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Prolonged bubble production by transient isobaric counter-equilibration of helium against nitrogen

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D'Aoust, B. G., K. H. Smith, H. T. Swanson, R. White, L. Stayton, and J. Moore. 1979. Prolonged bubble production by transient isobaric counter-equilibration of helium against nitrogen. Undersea Biomed. Res. 6(2): 109–125.—The production of systemic gas bubbles by isobaric counter-equilibration of helium against 5 atmospheres saturated nitrox (0.3 ATA O_2 in both mixes) in awake goats was demonstrated. Sixteen animal exposures (8 dives, 2 animals per dive) to a sudden isobaric gas switch from saturation on N_2 to He were conducted; 8 saturations occurred at 132 fsw and 8 at 198 fsw. Central venous bubbles were detected acoustically by means of a Doppler ultrasonic cuff surgically implanted around the inferior vena cava of each animal. Bubbles occurred from 20 to 60 min after the switch in both the 132 fsw and 198 fsw exposures, but were not always present in the 132 fsw exposure, and did not persist for as long. Bubbles or other Doppler events were often detected for the entire isobaric period—12 h—following the gas switch in the 198 fsw exposures. Decompressions were conducted according to the USN saturation tables and were uneventful, with only occasional bubbles. Supersaturation ratios calculated to have occurred for a considerable period after the gas switch were approximately 1.15 (tissue gas tension π, divided by ambient hydrostatic pressure, P) with maxima at 1.26 for the faster tissues. These values are limiting ones in USN decompression *only* for the slower tissues. In general, therefore, these results argue for reducing the permissible ascent criteria for the faster tissues—assuming bubbles are to be avoided—and allowing more time at stops for non-saturation decompression. Gas switches from a more soluble to a less soluble and/or more rapidly diffusing gas should therefore be avoided until physiological limits are well worked out.

helium	isobaric
nitrogen	bubbles
counter-equilibration	Doppler
ultrasound	counterexchange
counterdiffusion	gas elimination

It is now an accepted fact that parameters other than inert gas pressure should be considered both in decompression table calculations and in understanding decompression sickness. This understanding is based largely on original experiments involving gas switching or sequencing: one of the first such demonstrations, conducted by Keller off the coast of Southern California in 1962 (Keller 1968) used the transient undersaturation occasioned by the different uptake and

elimination rates of different inert gases, particularly helium and nitrogen, to gain a decompression advantage.

However, in March of 1970, Blenkarn, Aquadro, Hills, and Saltzman (1971) reported for the first time that gas sequencing could be a potential hazard under isobaric conditions, i.e., when no decompression had occurred. The urticaria observed were similar to skin bends and were definitely attributed to sequential changes in breathing gas involving helium, neon, and nitrogen in two different sequences. Because these authors were convinced on theoretical grounds that ". . . the total tension of N_2 and helium will show a transient fall and therefore cannot exceed the external hydrostatic pressure . . . ," they ruled out bubbles as an etiologic agent in favor of a potentially osmotic mechanism. There was, of course, in vitro experimental precedent (Kylstra, Longmuir, and Grace 1968) for this view, albeit using a much more soluble gas. However, due to insufficient data, the low calculated osmotic potential (Hemmingsen 1970) and the improbability of encountering a biological membrane that passes water faster than gas, this explanation did not seem capable of explaining the phenomenon observed (Halsey and Eger 1973). In 1971, the phenomenon was again encountered by the Philadelphia group (Lambertsen, Gelfand, and Clark 1978), also during studies of pulmonary function at depth under isobaric conditions. They described the isobaric formation of tissue and blood bubbles as a result of supersaturation induced by the steady-state counterdiffusion of two gases with different solubilities and rates of diffusion (the bilayer model). No decompression was involved. This raised some serious questions as to the potential hazards of switching gases at depth. On this occasion, the possibility of supersaturation was re-examined and it was shown (Graves, Idicula, Lambertsen, and Quinn 1973a, b; Idicula, Graves, Quinn, and Lambertsen 1976) that it was possible both in vitro (Graves et al. 1973b) and in vivo (Idicula et al. 1976) to produce bubbles by the steady state counter-exchange of two gases of different solubility and diffusivity.

It is not yet clear whether the physical model described by Graves et al. (1973a) adequately represents the situation that continually produces bubbles in vivo; however, it is a useful working model for that particular steady-state situation. On the other hand, such a bilayer model is unnecessary to account for bubbles in certain transient situations where differences in diffusivity alone are all that is required to provide a critical supersaturation pressure. This is the logical opposite of the situation first exploited by Keller.

The experiments originally reported by the Philadelphia group depended upon the use of anesthetized animals to demonstrate the steady-state phenomenon in vivo and on physical models to demonstrate both the phenomenon and to confirm their theory (known as the Bilayer Model) in vitro. Up to this point, all models presented were "steady-state" models chiefly because of the circumstances under which the phenomenon had been observed, namely 1) suddenly breathing N_2 after He saturation (Blenkarn et al. 1971), and 2) breathing neon while surrounded by and saturated with helium (Idicula et al. 1976). More recently, Greene (1975) and Harvey, Wilson, and Hester (1978) described theoretical calculations of transients to be expected under a variety of isobaric circumstances, using a simple extension of existing multi-exponential models. These indicated unacceptably high supersaturations. As a result, our laboratory at VMRC became involved in isobaric experiments on awake goats under conditions that might be encountered operationally, i.e., those which men might have been called upon to endure were it not for the work reported above and the results reported here.

This paper describes work done in the period May 1, 1976 to September 30, 1976, and fully documents the appearance of acoustically detected bubbles in the venous return of goats after isobaric gas switching. To avoid implied acceptance of any particular physical model, we

prefer to use the term isobaric counter-equilibration for those situations approaching equilibrium and "counter-exchange" for those situations approaching a steady state. However, since gas transport begins and ends with diffusion, the distinction is academic relative to the data we present here. A short note on this matter appears elsewhere (D'Aoust, Smith, Swanson, White, Harvey, Hunter, Neuman, and Goad 1977).

