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NITROGEN ELIMINATION IN MAN DURING DECOMPRESSION

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Kindwall, E. P., A. Baz, E. N. Lightfoot, E. H. Lanphier, and A. Seireg. 1975. Nitrogen elimination in man during decompression. Undersea Biomed. Res. 2(4):285-297.–The effect of ambient pressure on inert gas elimination during decompression was investigated using human subjects breathing air in a dry hyperbaric chamber. This was done by measuring nitrogen recovery during three different decompression schedules following identical simulated dives. Five subjects were used, each with normal pulmonary function. In each case the simulated dives consisted of exposure for 40 min to air at 4 ATA corresponding to a depth of about 100 fsw and 28°C. Following these exposures each subject was decompressed in different experiments to 50 fsw (2.515 ATA) and to 10 fsw (1.303 ATA) while breathing a mixture of 80:20 helium-oxygen. In addition, two of these subjects were denitrogenated isobarically, at 100 fsw, breathing 80:20 helium-oxygen. Significant differences in nitrogen-elimination rate were observed, with nitrogen removed most effectively at 50 fsw and least at 100 fsw. To explain these unexpected results it is tentatively suggested asymptomatic bubble formation occurred at both 10 and 50 fsw.

gas elimination
bubble formation
breathing mixtures
pressure effects
inert gases

Uncertainties introduced by extending diving and tunneling operations to more extreme conditions, coupled with the danger and cost of decompression, demand more precise and reliable diving tables. Improving tables developed during many years of accumulated experiences requires a more thorough understanding of the decompression process, which in turn requires, among other things, careful measurement of gas elimination in human beings under carefully controlled conditions.

This paper provides exploratory data on this subject, which is at variance with existing decompression theories and which suggests the possibility of faster decompression schedules. Also included here is a tentative explanation for the observed behavior which suggests a new approach to decompression modeling.

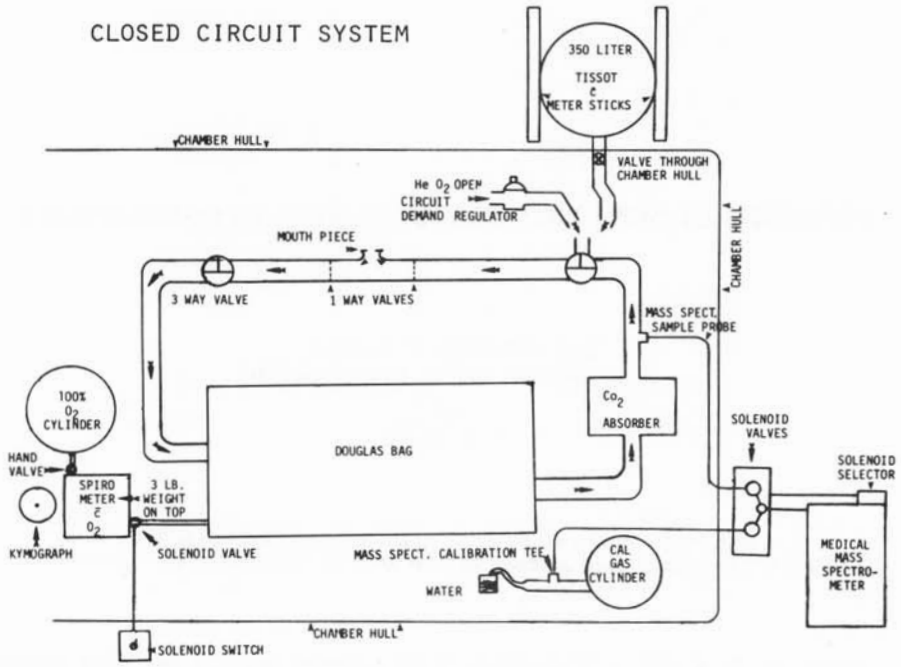

Fig. 1. Diagram of a closed-circuit system designed for measuring the quantity of inert gas eliminated from the lungs during decompression as a function of time.

METHODS

The primary purpose of this work was to measure as accurately as possible the quantity of inert gas eliminated from the lungs during decompression as a function of time. To do this we developed a closed-circuit system (shown schematically in Fig. 1) similar to that of Willmon and Behnke (1941).

