not expected to affect critically calculated O_3 concentrations during the first 3 weeks after the solar proton event, as NO and NO_2 do not affect O_3 concentrations significantly above about 45 km. Zonally averaged concentrations of chemical compounds were calculated on the basis of mean meridional circulation data [J. F. Louis, thesis, University of Colorado (1974)] and empirically determined time-dependent eddy diffusion coefficients (P. J. Crutzen, paper presented at the 4th Climatic Impact Assessment Program Conference, Cambridge, Mass., February 1974).
12. P. J. Crutzen, paper presented at the 16th International Union of Geodesy and Geophysics General Assembly, Grenoble, France, 25 August–6 September 1975.
13. Days 222 through 225 and 227 through 229 are used for the mean 8 days after the event. Day 226 was excluded because of a small sample size. Days 233 through 239 are used for the average 19 days after the event. Theoretical calculations were made for day 244 (1 September 1972).
14. The observations may be an underestimate of the depletion. Artifacts in the data due to spacecraft pitch errors show positive biases increasing with time at the upper levels. As a result, the O_3 content appears to increase above 1.1 mbar at 8 days and above 1.3 mbar at 19 days.
15. The O_3 content above 1 mbar exhibited a perturbation which disappeared a few days after the event, in accordance with a short photochemical removal time for an HO_x deposition.
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Venous Gas Bubbles: Production by Transient, Deep Isobaric Counterdiffusion of Helium Against Nitrogen

Abstract. *When awake goats were subjected to isobaric gas switching from saturation (17 hours) on 4.7 atmospheres of nitrogen (0.3 atmosphere of oxygen) to 4.7 atmospheres of helium (0.3 atmosphere of oxygen), bubbles detected by 5-megahertz Doppler ultrasound in the posterior vena cava 20 to 60 minutes after the switch continued for 4 hours. Similar experiments carried out at 6.7 atmospheres of inert gas and 0.3 atmosphere of oxygen produced more bubbles for as long as 12 hours after the gas switch. This is believed to be the first objective demonstration of the phenomenon of deep isobaric supersaturation under transient operational diving conditions at relatively shallow diving depths. Detection of bubbles by Doppler ultrasound confirms the potential importance of the phenomenon to shallow saturation diving and holds promise for better quantification of its effects as well as those of its counterpart, isobaric undersaturation, which can confer a decompression advantage.*

Isobaric supersaturation (*1, 2*) and the resulting production of cutaneous and deep-tissue bubbles by counterdiffusion at constant pressure of two or more gases with unequal permeation rates has been identified in man (*1, 2*) and demonstrated in animals (*3–5*) both in vitro and in vivo (*6*); it is generally considered to explain certain abnormalities that can be encountered in relatively deep (greater than 100 m) saturation diving (*6*). Two interrelated forms have been distinguished: (i) "superficial isobaric counterdiffusion" through skin and other tissues in direct contact with the ambient atmosphere, and (ii) "deep isobaric counterdiffusion" between tissue fluids and capillary circulation (*6*). Each is capable of supersaturating tissue, and the superficial form has been shown to produce not only gas lesions in man (*7*), but also continuous gas embolism in animals (*3–5*) under steady-state conditions. However, the probability of risk from the phenomenon in "deep" tissues in shallow-water diving involving transient gas switching rather than steady-state experimental situations is not known (*8*).

We now report the in vivo production of bubbles detected with Doppler ultrasound (*9*) in awake goats after a rapid isobaric switch of the inert gas in the chamber from nitrogen to helium at 40.2 m (132 feet) and 60.35 m (198 feet) of seawater (7 atm absolute) (all measures are expressed in terms of meters of seawater). These are the shallowest depths at which this phenomenon has been demonstrated. Further, the fact that it was produced by transient rather than steady-state conditions is of both practical and theoretical importance to the physiology and medicine of diving, particularly in reference to projected submarine rescue procedures requiring successive exposure to different inert gas atmospheres at these pressures.