The problem

Specifically, our attention was drawn to the possibility of isobaric gas exchange problems during a submarine rescue procedure with the Deep Submergence Rescue Vehicle (DSRV) being used to rescue personnel from a crippled submarine. As originally planned, this rescue procedure would require individuals saturated with air at pressures up to 132 fsw to be rapidly transferred into a helium/oxygen environment in which the partial pressure of oxygen is 0.3 ATA. This rapid transfer from the air environment to the helium/oxygen environment could possibly cause isobaric supersaturation in the body. If the supersaturation reached sufficient (but as yet undetermined) levels, bubble formation and signs of decompression sickness might occur. After the transfer to the helium/oxygen environment, these individuals would require decompression to the surface, which would further predispose them to bubble formation and any decompression sickness that might have started with the initial inert gas transfer.

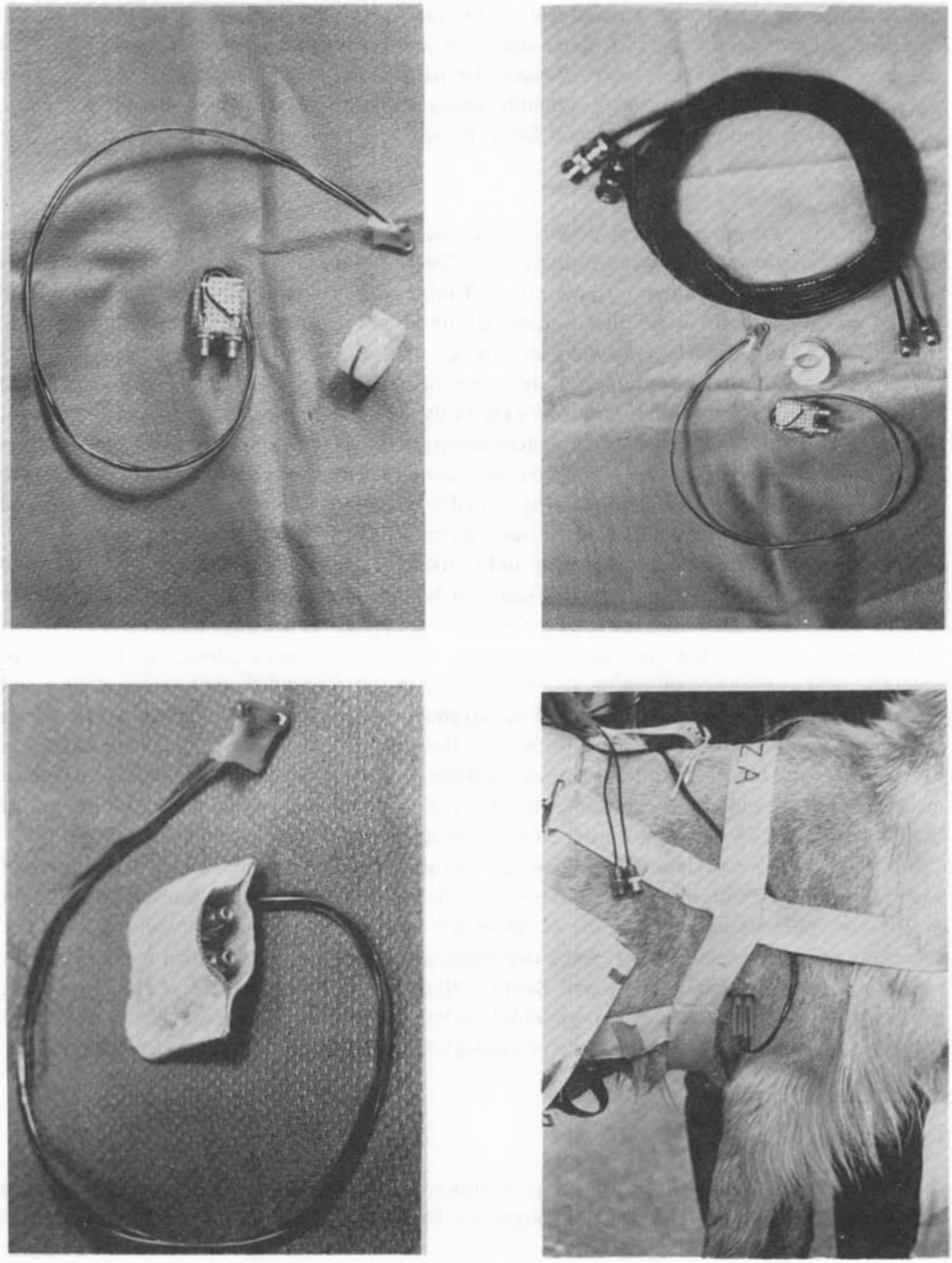
The Doppler bubble detector (Spencer and Clark 1972; Haugen and Belcher 1976) has been used to demonstrate the presence or absence of bubbles during decompression. It has been able to detect bubbles before the onset of serious symptoms of decompression sickness, and often detects emboli when no symptoms appear. This device can be considered both a more objective and a more conservative way of testing non-saturation decompression profiles and relating serious symptoms to the actual occurrence of separated gas. If rapid transfer from nitrogen to helium can cause bubble formation, then to the extent such bubbles are formed in or may enter the bloodstream, the Doppler bubble detector is the obvious tool with which to monitor subjects objectively during and after the gas exchange procedure. The effects of bubbles produced by supersaturation alone, without decompression, can thus be assessed.

Since decompression sickness has long been identified with the unphysiological evolution of gas in the form of bubbles and this bubble formation is a result of supersaturation of gases in the tissues; bubbles may herald the onset of any problem such as that resulting from the switching of inert gases. Further, since decompression itself has been shown to decrease the rate of nitrogen elimination (D'Aoust, Smith, and Swanson 1976), isobaric bubble formation provides a new and powerful experimental technique with which to assess the effects of bubbles on gas elimination, without the physiologic complications inherent in decompression.

METHODS

Preparation of animals

Under surgical anesthesia, a right lateral thoracotomy was made to expose the required major vessels of the heart. A Doppler ultrasonic bubble detection cuff (Haugen and Belcher 1976) was placed around the posterior vena cava, and the tube-enclosed leads for the Doppler probe were run subcutaneously to one side of the back approximately 5 cm posterior to the scapula, where they exited via a subcutaneously implanted storage pack, as shown in Figs. A to D. The pulmonary artery was catheterized by way of the jugular vein with a 7F Swan-Ganz catheter. From this catheter, blood samples were taken for blood inert gas content analysis. A post-surgical recovery period of one to two weeks was allowed before experimentation.



