addition, samples of blood were analyzed by pH/blood gas analyzer (IL Micro 13–03/213–05, Instrumentation Laboratory, Inc. MA, U.S.A.) for oxygen and carbon dioxide gas tension. The volume of the gas sample was 20 μl and that of the blood sample was 300 μl.

Results

Several samples (3~6) of bubbles, along with blood, were able to be taken

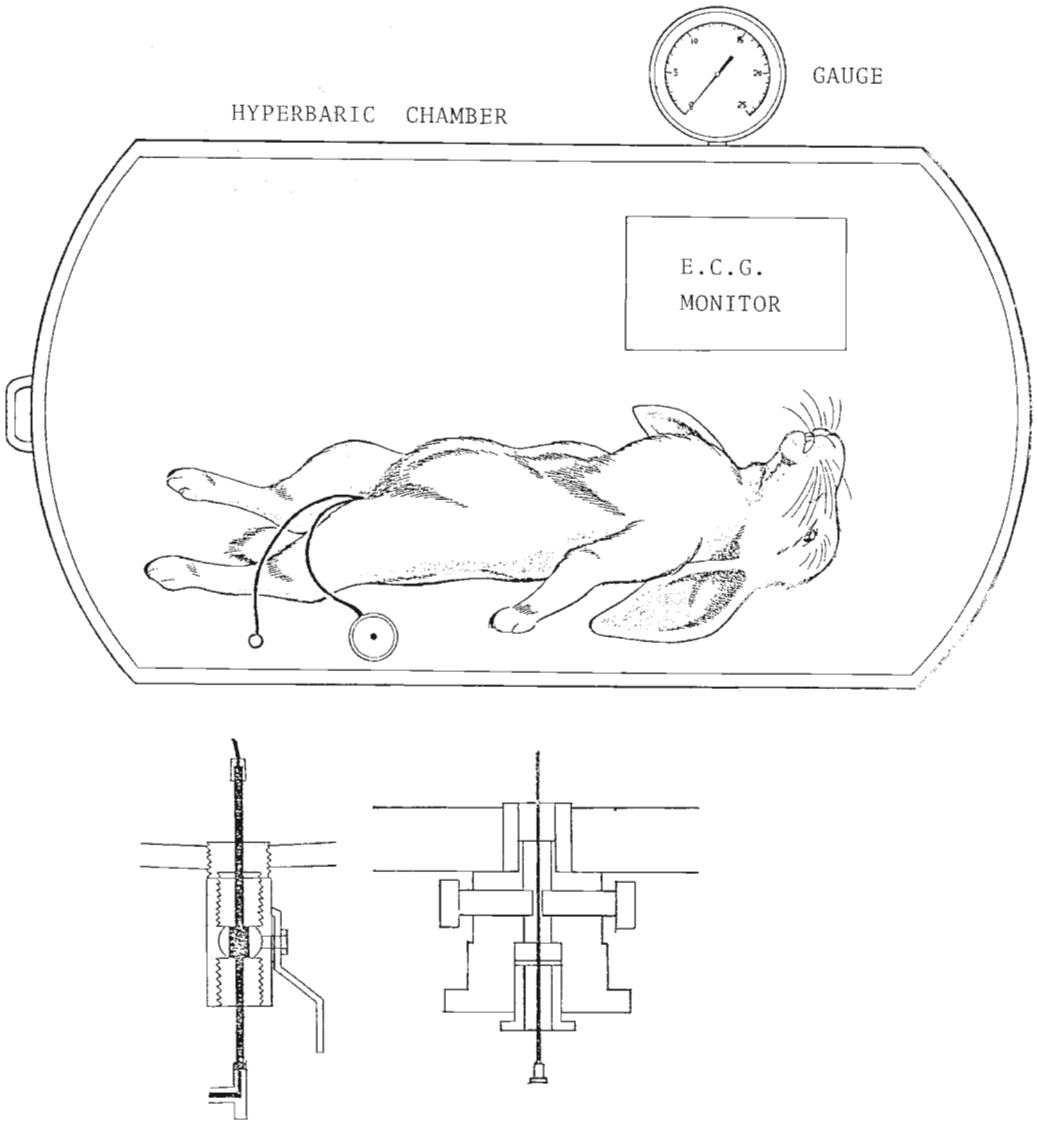

Fig. 2. Schema of Collection Method, The venous catheter passes through the chamber wall. The arterial catheter is connected to the high pressure stopcock valve.

from eleven rabbits at timed intervals after decompression. It was impossible to take bubbles sufficient for the analysis from the other rabbits.