Use of continuous-wave Doppler ultrasound for detection of vascular bubbles has become an accepted technique in hyperbaric physiology; the system and counter in use in our laboratory are theoretically capable of detecting bubbles 1 μm in diameter and have been experimentally demonstrated to detect 10-μm bubbles (*9*).

Eight adult goats weighing between 40 and 70 kg had Doppler ultrasonic transducer cuffs surgically implanted around the posterior vena cava (*9*). Animals were exposed in pairs to one of two different regimens. The first consisted of saturation to 40.2 m of seawater in normoxic nitrogen. Compression was at the rate of approximately 4.6 m/min, varied slightly as required to minimize noise-induced anxiety in the animals. The animals were held for 17 hours at 40.2 m at an O_2 pressure of 0.3 atm [the remainder was N_2 (CO_2 less than 0.09 percent)], after which it was assumed that saturation was virtually complete.

Isobaric gas flushing of the N_2-O_2 environment with He-O_2 was accomplished within 5 minutes at a flow rate of approximately 17 m^3/min [600 standard cubic feet per minute (SCFM)] for the 40.2-m dives, and 19.8 m^3/min (700 SCFM) for the 60.35-m dives. After the gas exchange, the residual chamber N_2 percentage varied from 0.3 to 5 percent as a maximum. These kinetics allow mathematical treatment of the gas switch as essentially a step function for all but the fastest tissues.

Ultrasonic Doppler monitoring and recording of bubble signals began 5 minutes before switching gases and continued for the duration of the isobaric phase of the dive and at regular intervals during the subsequent decompression. The earliest bubbles were detected 20 minutes after the first 40.2-m gas switch and continued to be detected in varying numbers for 4 hours. Two more 40.2-m dives were carried out with very few bubbles detected both in the same two animals and in another pair (*10*). The isobaric switch from saturation at 60.35 m produced bubbles in every case, which suggests that a threshold may exist near 40.2 m for isobaric bubble formation. After the switch from the 60.35-m saturation, bubbles were detected as early as 30 minutes, lasted several hours, and were detected for as long as 10 or 11 hours under isobaric conditions. No serious skin lesions were observed in this study; however, it is not possible to exclude such results because of the greater difficulty in perceiving skin discoloration in these animals.

Figure 1 shows a combined plot of Doppler bubble signal counts after an isobaric gas switch at 60.35 m and calculated curves showing the fractional saturation of N_2 and He and the total supersaturation ratio (N_2 + He) (Fig. 1A) and the total excess inert gas concentration after the isobaric switch for three pairs of N_2 + He half-times, corresponding to 13 + 5, 93 + 41, and 139 + 63 minutes, respectively (Fig. 1B) (*11*). The long period over which bubble signals were heard is striking. This immediately identifies bubbles with the so-called "slower" tissues. Although the approximately unimodal distribution of bubbles with time (Fig. 1A) may suggest the importance of a particular half-time (*12*), other experiments show either fairly constant rates of bubble production or bimodal