Figs. A, B, C, and D. Doppler ultrasonic transducer (5 MHz) and cuff showing *A*, how transducer fits into nylon cuff with stainless steel clip, and *B*, lead arrangement. Small connectors are miniature co-axial connectors (Amphenol Sub-Miniax 27-109) mounted on a circuit board which is then potted with epoxy and silicon rubber into the dacron felt pack; *C*, dacron pack which was stitched subdermally; dermal tissue healed into the dacron felt surface, providing an antiseptic seal and allowing convenient access to the animal as shown *D*, on animal with harness and strain-relieved leads.

Inert gas analysis

Inert gas content in venous blood was determined by sampling through the catheter into a 10-ml glass syringe filled with gas-free saline diluent according to the method of D'Aoust and Swanson (1974); samples were analyzed according to the method of Groom and Farhi (1967) and Groom, Morin, and Farhi (1967). By using pure neon as a carrier gas, helium could also be analyzed.

Blood samples were taken for a period of up to one hour after the inert gas switch. This represented a practical compromise between the decompression needed by the technician and the necessity for a reasonable post-switch sampling period. Because of our unwillingness to subject personnel to the gas switch even though they were not saturated with nitrogen, blood sampling was begun 10 to 20 min after the gas switch, by which time helium levels were already quite high and nitrogen levels quite low in the mixed venous blood. For this reason, only representative post-switch values are presented in Table 1. With some variation, these are as expected on the basis of past work (D'Aoust et al. 1976). On subsequent experiments at 198 fsw, blood gas sampling was omitted because of the obvious decompression constraints on personnel at this depth.

Ultrasonic Doppler detection of bubbles

Doppler bubble detection equipment (developed on ONR contract N00014-69-C-0402 (Haugen and Belcher 1976; Belcher 1976)) was used to detect bubbles in the posterior vena cava with the cuff-type implantable sensors shown in Figs. B, D surgically implanted in the experimental animals. Ultrasonic transducers using a carrier frequency centered on 5 MHz were used, and Doppler monitoring and recording began 5 min prior to the gas switching and continued for the duration of the bottom time after the switch to helium/oxygen. During the final decompression phase from 132 fsw and 198 fsw to the surface using the USN Saturation Decompression Table, the signal from the Doppler emboli detector was monitored but not recorded.

GENERAL EXPERIMENTAL PROTOCOL

Animals instrumented as described were equipped with a harness of webbing, shown in Fig. C, to restrain the animals and to provide strain relief for the catheter, Doppler, and ECG leads.

TABLE 1

AVERAGE MIXED VENOUS BLOOD HE AND N_2 CONTENT ANALYZED BY VAN SLYKE EXTRACTION AND GAS CHROMATOGRAPHY AFTER AN ISOBARIC GAS SWITCH FROM 4.7 ATM N_2/0.3 O_2 TO 4.7 ATM HE/0.3 ATM O_2 AT 132 FSW (5 ATA)

	Time after switch			
	min			Δ, %
	20	50	80	(80–20 min)
N_2 % Saturation	21.3	13.5	6.5	−14.8
He % Saturation	77.0	84.3	93.3	+16.3

$n = 4$.

In addition, for the sake of hygiene and environmental cleanliness, a large plastic bag for catching feces and a rubber baffle connected to a "cystoflow" urine collection bag were attached to the animals. Once inside the chamber, instrumentation leads were hooked up and performance checked. A supply of food and water was accessible to the animals during the entire compression period. After a check of all systems, the chamber was compressed to 15 fsw on air, held at that depth while all sensors and systems were further checked, and then compressed to the final experimental depth at 30 ft per minute (fpm) on pure nitrogen.

The animals were held at the experimental depth for 16 h to allow saturation. This would provide virtual saturation of all tissues except those with a 360 (85%) and 480 (77%) min half time (See Fig. 9 for 480/240 (N_2/He) tissue pair).

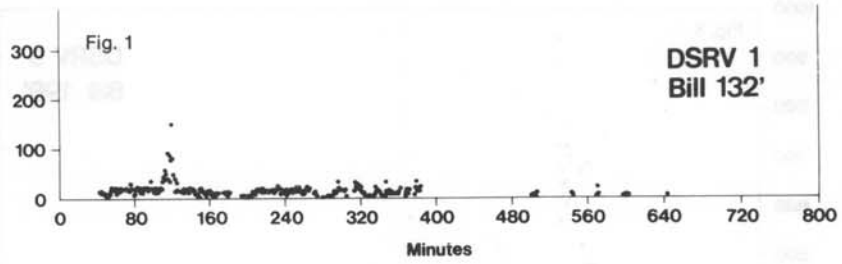
For studies at 132 fsw, immediately prior to the switch, a technician was compressed in the entry lock to within 2 fsw of the experimental depth on helium/oxygen. The gas switch was then carried out over a period of 5 to 7 min at a flow rate of 600 scfm. This usually provided a residual nitrogen percentage that ranged between 0.3 (at a minimum) and 5.0% (at a maximum). The maximum additional nitrogen percentage, potentially due to elimination from the animals after the switch, was approximately 0.5% and was considered negligible for our purposes.