All rabbits from which samples could be taken died of the "chokes" within 30 min (mean±S.D.=15±7) after the end of decompression. While the animals were still alive, bubbles and blood samples could be taken from the rabbits.

The three typical cases of changes in the bubble composition and blood gas tension after decompression are presented in Figs. 5~7. The gas tension of

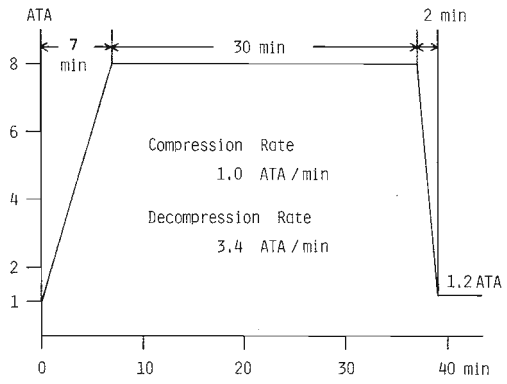

Fig. 3. Compression-Decompression Profile.

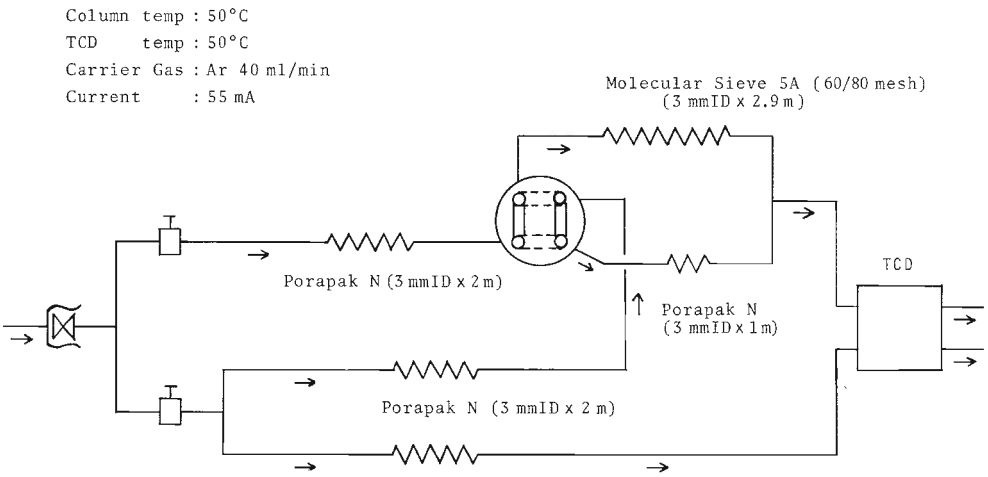

Fig. 4. Flow Line System of Gas Chromatograph and Analysis Conditions.

oxygen in the venous blood decreased with the post-decompression time. On the contrary, the gas tension of carbon dioxide increased. The percentage of carbon dioxide in the bubbles appears to decrease at first and then increases gradually, while that of oxygen appears to change in the opposite manner.

The results of all bubble samples of the eleven rabbits were plotted against the mean time after the end of decompression (Fig. 8). The percentage of carbon dioxide in the bubbles appears to decrease at first and then increases gradually, while that of oxygen appears to change in the opposite manner.

Table 2. Changes of Gas Composition of Bubbles With Post-Decompression Time Calculated From Regression Curves of Each Gas

Time / Gas	5 min	10 min	15 min
O_2	8.16%	15.51%	3.86%
CO_2	6.18	1.08	7.98
N_2	88.81	81.46	91.61

The changes in each gas with the post-decompression time calculated from the regression curves are presented in Table 2.