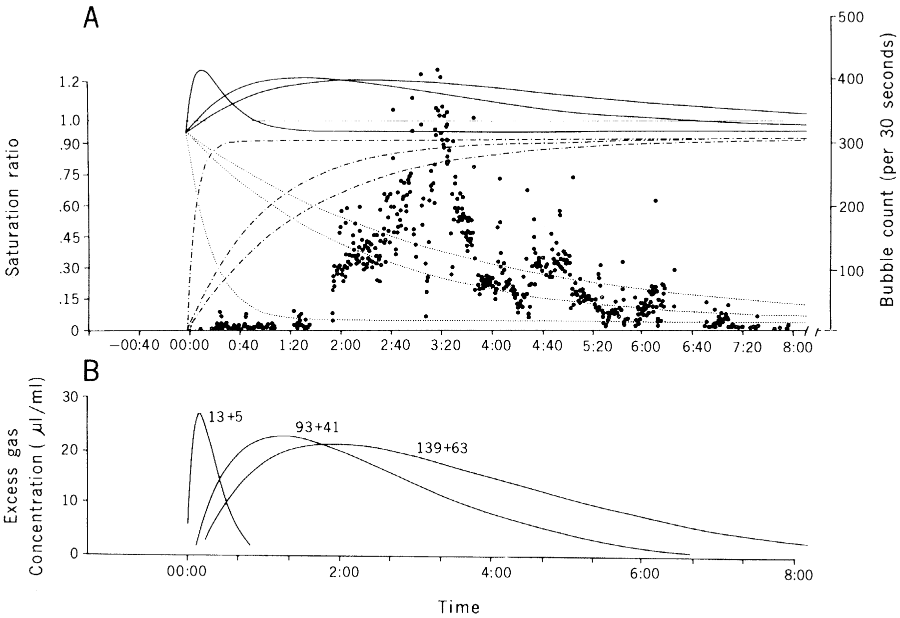

Fig. 1. (A) Bubble counts (right-hand ordinate) plotted against time (in hours and minutes) with calculated gas saturation and total supersaturation plotted on the same time scale. Only inert gases He and N_2 have been included in the computation; thus the initial fractional saturation is less than 1.0 (0.956) at time zero. Values for N_2 (········), He (– · –·), and total gas tension (——) are plotted for the 13 + 5, 93 + 41, and 139 + 63 N_2 + He pairs of half-times. At every point in time, total gas tension is the sum of the He and N_2 fractional saturations. (B) Excess gas concentration [the excess volume of gas (microliters per milliliter at standard temperature and pressure)] dissolved in the tissue as a result of supersaturation. The maximum gas concentration precedes the maximum supersaturation by approximately 30 minutes in the 93 + 41 tissue pair; similar results were seen for the other tissue pairs.

and trimodal counts with time for approximately the same time period. Speculation as to the precise tissue half-times associated with bubbles, therefore, cannot yet be supported by our results; rather, the time of first appearance and the total duration of bubble signals under isobaric conditions are more reliable criteria with which to establish critical supersaturations and critical tissue half-times. This time ranged between 20 and 60 minutes for the goat, although an identical experiment on a pig showed a much greater latency (*13*).

A second consideration refers to the theoretical curves of supersaturation and gas concentration with time. Because of the different gas fractions composing the supersaturation ratios, the maximum excess gas concentration (calculated from Henry's law and an assumed average tissue composition of 15 percent fat), does not coincide with the time of maximum supersaturation for the slower tissues; the greatest discrepancy of this sort is shown for the tissue pair at 93 + 41 minutes (*12*), for which the calculated maximum excess inert gas concentration occurred 70 minutes after the gas switch, and the highest supersaturation ratio occurred after 90 minutes. Also, the most extreme supersaturation and the greatest excess gas concentration occurs rapidly but briefly in the fastest tissues, whereas the slower tissues exhibit less extreme values for a longer period.

In interpreting Fig. 1, it is essential to understand the arbitrary nature of tissue gas-tension calculations. It is accepted (*14–18*) that He saturates and desaturates the body faster than N_2. This result is related to its more rapid aqueous as well as gaseous diffusion (*19*). However, because the multiexponential parallel-compartment model (*16, 20*) has been used in our calculations, we have arbitrarily paired He and N_2 half-times that we must then assume refer to the same actual tissue elements. This assumption itself contradicts part of the rationale supporting use of a multiple parallel-compartment model, since the latter overcomes the lack of physiological reality by having a spectrum of half-times known to span a realistic physiological range of rates (*16, 20*). With two gases, however, there is no way to decide which He half-time is best applied to which N_2 half-time. On the other hand, the use of a constant ratio of permeation rates for N_2 and He for every half-time is obviously an oversimplification because He diffuses faster, is less soluble, and has a lower fat-water partition coefficient than N_2 (*18*). We have used the pairing shown in Fig. 1 only because it is consistent, has been used in our operational decompression model (*11, 12*), and demonstrates the kinds of relationships that must be examined in these situations. Green (*7*) and Harvey and Lambertsen (*21*) have presented theoretical treatments concerning expected maximum supersaturation as a function of the N_2 + He diffusion ratios and the potential problem in operational diving.