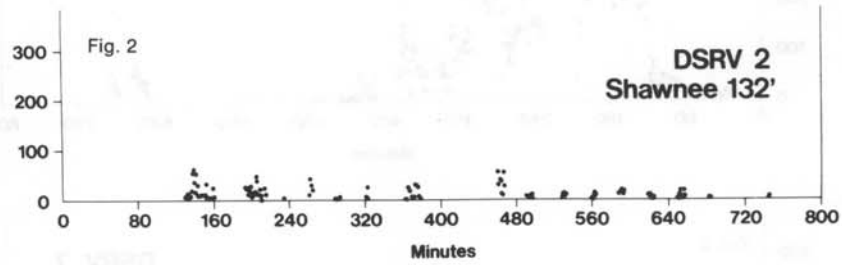
RESULTS

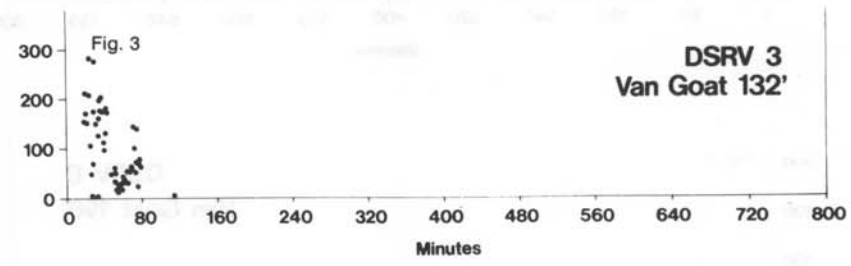
Mixed venous blood helium and nitrogen content are shown in Table 1 at three different times after the gas switch. It is clear that at this time, mixed venous blood levels of both gases were changing at a similar rate. Expressed as a percentage of maximum capacity (obtained by multiplying the solubility of each gas by the saturation pressure), the data summarized in the fourth column of Table 1 showed an approximately linear rate of change of −14.8% of maximum capacity per hour for nitrogen and +16.3% per hour for helium. Because of the inability to sample mixed venous blood immediately after the gas switch or for longer than an hour, no attempt has been made to extract compartmental constants from these data, which remain only supportive of changes that must have occurred.

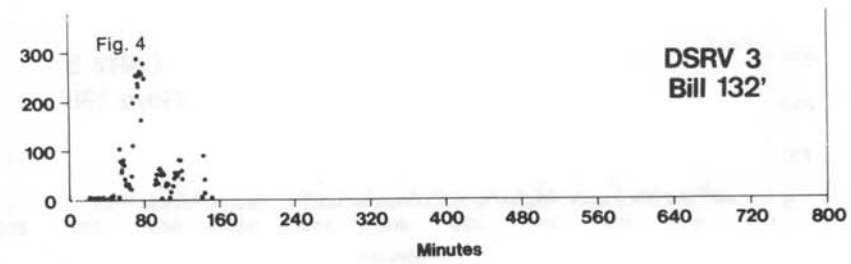
Because of frequent problems with corrosion in the internal connections of the leads of the Doppler cuff, there were occasional gaps in the records of some of the dives, occasioned by either a noisy signal or no signal at all. If this occurred, the dive was aborted. However, if the signal became poor or intermittent a reasonable time after the switch, the entire dive was continued to observe the subsequent effects of decompression. This explains some of the gaps in the record on Dives 1, 5, 7, and 8, whereas the remaining figures record a continuously "intact" signal. As more experience was gained, extra precautions produced more reliable results and subsequent experiments were carried out without further difficulty.

In Fig. 1, from the first dive of the series, the count rate was between 0 and 100 bubbles per minute. The same is seen in Fig. 2. All counts should be considered as *relative* values rather than absolute numbers of bubbles since the "counting efficiency" of the entire system varies with each surgical implant on each animal. However, all the dive records were processed by one person, who also adjusted the sensitivity of the counter to the same level. It can therefore be assumed that comparisons between different dives are valid. The second and third dives at 132 fsw (Figs. 3 and 4) showed very few bubbles compared to the first dive. For this reason, the next 5 dives were carried out at 198 fsw. (The missing dive numbers in the sequence 4 and 6 are dives that were begun but were aborted due to failure of Doppler signals and are not included here).

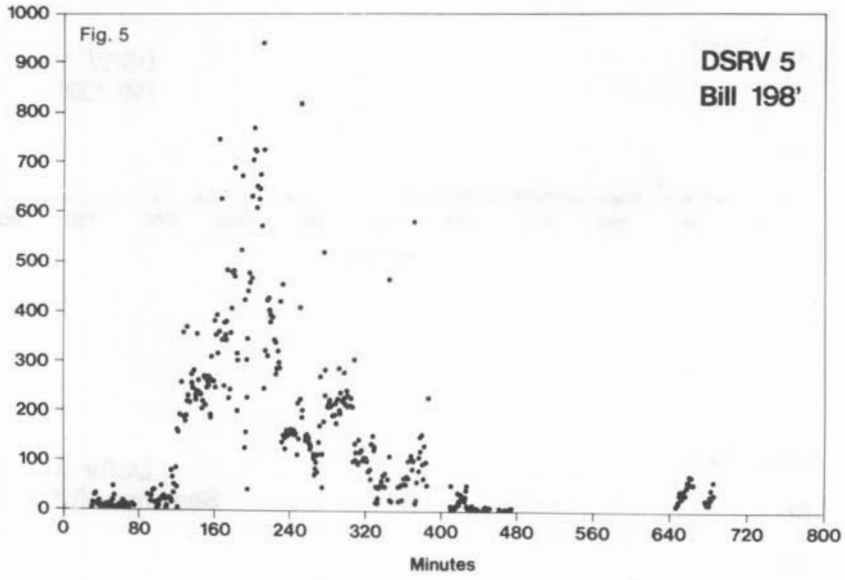


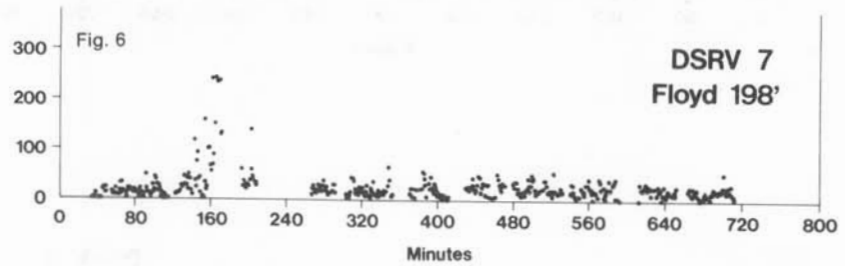


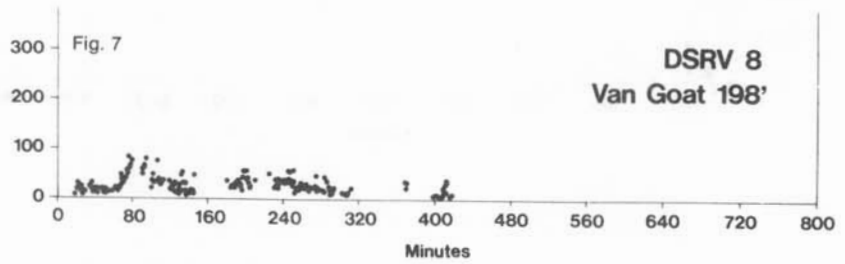


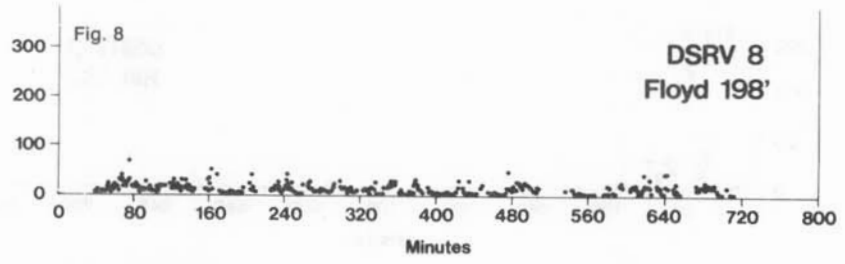


Figs. 1–4. See Fig. 10 for legend.