Approximately 50 liters of helium-oxygen (80:20) was introduced into a heavy vinyl Douglas bag after the bag and connecting tubing had been flushed free of nitrogen and evacuated to a standard volume by hanging a 3.5 k weight on the Tissot spirometer. Volumes before and after the experiment were measured by transferring the contents of the bag to the spirometer.

Quantitative determinations of helium, oxygen, nitrogen, and carbon dioxide present in the closed circuit were made during the course of the experiment using a Scientific Research Instruments, Inc., MS-8 medical mass spectrometer in respiratory mode. This machine was modified to yield a reproducible change of 100 ppm (1/100th of 1%) for the inert gases, nitrogen and helium, when their concentrations were in the range 0.2 to 6%.

The mass spectrometer was calibrated using calibration gas supplied by Matheson Gas Products, Joliet, Illinois, after discussing the matter with their works manager and defining our specific needs and accuracy requirements. This gas was analyzed by Matheson to tolerances of 100 ppm using the Bendix Thermal Conductivity Gas Chromatograph with a 5Å molecular sieve for the helium and the nitrogen. The CO_2 was analyzed with a Porapak R column (Waters Associates). The oxygen was analyzed with the Beckman E-2 Paramagnetic Oxygen Analyzer with a full-scale span of 18 to 23%. All of the above results

were compared with Matheson primary standards prepared by weight at East Rutherford, New Jersey, and traceable back to the National Bureau of Standards. To insure internal consistency within the experiments, each succeeding bottle of calibration gas used was cross-checked with its predecessor using the MS-8 mass spectrometer. The stainless steel sample and calibration cannulas were of equal 10-ft length and had an internal diameter of 0.019 in.

Six experienced scuba divers who were nonsmokers were used as subjects. They had normal pulmonary function tests. Each subject breathed chamber air supplied by Teflon-ringed, low-pressure air compressors at a depth of 100 fsw (4.03 ATA) in the dry chamber for 40 min and was then switched to open-circuit helium-oxygen breathing via scuba mouthpiece with nose clip for 3 min during decompression to either 50 fsw (2.515 ATA) or 10 fsw (1.30 ATA) to accomplish lung rinsing. Decompression rates were similar (valve wide open). On two occasions lung rinsing was accomplished isobarically with the

TABLE 1

N_2 elimination breathing 80:20 He-O_2 following
40 min of air breathing at 100 fsw

L.M.	WEIGHT: 79.8 kg HEIGHT: 177 cm		
Minutes of Decompression	Depth of Decompression Stop		
	100 fsw (ml/cc STPD)	50 fsw (ml/cc STPD)	10 fsw (ml/cc STPD)
5	146	209	148
10	319	405	313
15	425	570	435
20	534	702	532
25	630	823	627
30	706	951	716
35	795	1054	796
40	879	1135	900
45	940	1213	959
50	997	1293	1034
55	1060	1362	1102
60	1125	1430	1149
65	1170	1503	1214
70	1220	1555	1294
75	1266	1627	1345
80	1306	1688	1400
85	1347	1753	1467
90	1377	1827	1505

subject remaining at 100 fsw after being switched to helium-oxygen and continuing to remain there on closed circuit during the measurement period. All depths were verified during each dive with a dead-weight piston gauge connected to the chamber. Following the lung rinse, the subjects were switched to breathing 80:20 helium-oxygen from a closed-circuit Douglas bag system for 90 min, during which time the nitrogen accumulation in the Douglas bag was measured at 5-min intervals. Make-up oxygen was added to the closed circuit as needed and CO_2 was scrubbed out with Baralyme. To rule out nitrogen diffusion through the bag walls and tubing, the closed-circuit system filled with helium-oxygen was taken to 100 fsw for 96 min without a subject in the circuit. No rise in the N_2 level was seen on repeated sampling.