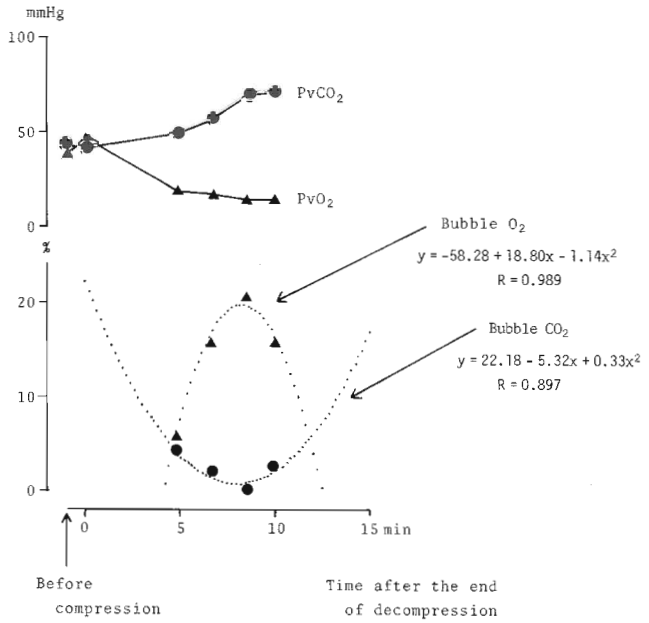

Fig. 5. Changes of Bubble Composition and Blood Gas Tension After Decompression. (Case No. 4)

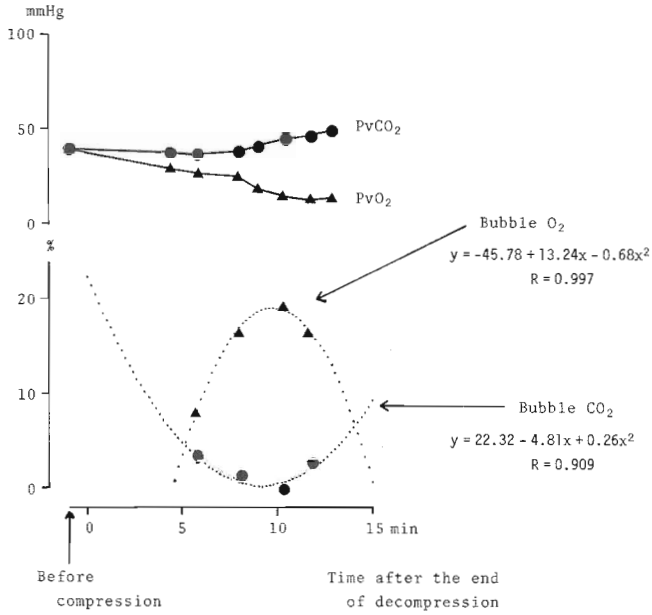

Fig. 6. Changes of Bubble Compositon and Blood Gas Tension After Decompression. (Case No. 7)

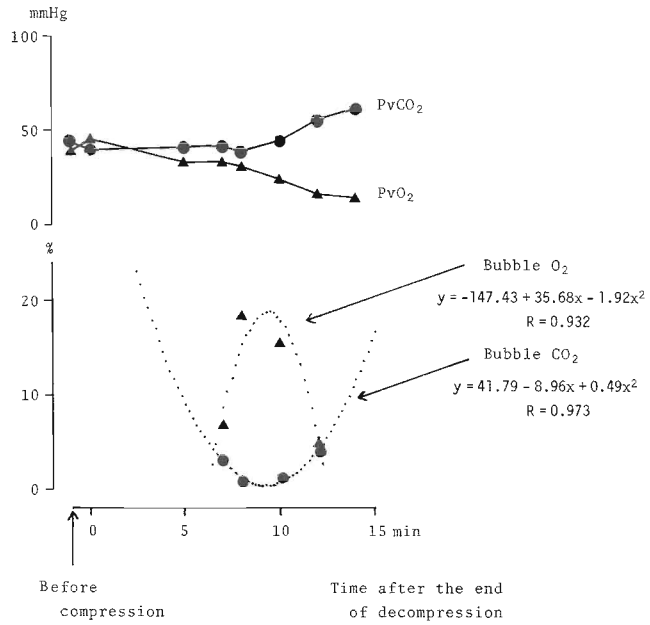

Fig. 7. Changes of Bubble Composition and Blood Gas Tension After Decompression. (Case No. 10)