Figs. 5–8. See Fig. 10 for legend.

Note that there are both time-varying levels of bubble counts, e.g., Fig. 5, and relatively constant counts (Figs. 6, 7, and 8) with the same exposure. This raises a question about the kinetics of the supersaturation "front" passing through the tissues. Since multiple parallel exponential models do not provide for the actual amount of gas dissolved or give any guidance about the half times of He and N_2 in the same tissue, we have used the procedure of Greene (1975) and Harvey et al. (1978) to provide only a representation of supersaturation of different tissues.

Figure 9 is plotted to the same time scale as Figs. 1–8, 10, 11 and shows calculations for the 132 fsw dive. By superimposing the curves in Fig. 9 on the 132 fsw dives, it is possible to estimate which half times might coincide with maxima or minima in the bubble count. For example, the maximum count shown in Fig. 5 occurred at approximately 200 min (D'Aoust et al. 1977). Thus, tissues with half times faster than this must have been involved, since bubble formation, growth and transport all preceded detection. On the other hand, Figs. 7 and 8 show a strikingly constant count rate and no particular time constant is evident. Such a response suggests the role of factors, unrelated to those affecting equilibration rates, that are not yet clear; however, they may be related to platelet activity and coagulation function. In this connection, it is interesting that in one recent experiment where platelet function inhibitors were used, a very clearly phasic bubble count response resulted. This observation, which is the subject of further study, might be interpreted as having been due to the absence of a

Fig. 9

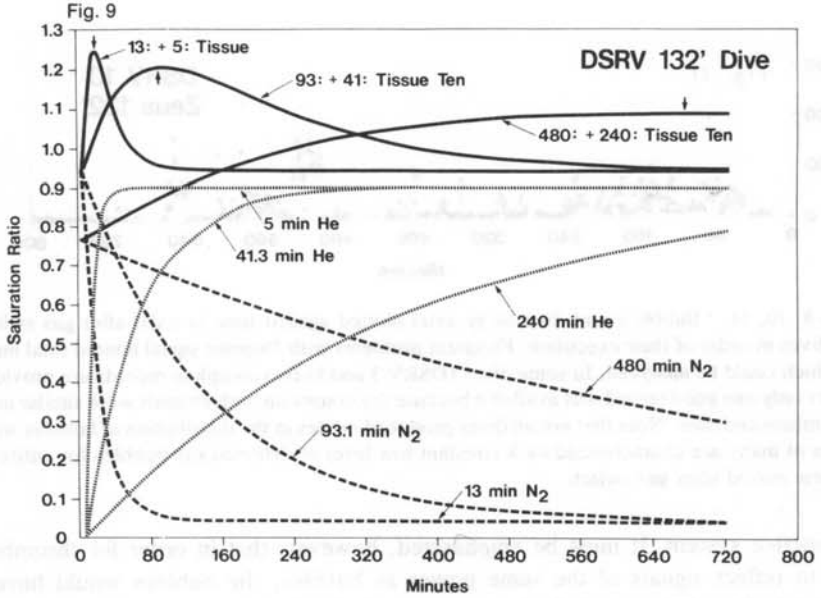
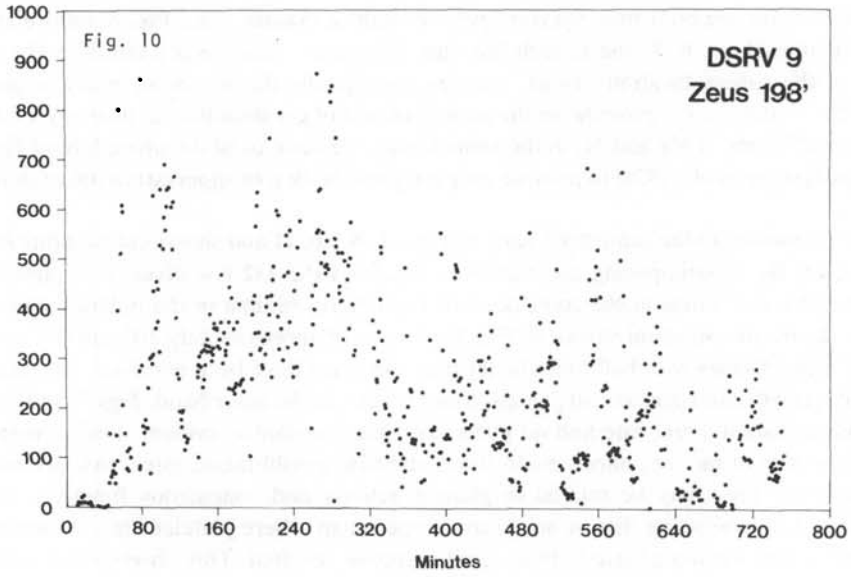
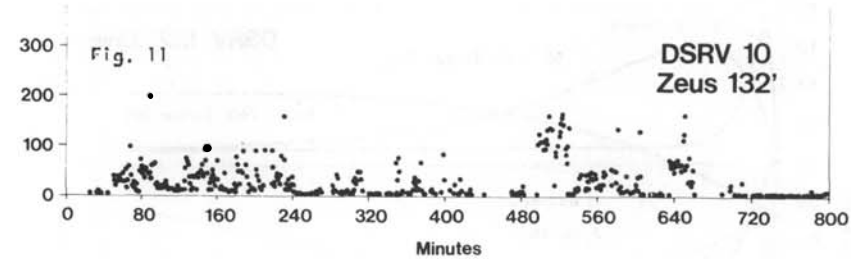