Dives for each subject were separated by at least 48 hours. All subjects were clothed identically in light fireproof jump suits. By means of cooling coils, heating coils, and fans under the floor, chamber temperature was maintained at $28^{\circ}C \pm 0.5^{\circ}$ except during pressurization and decompression (average $28^{\circ}C$ during runs). The temperature peaked at

TABLE 2

N_2 elimination breathing 80:20 He-O_2 following 40 min of air breathing at 100 fsw

N.T.	WEIGHT: 66.7 kg HEIGHT: 166 cm		
Minutes of Decompression	Depth of Decompression Stop		
	100 fsw (ml/cc STPD)	50 fsw (ml/cc STPD)	10 fsw (ml/cc STPD)
5	79	180	150
10	229	386	338
15	316	544	455
20	403	671	582
25	446	777	670
30	523	866	756
35	584	984	818
40	638	1056	874
45	673	1137	938
50	709	1228	986
55	744	1278	1039
60	776	1347	1103
65	819	1394	1103
70	845	1458	1160
75	879	1520	1194
80	890	1591	1210
85	934	1639	1256
90	948	1684	1271

38°C during the 2.1-min compression to 100 fsw but returned to 28° in less than 2 min. During decompression to 50 fsw from 100 fsw the temperature low point was approximately 13°C, returning to 28° in 3 to 4 min. During decompression to 10 fsw from 100 fsw the temperature low point reached approximately 9°C, returning to 28° in 3.5 to 4 min.

Subjects sat in the same relative positions for all dives. All subjects had fasted for at least 8 hours before entering the chamber. Adequate data were obtained from five subjects (12 dives) which could be reduced to STPD values. The amount of nitrogen eliminated was computed each 5 min by multiplying the calculated bag volume by the observed nitrogen percentage in the bag, after subtracting the initial 2-min value on closed circuit (see Tables 1-5).

TABLE 3

N_2 elimination breathing 80:20 He-O_2 following
40 min of air breathing at 100 fsw

T.J.	WEIGHT: 78.2 kg HEIGHT: 180 cm	
Minutes of Decompression	Depth of Decompression Stop	
	50 fsw (ml/cc STPD)	10 fsw (ml/cc STPD)
5	143	117
10	319	321
15	468	491
20	584	598
25	717	710
30	834	805
35	918	886
40	1030	978
45	1130	1052
50	1195	1124
55	1266	1188
60	1342	1251
65	1402	1297
70	1473	1349
75	1502	1401
80	1538	1454
85	1579	1488
90	1639	1544

TABLE 4

N_2 elimination breathing 80:20 He-O_2 following 40 min of air breathing at 100 fsw

C.R.	WEIGHT: 56.5 kg HEIGHT: 167 cm	
Minutes of Decompression	Depth of Decompression Stop	
	50 fsw (ml/cc STPD)	10 fsw (ml/cc STPD)
5	131	113
10	264	255
15	391	347
20	485	438
25	554	507
30	728	587
35	801	648
40	881	700
45	962	752
50	1039	789
55	1192	824
60	1145	855
65	1234	886
70	1289	914
75	1348	951
80	1388	972
85	1429	998
90	1477	1018

RESULTS

Average nitrogen elimination of the subjects at 50 fsw was 1726 ml, whereas the average of the same subjects at 10 fsw was 1441 ml, representing a 20% increased elimination at 50 fsw (Tables 1-5). No subject eliminated more nitrogen at 10 fsw than when compared to his own 50-fsw run. Two dives were made with isobaric denitrogenation at 100 fsw where the subject did not change depth following air exposure. These two subjects individually eliminated less nitrogen at 100 fsw than they had either at 50 fsw or 10 fsw, averaging only 1163 ml.

Data from the 50-fsw and 10-fsw decompression stops were compared at 90 min using analysis of variants. The differences in gas elimination were found to be significant ($P < .025$). Differences in body weight were not considered in analyzing the data from these five subjects.