Calculations made from accepted models for He and N_2 predict supersaturation in all perfused or "deep" tissues produced by isobaric counterdiffusion, without decompression (Fig. 1). These predictions are confirmed by the presence of gas bubbles detected by Doppler ultrasound. The demonstration of this phenomenon in large animals suggests its importance to human divers at relatively shallow depths. Reversing the direction of the gas switch (that is, from He and O_2 to N_2 and O_2) should provide undersaturation and therefore a decompression advantage (*11, 18*).

An attractive alternative diffusion-dependent model has been described by Tepper (*23*), which can account for higher supersaturation ratios than the summing approach described above and used by Green (*7*) and Harvey and Lambertsen (*21*). Deciding on the most useful model will be facilitated by the judicious use of gases of diverse physical properties in counter studies in vivo, such as those described above, as well as in vitro. The prediction of the diffusion model of Tepper (*23*) more accurately corresponded to the actual depths at which human symptoms have been encountered.

Two of us (C.A.H. and W.L.H.) performed identical gas-switching studies with human volunteers at 3 and 4 atm absolute; we saw no effects at 3 atm absolute, but at 4 atm absolute we observed and photographed the production of urticaria and blotchy subcutaneous skin lesions similar to those reported by Blenkarn *et al.* (*2*) and Lambertsen *et al.* (*1*). These subjects were monitored by ultrasonic Doppler probes placed over the pulmonary artery, but no bubbles were detected. One probable limb bend was observed and successfully treated by pressurizing with He and O_2 at an additional atm of pressure. This additional 25 percent increase in pressure, while relieving the limb bend (a "deep" tissue incident) exacerbated the urticaria and subcutaneous lesions. Procedures therefore should take into account the sum of the inert gas tensions as well as the total excess gas present; as stressed by Buhlman (*18*), decompressions can be either helped by appropriate or hindered by inappropriate inert gas sequencing. More important, we now have an appropriate technique for testing critical concepts such as deep-tissue half-times (*14*), diffusion versus perfusion limitations, gas-induced fluid shifts (*24*), preexisting gas micronuclei (*21, 22*), and appropriate ascent criteria in a way that is insensitive to the experimental difficulty inherent in decompression.

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8. The first reports identifying this phenomenon as a gas bubble lesion associated with cutaneous gas lesions and vestibular derangement in man were those of C. J. Lambertsen's group (*1, 2*) and were presented at the Fifth Symposium on Underwater Physiology in 1972. They demonstrated that man develops cutaneous gas lesions at 37 atm absolute breathing N_2 or Ne at high ambient pressures of He. Experimental confirmation by Idicula *et al.* (*3*) demonstrated copious production of bubbles in anesthetized pigs under a total ambient pressure of 1 atm when N_2O was respired and the animals were surrounded by He. The severity of lesions in the latter experiment was directly proportional to the solubility of the gas respired. This result identifies solubility and therefore total gas concentration as one of the critical parameters in predicting bubble formation and is confirmed by other research [E. Hemmingsen, *Science* **167**, 1493 (1970); B. G. D'Aoust and L. S. Smith, *Comp. Biochem. Physiol.* **49**, 331 (1976); D. L. Beyer, B. G. D'Aoust, E. Casillas, L. S. Smith, paper presented at the Sixth Symposium on Underwater Physiology, San Diego, 6 to 10 July 1975.
9. D. Haugen and E. Belcher, "Final report ONR N00014-69C-0402" (Applied Physics Laboratory, University of Washington, Seattle, 1976); E. O. Belcher, thesis, University of Washington (1976).] Under a surgical plane of anesthesia, a right lateral thoracotomy was made to expose the required major vessels of the heart. The Doppler ultrasonic bubble detection cuff was placed around the posterior vena cava, after which the chest wall was closed; the leads from the Doppler cuff were run subcutaneously to the lateral dorsum of the back approximately 5 cm posterior to the scapula, where they exited through a Dacron-covered storage pack (which allowed healing) with a sterile seal around the connectors. Further details are available in K. H. Smith and B. G. D'Aoust ["Final report ONR N000129-76MB-498" (Virginia Mason Research Center, Seattle, Wash., 1976)].
10. The appearance of bubbles in the first 40.2-m experiment but not in two subsequent ones (either with the same pair of animals or with two more naive subjects) suggests the potential importance of a possible fright reaction to an initially high noise level associated with gas flushing. Such a reaction may have physiologically predisposed the animals to bubble production through vasoconstriction and resulting lower perfusion of slow tissues. Gas flushing in subsequent experiments was carried out in such a way as to slowly increase the onset of noise during the gas flush.
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12. The total tissue tension and fractional saturation values for He and N_2 (Fig. 1) have been computed from the equation