Fig. 9. Calculation of supersaturation and saturation fraction (ordinate). Variation with time (abscissa) after gas switch for 132 fsw. Total inert gas pressure (_____) is plotted along with individual saturations of each gas. Inert gas saturation of nitrogen (-----) and helium (•••••) is shown individually. At all times, nitrogen and helium partial saturation fractions must add up to total saturation fraction for tissue pairs illustrated. "Tissue pairs" calculated for Fig. 9 are labeled with the nitrogen half time first and the helium half time second. Thus, the faster tissue pair plotted is 13-min nitrogen half time summed with a 5-min helium half time. Intermediate tissue pair combines a 93-min half time for nitrogen with a 41-min half time for helium, and the longest tissue pair combines a 480-min half time for nitrogen and a 240-min half time for helium. Thus the transport ratios for nitrogen to helium in three pairs of tissues are 2.6, 2.27, and 2, respectively, and different rate of equilibration of 2 different inert gases dictates the maximum possible supersaturation in any one tissue.





Figs. 1–8, 10, 11. Bubble counts/minute (y axis) plotted against time (x axis) after gas switch on 8 different dives in order of their execution. Frequent problems with Doppler signal limited total number of records which could be analyzed. In some dives (DSRV 3 and 8) two complete records are provided, and in all others only one good record was available because the counts on both animals were similar in respect to both numbers and time. Note that not all dives produced modes in the distribution of bubbles with time, and results of many are characterized by a constant low level of detected gas bubbles for entire bottom time isobaric period after gas switch.

bubble-reactive system. It must be emphasized, however, that in order for thrombi or fat globules to reflect signals of the same power as bubbles, the bubbles would have to be approximately 10 or 100 times their size, respectively (Wells 1969). It is therefore unlikely that such targets are a significant source of Doppler events.

The limitations of the models described above (shown in Fig. 9), which are currently used to compute decompression, need emphasizing. Simple parallel-compartment models are not adequate for these studies. In the situation of transient counter-transport, we are no longer dealing with just one gas; it is therefore necessary to emphasize that each calculation we have made is of the *total gas supersaturation* for a "pair" of tissue half times. Choice of these half times required an arbitrary guess about *which helium half time was most realistically paired with which nitrogen half time*. Or, in other words, what are the relative rates of N_2 and He in each tissue? Or at each point where a bubble forms? Thus, for experiments of this sort on

counterdiffusion, it is necessary to make some assumptions that were unnecessary when dealing with only one inert gas. Further, it is unlikely that the *rate* of helium equilibration in all tissues bears a *constant* ratio to that of nitrogen (Bühlmann 1975). For these reasons, the pairs of half times shown are somewhat arbitrary. They are derived from our own tables and experience and are described elsewhere (Smith 1976). The method of calculation presented by Baz, Lightfoot, Tepper, and Lanphier (1977) may be preferable to the method used here for calculation of potential supersaturation. We have used the parallel exponential model here *as much to emphasize its inadequacy* as to illustrate both the transient nature of supersaturation in any particular tissue and the resulting *average* long duration of whole body supersaturation after a gas switch. The total tissue inert gas tension, Π, has been calculated by summing the equation

$$\pi_2 = f_{D_1} + fR\,(T - 1/R) + (\pi_1 - fD_1 - fR/K)e^{-t_{\frac{1}{2}}} \text{ for each inert gas,}$$

where T = stop time, min; π_1 = initial gas tension at T = 0; π_2 = gas tension at T; D_1 = depth at T = 0; R = rate of change of pressure dP/dt in fsw/min; f = inert gas decimal fraction; $t_{\frac{1}{2}}$ = tissue half time in min; and K = tissue constant = $0.693/t_{\frac{1}{2}}$.

Since R = 0 in these isobaric gas switches, the equation simplifies to $\pi_2 = fD_1 + (\pi_1 - fD_1)e^{-Kt}$ for each gas, and $\Pi = \pi_2 N_2 + \pi_2 He$ describes the total supersaturation shown in Fig. 9. Thus, at all times the total tissue inert gas pressure equals the sum of the decreasing nitrogen pressure and the increasing helium pressure. Note that helium saturates so much more quickly than nitrogen and that supersaturation (at least by calculation) may last for several hours. This is supported by the results shown in Figs. 1–8, 10, 11.

Two very important points to be emphasized are 1) the long duration of bubbles observed, and 2) the relatively low supersaturation ratios calculated for three (arbitrary) pairs. The latter observation demonstrates that bubbles can form and grow in tissues at low supersaturations and indicates the potential risk associated with supersaturation ratios of less than 1.2 at these depths. It is of interest to note that the lethal effect of this ratio of supersaturation on fish at 1 atm total pressure has been known for some time (Marsh and Gorham 1905; D'Aoust and Smith 1974; Ebel, Raymond, Monan, Farr, and Tanonaka 1975), and is a source of considerable environmental concern (Legg 1974; Weitkamp and Katz 1974) in the U.S. Pacific Northwest.

Note (from Fig. 9) that the maximum supersaturation levels—expressed as a ΔP—increase markedly as depth is increased but plateau if expressed as a pressure ratio, $^{\pi 2}N_2 + {}^{\pi 2}He/P$ or Π/P. This is due to the drop in percentage of oxygen in the breathing mix. The distinction is important in isobaric studies since gas transport into a bubble depends directly upon ΔP, whereas the pressure ratio determines the potential change in volume. This has important implications for future work (Yount *in press*).

DISCUSSION

The objective of this research was to determine whether or not isobaric bubble formation and subsequent decompression sickness can occur in a goat exposed to a situation that might be encountered operationally—a rapid switch from a nitrogen/oxygen breathing mixture and environment to a helium/oxygen breathing mixture and environment while remaining at the same hydrostatic pressure of 132 fsw.

The results of this study were unexpected, so much so that we have been encouraged to consider more quantitative ways of describing gas transport and decompression stress. We do not have—at the present time—a mathematical model that can account for the factors that we now know are important in bubble formation and growth in decompression sickness.