TABLE 5

N_2 elimination breathing 80:20 He-O_2 following
40 min of air breathing at 100 fsw

T.B.	WEIGHT: 80.9 kg HEIGHT: 178 cm	
Minutes of Decompression	Depth of Decompression Stop	
	50 fsw (ml/cc STPD)	10 fsw (ml/cc STPD)
5	206	202
10	387	392
15	531	557
20	663	675
25	906	780
30	930	974
35	1030	1066
40	1137	1170
45	1231	1235
50	1309	1344
55	1462	1490
60	1528	1529
65	1607	1573
70	1687	1650
75	1770	1700
80	1847	1746
85	1920	1834
90	2004	1869

Again using analysis of variants, the data from two of the subjects' nitrogen gas elimination at 100 fsw, 50 fsw, and 10 fsw were not found to be significant ($P < .1$). When body weight was taken into consideration in terms of milliliters of nitrogen eliminated per kilogram, analysis of variants still only yielded a significance of $P < .1$. However, using the analysis of variants, the experimental error expressed as the standard deviation was 1.92 ml of nitrogen per kg and the average of the six readings was 19.59 ml of nitrogen per kg. Thus, when averages of each pair of nitrogen-elimination readings in ml/kg at each depth were compared to the overall mean, the 100-fsw values were minus 2.83 SEM ($1.926 \div \sqrt{2}$) away from the overall mean ($P < .00235$). The 50-fsw averages were plus 3.289 SEM away from the overall mean ($P < .00135$). Nonetheless, the 10-fsw averages between these two subjects were not statistically different from the overall mean. This, of course, is to be expected since the 10-fsw values lay between the 100-fsw and 50-fsw values numerically and do not, therefore, differ materially from the mean. However, using the normal distribution and the

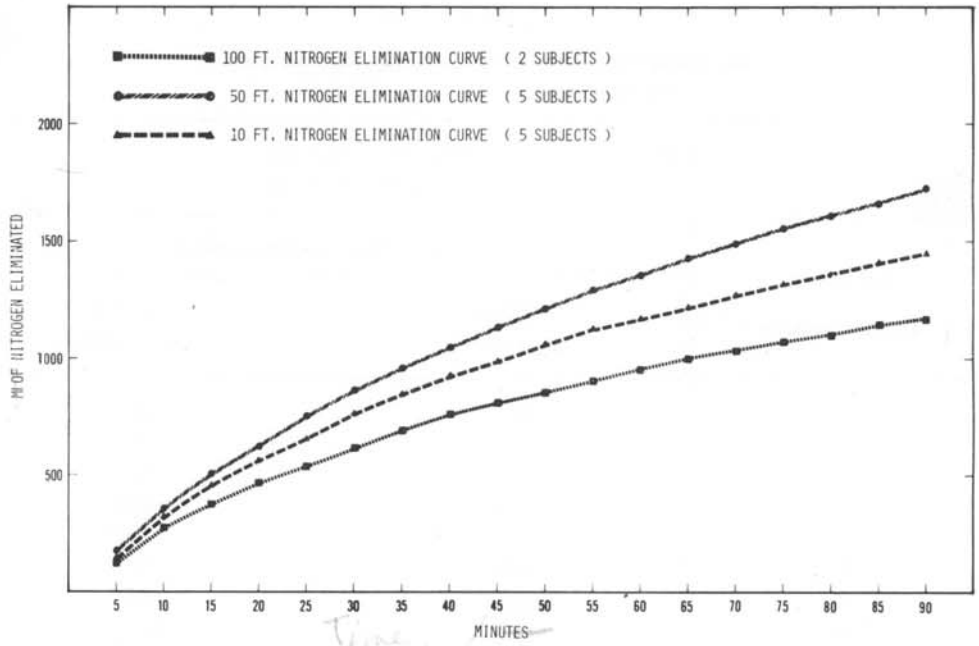

Fig. 2. Nitrogen elimination breathing 80:20 helium-oxygen following 40-min exposure at 100 fsw breathing air.

estimated experimental error provided by the ANOVA, the 100-fsw and 50-fsw values were demonstrated to be highly significant in the two subjects of five denitrogenated at all three washout depths.

These data tend to confirm Willmon and Behnke's 1941 observations that nitrogen elimination seemed to be greatest for decompression depths between 50 and 60 fsw, following similar 100-fsw dives. Furthermore, it does not appear possible that these differences resulted from random errors since essentially no overlap of data occurred in any of the comparisons except for subject T.B., as shown in Table 5. The consistency of these results is further emphasized in Fig. 2, where averages of cumulative elimination are shown for each condition tested as a function of time.