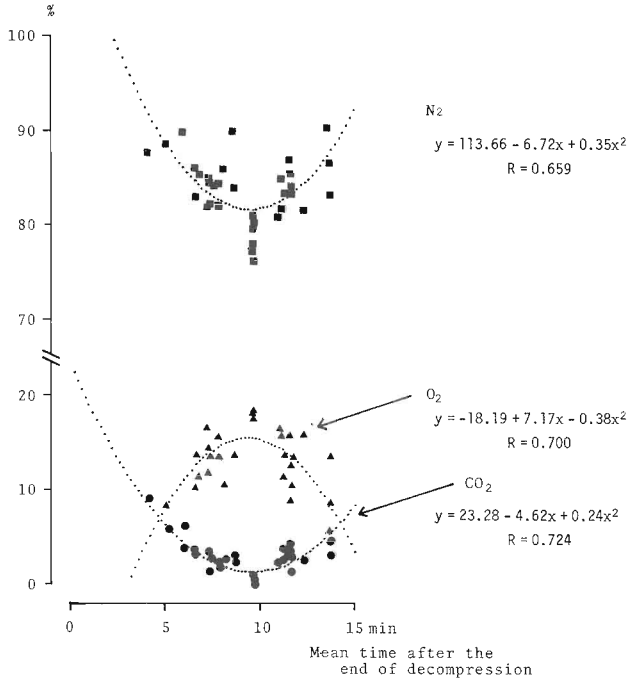

Fig. 8. Change of Bubble Composition After Decompression.

Discussion

The formation of bubbles produced by decompression can be divided into four distinct processes as follows (Hills [11]):

(I) Supersaturation of the solution
(II) Nucleation: Inception of the gas phase as minute specks (nuclei), if not already present
(III) Growth: Transfer of gas molecules from the solution into the gaseous phase
(IV) Coalescence

According to Henry's law, the concentration of gas dissolved in a liquid is at equilibrium proportional to the partial pressure (p) of the gas in contact with the liquid. This pressure determines the gas tension (t) in the liquid. If the hydrostatic pressure (P) in the liquid is P atmospheres, the difference $t-P \equiv \Delta p$ is the primary driving force for the bubble formation. When the formation of the gaseous phase is suppressed, a solution that contains the gas in excess is said to be supersaturated. Decompression provides one means of supersaturating a gas solution and a driving force for bubble growth.

For the de novo formation of bubbles in a homogenous liquid at rest containing dissolved gas, it is necessary that Δp be of the order of 100~1000 atmospheres (Harvey [1]). Since a Δp of 100~1000 atmospheres cannot exist in the resting animal, there has been little doubt that most bubbles formed in a resting animal come from the minute gas nuclei present in the blood and tissues. Once produced, bubbles may grow by diffusion of any gas into the bubbles.

Since the pressure for bubble formation increases with the decreasing gas solubility, the gas concentration rather than the tension appears to be the determining factor (Hemmingsen [12]). Nitrogen, oxygen and carbon dioxide would enter the bubbles in proportion to their concentration and at a rate depending on the diffusibility. Thus, bubbles formed in the body may not be expected to contain the estimated concentration of nitrogen, oxygen and carbon dioxide corresponding to their partial pressure in the blood. Although governed by Henry's law and the Law of Diffusion, the complicated interrelationship between the many other factors makes it difficult to ascertain the composition of a gas mixture in a bubble accurately. Therefore, it is obvious that the composition of bubbles may change very easily. Bubbles will always contain water vapor corresponding to its saturation pressure at the existing temperature, but the concentration of water vapor in the bubbles was not considered in this study.

Harvey *et al.* [13] have presented a differential equation for the growth rate of a gas bubble in terms of the rate of its radius change. It is assumed that:

1) The bubble is spherical with a radius (r);
2) It contains molecules of a single ideal gas;
3) The gas is distributed up to the gas-liquid interface;
4) Gravity is neglected so that the external pressure (P) on the bubble is uniform throughout;
5) The bubble grows in a state of mechanical quasi-equilibrium;
6) The concentration of dissolved gas in the fluid is uniform except in the shell surrounding the bubble;
7) The diffusion gradient is uniform through the shell;
8) No gas is produced or consumed within the bubble.