Since steady-state counterdiffusion (Lambertsen and Idicula 1974) has been demonstrated by Graves et al. (1973a) to be capable of generating total gas supersaturations *in vitro* of as much as 30% of the ambient pressure, there is a tentative explanation of several problems encountered in deep saturation diving in the last several years (Blenkarn et al. 1971; Lambertsen and Idicula 1974). However, the significance of isobaric bubble production to diving medicine is not limited to the potential additional hazard of subsequent decompression, or recompression with He (Strauss and Kunkle 1974) since even without these treatments, tissue and vascular bubbles can have significant effects. Bubbles have been demonstrated to cause platelet and red cell aggregation (Philp, Schachem, and Gowdey 1971), reduce platelet and fibrinogen survival (Slichter, Stegall, Smith, and Harker 1974), and cause the release of serotonin, adenosine, and bradykinin (Chryssanthou 1973). That this response is probably a universal one in vertebrates is supported by some experiments with fish (Casillas, Miller, Smith, and D'Aoust 1975; Casillas, Smith, and D'Aoust 1976; Smith 1976).

From preliminary hematologic studies done in this laboratory (Smith, Stegall, Harker, and Slichter 1973; Slichter et al. 1974), it is apparent that hemostatic abnormalities do occur after asymptomatic hyperbaric exposure as the result of bubble formation. These abnormalities include both the activity of coagulation systems and the survival of hemostatic factors such as platelets. In addition, endothelial damage has been demonstrated to accompany these platelet changes and may affect platelet and fibrinogen times. Bubble/platelet interaction has also been shown to have this effect. The possibility exists that such endothelial damage is caused mechanically either by moving vascular emboli or by actual bubble formation between the endothelial cell layer and the connective tissue of the vessel wall (Harker and Finch 1969; Harker and Slichter 1970). Such changes may have additional and far-reaching systemic effects.

For example, diving-induced deafness and vestibular dysfunction have been recognized as important problems in individuals exposed to compressed gas atmospheres (Harris 1971; McCormick, Higgins, Daugherty, and Johnson 1972; Kennedy 1976), and may also be a potential risk in isobaric counterdiffusion. The condition is seen in almost every phase of human diving and appears to be most prevalent where gases of different physical properties are sequentially employed during decompression to facilitate the removal of inert gas from the body. Vertigo, vestibular disorientation, nausea, and auditory loss have been demonstrated after gas switching during decompression from deep dives. The etiology of these symptoms has not been demonstrated, but it is hypothesized that gases having different diffusion rates and solubilities may predispose to the onset of these signs and symptoms.

On the other hand, vestibular problems have been caused by a gas switch *in the opposite direction* from that reported here (Blenkarn et al. 1971; Lambertsen and Idicula 1974), and may be due to the unique architecture and physiology of the inner ear (Hills 1977).

Thus, the Boyle's law expansion of preformed gas nuclei on decompression is not the only mechanism by which systemic bubbles can originate and have deleterious effects. It would appear that *any* bubble formation in the isobaric phase of hyperbaric exposure is to be avoided; bubbles formed as a result of an isobaric breathing gas switch could not only affect gas elimination at the tissue level, as outlined above, but could also further affect lung function and thus lower the permissible decompression rate even more.

Decompression tables used currently by industry and the U.S. Navy (Workman and Bornmann 1975) allow (even for helium/oxygen) supersaturation ratios as well as ΔP values in the faster tissues to exceed by a considerable margin the maximum total tensions that we have calculated (Fig. 9) to occur in tissues of these half times at different times after the gas switch. This is shown in Table 2, which compares limiting supersaturation ratios at 0 and 60 m depth (0 and 198 fsw) used in the U.S. Navy tables with the total levels calculated to have occurred as a result of our gas switch. Numbers to the right in parentheses refer to the time in minutes after the switch when the maxima occurred (see Table 2). Surface values used in the USN tables illustrate the greater decompression "insult" allowed for all tissue half times at the surface. Doppler monitoring of subjects after dives producing these supersaturations reveals far fewer (if any) bubbles than were observed during these experiments, indicating the importance of ΔP as well as pressure ratio in considering ascent criteria (see Table 2). Decompression *per se* must be considered a more extreme insult than isobaric counter-transport, if only because of the greater *potential* volume change involved. Accordingly, permissible supersaturation ratios should probably be reduced; the question is by how much?

Fortunately, the experimental procedures that have raised these questions appear also to be the most appropriate techniques for resolving them. In other studies (D'Aoust et al. 1976), we have shown that decompression from saturation at a depth as shallow as 33 fsw can decrease the rate of nitrogen elimination. This is consistent with the observations of Hempleman (1960) and Heimbecker, LeMire, Chen, Koven, Leask, and Drucker (1968). In such a situation, one can no longer apply classical calculations of normal desaturation rates (Kety 1951) because perfusion at the tissue level may have been altered. On the other hand, using the technique of isobaric counterdiffusion, *only* the gas partial pressures need be considered; the supersaturation is caused not by a decrease in hydrostatic pressure but by the actual difference in equilibration rate of the inert gases themselves. This can be assumed to be a much less stressful situation than decompression, and more important, the degree of supersaturation causing the bubbles can be calculated with much more confidence than has ever been possible in decompression experiments. Further, gas elimination can be studied in this situation to compare its efficiency with that in the situation after decompression. Thus, it should at last be possible actually to determine the relationship between a given "average supersaturation" and the appearance of vascular bubbles to evaluate the physiological reality of certain half times. It

TABLE 2

COMPARISON OF SUPERSATURATION RATIOS CALCULATED AFTER A GAS SWITCH (GS) AND THOSE ALLOWED BY U.S. NAVY TABLES (USN) AT 60 MSW (USN) AND AT SURFACE

	Tissue Half Time, min									
	5		10		40		60		240	
	USN	GS	USN	GS	USN	GS	USN	GS	USN	GS
Surface	2.60	1.02	2.242	1.04	1.82	—	1.80	1.0	1.61	<1.0
	1.6	0.02	1.24	0.04	0.82		0.80	0	0.61	0
60 m	1.66	1.26(10)	1.52	1.25(20)	1.29	1.22(90)	1.28	1.21(140)	1.09	1.09
	3.93	1.54	3.09	1.49	1.72	1.31	1.66	1.25	0.53	0.53

ΔP values, i.e., tissue nitrogen tension - hydrostatic pressure expressed in atm are shown under each ratio. Notice the differences in permissible ΔP values (USN) and those calculated to have occurred during the bubble-producing gas switch.

may also be possible to determine the suitability of different ascent criteria, such as the critical released gas volume concept of Hennessy and Hempleman (1977), or a similar volume-dependent stress concept suggested by D'Aoust and Smith (1974) and D'Aoust et al. (1977).