DISCUSSION

The above-described results are anomalous in that they would not be predicted either from the perfusion-limited model of Haldane (Boycott, Damant, and Haldane 1908) or from consideration of diffusional resistance within the body (Harvey 1951). They must then result either from some artifact of the procedure used or from some as yet unrecognized aspect of decompression. They are potentially important because they suggest possibilities for maximizing gas elimination rates not apparent from current decompression models. An explanation for the anomaly should therefore be sought. It is our current belief that it results from gas nucleation during the 50-fsw and 10-fsw dives, but this hypothesis has yet to

be proven. We present the reasons for our belief below, but we are also continuing our investigation both experimentally and mathematically.

The physical and chemical bases for elimination of such gases as nitrogen from the body are simple in concept even if complex in detail. If no nitrogen enters with the inhaled gas during decompression, the elimination rate can depend only upon the initial gas distribution, body geometry and chemical composition, the effective diffusivity of nitrogen in blood and tissue, and the effective transport capacity of the circulating blood. These factors in turn depend upon the physiological state of the subject, through possible changes in geometry and flow distribution, and on the physical state of the nitrogen, via possible nucleation and departures from ideal gas behavior.

At first sight, all of these factors are constant for any one subject in the above experiments and gas-elimination behavior should be the same for all three decompression schedules used. Since this is not what is observed, it is necessary to take a second look and we have considered the following possibilities: *systematic bias,* introduced by the experimental procedure; *change of physiological state,* introduced by differences in environment; and *change in the state of body nitrogen,* introduced by differences in ambient pressure. These are discussed in turn below. Random errors are unlikely to be important but both the accuracy and precision of the experimental technique must be further tested.

BIAS IN THE EXPERIMENTAL PROCEDURE

Three possibilities of experimental bias are worth considering here: unequal losses of nitrogen during the first 5 min of decompression, recirculation of nitrogen in the closed loop, and nitrogen leakage through the skin of the subjects.

Measurement losses

Because of inherent limitations of our experimental method, nitrogen elimination measurements were not absolute. It is clear that large quantities of nitrogen were eliminated both during the 3-min lung rinse and during the next 2 min for which elimination was not included in the measurements of Tables 1-5. The lung rinse was necessary because of the large and variable nitrogen content of the lung. Discard of measurements for the next 2 min was made to avoid errors resulting from undetected leaks or diffusion from the water in the spirometer during evacuation to baseline pressure. Nitrogen measurement was recorded only after the subject was securely on the closed circuit and all valve shifts had been accomplished. Tidal volumes and minute volumes were not recorded.

Fortunately this gap in the elimination record is unlikely to have a significant effect on the results since the losses were probably small compared to the total amount of nitrogen collected. This can be seen by looking at the short-time behavior in Table 1, which is representative of the results obtained.

Linear extrapolation of these figures predicts that nitrogen eliminated during the 5 min for which data are unavailable is about 12% of total nitrogen recovered and that differences relative to the mean should not be more than about 20% of this 12. Such an extrapolation is reasonable for all but the very fast-responding tissues, such as the kidneys and coronary circulation, which must be excluded along with the lungs. The measurements shown should then be representative of all the tissues of normal interest during decompression within an uncertainty of only 2-3%. This uncertainty is small relative to the observed differences. Improvements now incorporated into the system cut this initial loss of measurement time from 5 min to 3 min.

Recirculation effects

Initial back pressure of nitrogen was reduced to very low levels at the start of each decompression and the recirculation volume was always essentially the same. The net effect of nitrogen accumulation, which averaged less than 5% of total recirculating gas volume at the ends of the runs, would be to retard elimination, most strongly when elimination rate was largest. This effect, then, is to *decrease* the observed differences without changing the results qualitatively.

Diffusion across the skin

Nitrogen diffusion across the skin had to be considered in analyzing our results since others (Behnke and Willmon 1941; Klocke, Gurtner, and Farhi 1963; Idicula, Graves, Quinn, and Lambertsen 1972) have demonstrated inert gas transport across the intact skin. The skin of our subjects was at all times exposed to the ambient nitrogen partial pressure in the chamber during the measuring stop, despite the fact they breathed He-0_2 via mouthpiece.