$$\pi_2 = fD_1 + fR(T - 1/K) - (\pi_1 - fD_1 - fR/K)e^{-KT}$$

where T is the step time in minutes, π_1 is the initial gas tension at $T = 0$, π_2 is the final gas tension at T, D_1 is the depth at $T = 0$, R is the rate of change of pressure (dP/dT) in meters per minute, f is the inert gas decimal fraction, K (the tissue constant) is $0.693/T_{1/2}$, and $T_{1/2}$ is the tissue half-time in minutes. Saturating He tensions and desaturating N_2 tensions were calculated and summed for discrete pairs of N_2 + He half-times as follows: 13 + 5, 22.5 + 9, 37.4 + 15, 60.2 + 25, 93 + 41, 139 + 63, 200 + 94, 278 + 138, 372 + 182, 480 + 240. The rationale for this procedure has been described by Smith (*11*). The excess gas concentration was calculated for all tissues by assuming an average fat composition of 15 percent by weight for all tissues and by finding the difference between the excess inert gas fraction and the same gas fraction at a saturation ratio of 1.00.
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17. H. V. Hempleman, in (*14*), p. 331.
18. A. A. Buhlman, in (*14*), p. 348.
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Carbon-13/Carbon-12 Ratio Is Relatively Uniform Among Honeys

Abstract. *The variability of the carbon-13/carbon-12 ratio in honeys was evaluated preliminary to use of the ratio to detect the addition of high-fructose corn syrup to honey. Eighty-four honey samples representing 34 states and including 37 floral types from 17 plant families were analyzed. The mean value of the per mil increment in carbon-13 ($\delta^{13}C$) for all samples is −25.2 per mil, and the coefficient of variation is 3.7 percent. This is the smallest variation yet encountered for a honey constituent or physical property. The range and magnitude of the values suggest that the floral sources are C_3 plants.*

We have undertaken to develop methods to detect the undeclared addition to honey of high-fructose corn syrup (HFCS), a new, highly refined syrup now produced in large quantity (*1*). Its similarity to honey in major components and in minor oligosaccharides and the great variability of the composition of honey make most approaches unfruitful.

When inorganic carbon is converted to living matter during photosynthesis, an isotope effect produces differences in the $^{13}C/^{12}C$ ratios among the various reservoirs of the carbon cycle (*2*). The organic compounds of cells invariably have a slightly lower $^{13}C/^{12}C$ ratio than the carbon dioxide and carbonate of the environment. Isotope variations among these reservoirs result from differences in chemical and physical properties of molecules containing different isotopic species (*3*).

In surveys of many plant families, Bender (*4*) and Smith and Epstein (*5*) demonstrated large differences in $\delta^{13}C$ values (*6*) among plants. Bender, in analyzing the family Gramineae, found that plants that initially fix carbon dioxide via the C_4 dicarboxylic acid pathway have $\delta^{13}C$ values in the range −10 to −20 per mil and those which follow only the C_3 cycle have $\delta^{13}C$ values of −22 to −33 per mil. Thus C_3 plants fractionate atmospheric carbon dioxide to a greater extent than do C_4 plants. Families that show crassulacean acid metabolism also have many examples of high $\delta^{13}C$ values. Smith and Epstein looked at many plant families and found several to be high in ^{13}C content ($\delta^{13}C$ range, −5.6 to −18.6 per mil), while those lower in ^{13}C content ($\delta^{13}C$ range, −23.2 to −34.3 per mil) comprise the bulk of the plant kingdom, lacking the C_4 pathway of carbon dioxide fixation.

Smith and Epstein (*5*) suggested that