In this connection, it may be significant that the only animal in our study (Zeus) that definitely showed signs of decompression sickness (favoring a limb) in the entire series of dives was also the animal having the highest average bubble count in both 132 fsw and 198 fsw dives (Figs. 10 and 11).

The dive on which this occurred was a decompression according to U.S.N. saturation for nitrogen; the Doppler signal was lost just prior to the switch, which was therefore aborted, leading to the decompression. No other *clear* signs of decompression sickness were observed in the study. However, it appears that detecting bubbles from helium may be an even more conservative method of testing decompression concepts than detecting those from nitrogen because of the more rapid diffusion of the gas. The equivalent transient gas switch carried out by Harvey (1977) and reported in an earlier paper (D'Aoust et al. 1976) produced, at 4 atmospheres, urticaria and skin lesions similar to those described by Blenkarn et al. (1971) and Lambertsen and Idicula (1974), but no bubbles were detected. We have no way of knowing whether in fact systemic vascular bubbles occurred; from our experience, it would seem likely.

Thus, both vascular bubbles and skin urticaria apparently can be produced both by transient supersaturations caused by the counter-equilibration of two gases and the steady-state supersaturation as a result of counter-exchange of two gases.

CONCLUSIONS

1. Isobaric counter-equilibration of nitrogen and helium can definitely produce bubbles within 20–60 min at a depth of 132 fsw. This involves computed supersaturation ratios as low as 1.15 or a ΔP of 24.7 fsw.

2. The number and duration of vascular bubbles caused by an isobaric gas switch from nitrogen/0.3 ATA oxygen to helium/0.3 ATA oxygen correlate with both the concentration of dissolved inert gas and the partial pressure gradients involved. More bubbles were heard for a longer time after the 198 fsw (7 ATA) isobaric switch than after the 132 fsw switch, and although we have not yet determined the minimum supersaturation threshold for the detection of bubbles by this technique, we would suggest, based on our results and the results of others, that after any exposure to a nitrogen saturation pressure of 66 fsw or greater, switching the breathing mix to helium should be avoided. Further, and also based on the experience of others, this suggestion may not apply to vestibular problems, although identical gas switches have been carried out on men at 66 fsw.

3. Individual variations were observed in the number of bubbles produced by isobaric counterdiffusion in different animals, as they have been observed in divers after decompression. Some individuals appear to get decompression sickness more readily than others, and it is probable that this is related to the same phenomenon we have observed in one of our goats that developed significantly more bubbles than the others both at 132 fsw and 198 fsw (Figs. 10 and 11). Whether this is due to different numbers and distribution of preformed micro-gas nuclei (LeMessurier 1972; Skripov 1974; Yount *in press*) or not remains to be determined. However, here again, the isobaric counterdiffusion technique may help to resolve this question.

4. Detecting and counting bubbles electronically is the final event in a complicated combination of physical and physiological processes. However, one can still assume on acoustic grounds that bubbles constitute most of the Doppler events we have observed (Belcher 1976; Belcher, Ehrenberg, and Lytle 1977). Further, because the potential volume change is less, the supersaturation produced by gas switching can be assumed to be a more gentle experimental procedure; isobaric supersaturation can thus be used as a "probe" to investigate both critical levels of supersaturation and the effect of bubbles on many systems. The information presented is thus of immediate practical and theoretical use: practical in that it provides a clear idea of the limits to be placed on gas switching, and theoretical in that it clearly shows that supersaturation ratios as low as 1.15, in conjunction with a ΔP of 25 fsw, can produce bubbles in the blood. This has immediate implications for decompression theory and practice and suggests that current ascent criteria should be reduced.

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D'Aoust, B. G., K. H. Smith, H. T. Swanson, R. White, L. Stayton, and J. Moore. 1979. Production prolongee de bulles par exposition a contre-equilibration isobare transitoire de l'helium et de l'azote. Undersea Biomed. Res. 6(2): 109–125.—La production de bulles de gaz par contre-équilibration de l'hélium et de 5 atmosphères de nitrox saturé (O_2 a 0,3 ATA dans les deux mélanges) chez le bouc vigile a été démontrée. On a realisé 16 expositions (8 plongées à 2 animaux chacune) a un changement abrupt de gaz (de N_2 à He) à saturation. Huit saturations ont été effectuées à 132 fsw, et huit à 198 fsw. Les bulles des vaisseaux centraux véneux ont été détectées par le moyen d'une manchette implantée autour de la veine cave inférieure de chaque animal, par détection à ultrasonique Doppler. Les bulles ont été observées 20–60 min après le changement de gaz, aux deux profondeurs; elles ne sont pas toujours apparues à 132 fsw, et elles n'ont pas duré aussi longtemps à cette profoundeur. Les bulles ou autres événements détectés par l'effet Doppler ont souvent duré 12 heures, la durée de la periode entiere de l'exposition isobare à 198 fsw après le changement de gaz. Les décompressions, réalisées selon les tableaux à saturation de la Marine américaine, se sont déroulées sans événement, avec quelques bulles rares seulement. Les rapports de sursaturation, calculés pendant une période importante après le changement de gaz, sont d'environ 1,15 (pression de gaz tissulaire π, divisée par la pression ambiante hydrostatique, P), avec les maxima à 1,26 pour les tissues plus rapides. Ce sont les valeurs-limites des tableaux americains pour les tissus moins rapides seulement. Ces résultats plaident donc pour une réduction des critères d'ascente pour les tissus plus rapides—si les bulles sont à éviter—et pour une plus grande durée des paliers pour la décompression non-saturation. Il faut éviter aussi des changements d'un gaz moins soluble à un plus soluble ou qui se diffuse plus rapidement, jusqu'à ce que les limites physiologiques soient mieux connues.

hélium
oxygène
contre-équilibration
ultrasons
contrediffusion
isobare
bulles
Doppler
elimination de gaz
changement de gaz

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