On the basis of these assumptions, the following differential equation was obtained for the time rate of the radius

increase, as shown in Eq. (1):

$$\frac{dr}{dt}=\frac{RTaD}{\Delta r}\frac{\Delta P}{P}\frac{r-(2\gamma/P)}{r-(4\gamma/3P)} \quad (1)$$

where:

r=radius in cm

R=gas constant, 8.3136×10^{7} erg/°C/mol

T=absolute temperature

a=solubility in mol/dyne-cm, defined by $c=a\tau$, c being the concentration in mol/cm^3 and τ the tension in dynes/cm^2

D=diffusion coefficient in cm^2/sec

Δr=thickness of the diffusion shell (3×10^{-3} cm); for $r<3\times10^{-3}$ cm, $\Delta r=r$

P=hydrostatic pressure in dynes/cm^2

τ=gas tension in water measured by gas pressure with which dissolved gas is in equilibrium

$\Delta P=\tau$-P, in dynes/cm^2

γ=surface tension in dynes/cm

t=time in seconds

Carbon dioxide, due largely to its high solubility (Table 3), may be an outstanding factor in the initiation and early growth of bubbles. The ratio of the expression RTaD/Δr is as follows:

$$N_2:CO_2=1:37.5$$

Under comparable conditions, carbon dioxide will enter or leave a gas nucleus about thirty eight times more rapidly than will nitrogen. It is possible that, during the early development of bubbles, the carbon dioxide concentration is much higher than that shown in the analysis.

Table 3. Solubility Coefficients for Various Gases in Biological Fluids at 37°C

Gas	Fluid			
	Blood α	Lean tissue α	Fat α	Olive oil α
H_2	—	—	—	0.0484
He	0.0159	—	—	0.0159
N_2	0.0130+	0.012+	0.062+	0.067
Ar	—	—	—	0.14
Ne	—	—	0.020	0.019
O_2	0.0223	0.023	—	0.112
CO_2	0.488	—	—	1.25

From Shilling *et al.* [14]

In this study, the regression curve of the carbon dioxide concentration in the bubbles at a mean time after the end of the decompression is obtained, as shown in Eq. (2):

$$Y=23.28+(-4.62)X+0.24X^2 \quad (2)$$
$$n=35,\ R=0.724$$

where:

Y=carbon dioxide concentration in the bubbles (%)

X=the mean time after the end of the decompression in minutes

n=sample number

R=coefficient of regression

From this equation, it is calculted that the bubbles would contain 23.28% carbon dioxide at the end of the decompression. It has not been known for certain where the original bubbles are formed. But, as the bubbles move out from the original site into the larger vessels where they are first available for analysis, carbon dioxide may continue to leave the bubbles. Again from Eq. (2), the bubbles would contain only 1.05% carbon dioxide 9.6 min after the end of the decompression. The rate of the decompression employed in this study was so severe that all animals from which samples could be taken died of the "chokes" within 30 min after the end of decompression.

As the gas tension of carbon dioxide in the venous blood increases thereafter probably because of gas embolism at the site of the pulmonary vein level, the concentration of carbon dioxide in the bubbles may increase proportionally.

It cannot be explained why the percentage of oxygen in the bubbles appears to increase at first, while the gas tension

of oxygen in the blood decreases with post-decompression time. Ackles *et al.* [15] have reported that, using mass spectrometry, the venous PO_2 and the muscle PO_2 in the decompressed dog increased rapidly (about 20~30 times the starting surface value) with post-decompression time and they returned to normal after several minutes. This interesting change of PO_2 in the vein and muscle demonstrated by using mass spectrometry may have some correlation with the change of oxygen concentration in the bubbles reported in this paper (Fig. 8). In any case, additional studies are necessary to resolve this problem.

Actual analysis of the bubbles in the live decompressed animals indicates that carbon dioxide may play an important role in the initiation and growth of bubbles. It has been reported that the higher the carbon dioxide content of gas inhaled during decompression, the higher the incidence of DCS (Mano *et al.* [16]). They concluded that the reduction of the CO_2 level in the gas inhaled during decompression and the increased elimination of dissolved CO_2 in the body tissues proved to be a highly effective procedure for reducing the incidence of DCS.

In view of this, Haldane's classical maximum supersaturation limit for avoiding DCS should be examined and possibly modified for gases other than nitrogen.

Acknowledgements

The author thanks Prof. H. Maeda and Asst. Prof. Y. Mano for their valuable advices and criticisms as well as Mr. M. Shibayama and Mrs. N. Kano for the excellent technical assistance they rendered.

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