If nitrogen diffusion across the skin alone could explain our data, then the elimination should have been maximal at 100 fsw and minimal at 10 fsw. Neither was the case; the maximal amount was eliminated at 50 fsw. Therefore this effect can only have tended to mask our results by decreasing the observed differences.

Summary

Although ambiguities were introduced by the experimental procedure, they are very unlikely to have affected the results qualitatively. Indeed, their primary effect was probably to reduce the differences observed and thus to mask the effect of decompression depth.

POSSIBLE CHANGES IN PHYSIOLOGICAL STATE

All our subjects fasted for at least 8 hours before each experiment because Cissick, Johnson, and Rokosch (1972) had recently published some controversial data indicating that nitrogen might be endogenously produced after a heavy protein meal.

Temperature was controlled as closely as possible (*see* METHODS). Balldin (1973) demonstrated that ambient temperature has a pronounced effect on nitrogen elimination. He also noted that body position is important. The effect of temperature transients is being eliminated in current experiments by using totally submerged subjects.

The PI_{O_2} must also be discussed as a possible factor influencing our results. In Willmon's and Behnke's original work (1941) their subjects breathed 100% oxygen at 100 fsw and those investigators felt that the resultant vasoconstriction may have decreased the amount of N_2 eliminated during isobaric washout. For this reason 80:20 helium-oxygen was used in these experiments. At 100 fsw this represented a PI_{O_2} of 0.81 ATA. At 50 fsw the corresponding PI_{O_2} was 0.50 ATA and 0.26 ATA at 10 fsw. The elimination of N_2 did not correlate with the PI_{O_2} at the measurement stop.

A comparison of the efficiency of air versus oxygen breathing on helium elimination at 40 fsw following 40 min exposure to helium-oxygen breathing at 120 fsw (Kindwall 1975) failed to show any difference in the amount of helium eliminated although the PI_{O_2} was 0.46 ATA breathing air and 2.21 ATA breathing oxygen.

It therefore seems unlikely that any significant change in physiological state was introduced directly by changes in decompression profile.

POSSIBLE CHANGES IN PHYSICAL STATE OF THE NITROGEN

In general one may consider here both departures from ideal gas behavior and possible nucleation of nitrogen to form either extravascular or intravascular bubbles.

The first of these possibilities can be quickly discarded in view of the relatively high temperatures and low pressures used. Even at 100 fsw the compressibility factor for nitrogen is between 0.99 and unity (Hougen and Watson 1947). Departures from ideality are therefore negligible throughout the range of experiments.

Nucleation cannot be so easily discarded, however. Using Doppler sonar, Smith and Johanson (1970) have demonstrated bubbles in the vena cava during standard asymptomatic decompression. There is also indirect evidence of intravascular bubble formation: blood studies showing loss of platelets following asymptomatic 100-fsw dives were carried out by Martin (1973) in England and Ackles, Korey, Moschos, and McBurney (1974) in Canada. These and other recent studies suggest the likelihood of gaseous nitrogen forming in the body under diving schedules permitted by all existing tables.

It is important to recognize that gas bubbles can have at least three major direct effects on nitrogen elimination, all resulting basically from the low solubility of this gas in both fat and water.

First, even a very small fraction of gaseous nitrogen in capillary or venous blood can increase the transport capacity for this gas remarkably. Since the molar concentration of nitrogen in gas is roughly 50 times that in adjacent blood, only 2% gas phase by volume is needed to double transport above that of nitrogen-saturated but bubble-free blood.

By the same token extravascular nucleation greatly reduces the diffusional driving force for nitrogen migration to the capillaries from the surrounding tissue. Thus, if tissue nitrogen nucleates in the extravascular space, bubbles will form in which total gas pressure is elevated above the ambient pressure only by action of surface tension and tissue forces. This pressure is indeterminate but certainly very small (Harvey 1951). Since the partial pressure of nitrogen in these bubbles will always be less than the total–because O_2, CO_2, and helium will also contribute–they act as a quite effective nitrogen *sink* competing with the blood for nitrogen.

Finally, if intravascular bubbles grow too large in a given capillary, they may retard or even stop the local flow. For example, Hallenbeck, Bove, (1975) have elegantly demonstrated that in severe decompression sickness documented bubble formation is associated with a blockage of the venous flow. Calculations have been reported (Baz, Lightfoot, Lanphier, and Seireg *in press*) indicating that bubble growth rates under our decompression at 10 and 50 fsw are such that bubbles will reach a diameter near that of typical capillaries during their transit of the capillary.

It is then possible to explain all of the observed behavior by the following hypothesis:

Nitrogen elimination at 100 fsw represents the combined effects of homogeneous diffusion and convective transport, as in conventional models. No assumption need be made as to the relative speeds of these two processes.

Enhanced elimination at 50 fsw results from intravascular bubble formation, which greatly increases transport capacity for given partial pressures of nitrogen in the blood.

Appreciable *extravascular* bubble formation occurs at this point, because of the increased driving force for nucleation; the driving force for diffusion of nitrogen from

tissues to blood decreases as a consequence. Also, bubbles now grow to such a size as to occlude capillaries. The somewhat lower elimination rates at 10 fsw result from either or both of these effects.

It should be noted that we arrive at this hypothesis by process of elimination rather than from positive experimental evidence. It must therefore be considered no more than a tentative explanation. At the same time it seems an attractive explanation, in reasonable agreement with known facts as opposed to accepted decompression theories.

The theory does depend upon a presumed large capacity of the systemic venous system and lungs to transport bubbles but this is not so unlikely as it might first appear. Once the capillary venous junction has been passed, the diameter of the venules and veins increases all the way back to the lungs. Thus, during reasonable rates of decompression there would be little danger of bubbles blocking circulation before reaching the lungs.

Our theory also presumes that the lungs are able to accept substantial volumes of inert gas in the form of relatively gross gas emboli over a period of one to several hours. Ilyan, quoted by Van Allen, Hrdina, and Clark (1929) was able to inject up to 2 liters of air into the jugular vein of the dog at a rate of 30 cc per min without causing symptoms. Extrapolating these data from the dog to a 70-kilo man, there would appear to be ample margin for handling this embolic load.

CONCLUSIONS

The consistency of the data presented, the agreement with Willmon and Behnke (1941), and the discussion of possible artifacts all suggest that the observed effects of ambient pressure on nitrogen elimination rate are real.

A relatively simple postulate of asymptomatic bubble formation, necessarily intravascular and quite possibly extravascular as well, explains the observations in a self-consistent way.

The potential practical importance of the observed behavior suggesting more effective selection of decompression stops, indicates that careful test of the hypothesis be made. These tests should include confirmatory dives with fully submerged subjects, direct measurements of gas formation if possible, and also additional theoretical analysis.

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Kindwall, E. P., A. Baz, E. N. Lightfoot, E. H. Lanphier, and A. Seireg. 1975. L'élimination de l'azote chez l'homme au cours de la décompression. Undersea Biomed. Res. 2(4):285-297.– L'effect de la pression ambiante sur l'élimination des gaz inertes pendant la décompression a été étudié chez cinq sujects à fonction pulmonaire normale qui respiraient de l'air dans une chambre hyperbare sèche. Nous avons déterminé le taux de récuperation de l'azote pendant la décompression selon trois schémas différents à la suite de plongées fictives identiques. Chaque plongée fictive comprenait une exposition à l'air à 4 ATA pendant 40 min à 28°C. Apres l'exposition, chaque sujet a été décomprimé jusqu'a 50 fsw (2, 515 ATA) ou a 10 fsw (1,303 ATA) selon les experiences, dans un atmosphère hélium-oxygène (80:20). Aussi, l'azote s'ait éliminé isobariquement des deux sujets à 100 fsw, dans un atmosphere helium-oxygène (80:20).

Nous avons observé des différences significatives des taux d'élimination de l'azote. L'élimination de l'azote le plus efficace a eu lieu à 50 fsw; la moins efficace à 100 fsw. Pour expliquer ces résultats inattendus, la formation de bulles gazeuses asymptomatiques à 10 fsw et à 50 fsw est invoquée.

élimination des gaz
formation de bulles
gaz inertes
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