

DIFFUSIONAL AND METABOLIC COMPONENTS OF NITROGEN ELIMINATION
THROUGH THE LUNGS: EFFECT OF PRESSURE

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SUMMARY PAGE

THE PROBLEM

To determine the diffusional and metabolic components of nitrogen elimination. Using correction factors for nitrogen elimination the possibility of improving decompression tables exists.

FINDINGS

The diffusional component of nitrogen elimination was separated from the metabolic component of nitrogen elimination using nitrogen washout procedures in helium-oxygen atmospheres over a period of 18 hours. The metabolic component was measured at 0.5 ml/min. This figure could be used for a correction factor in the calculation of decompression tables.

Cyclic variations in the ratio of expired to inspired nitrogen in 7 subjects participating in saturation dives to 200 feet and saturation-excursion dives to 800-1000 feet appear to provide evidence for delayed nitrogen excretion which might be related to metabolic nitrogen production.

APPLICATION

This information is important to Diving Medical Officers and Research personnel concerned with diving operations and decompression studies.

ADMINISTRATIVE INFORMATION

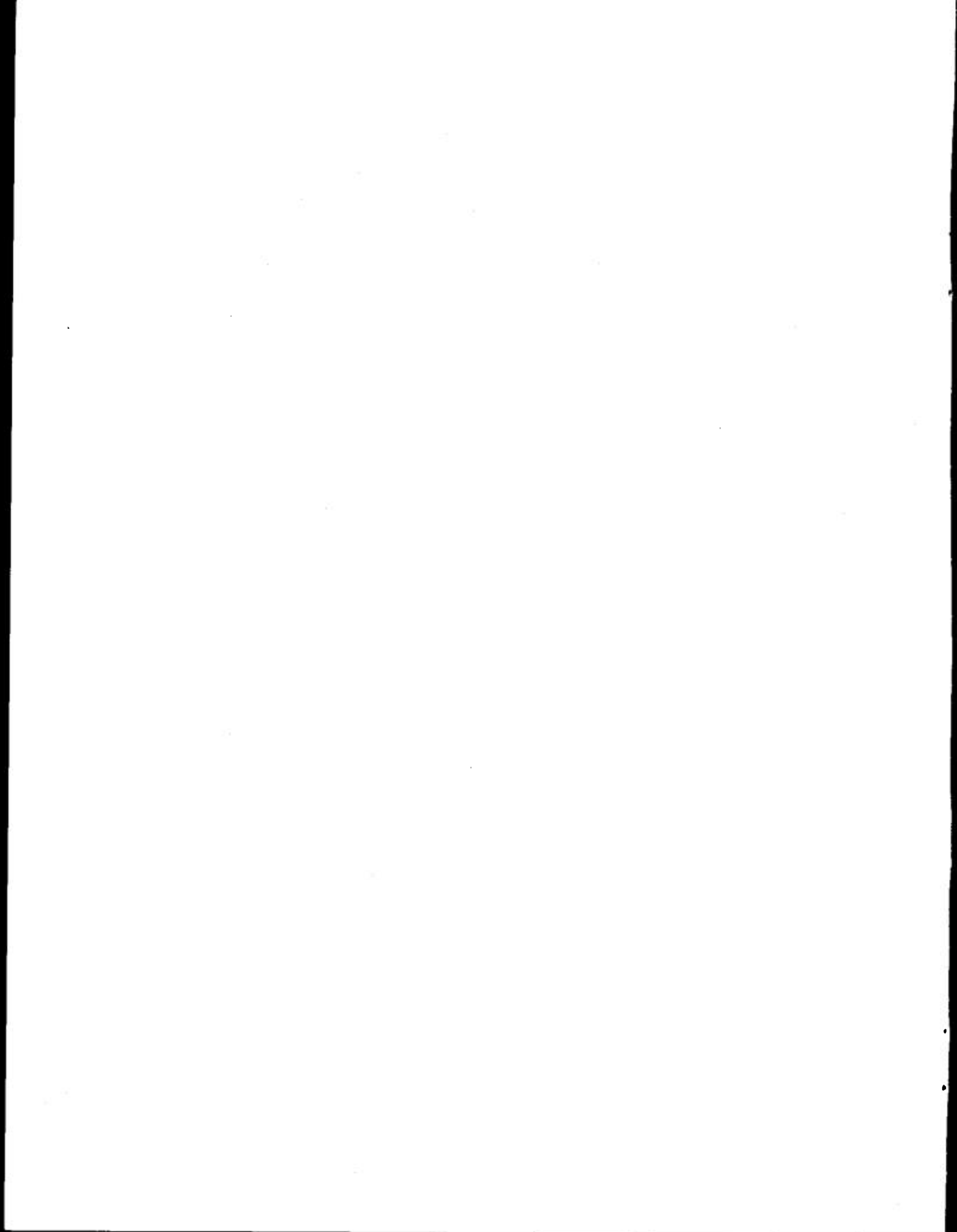
Part of this investigation was conducted under Bureau of Medicine and Surgery Research Work Unit MR041.01.01-0063BOKL and part was conducted during Sabbatical leave in Germany. The present report is Number 7 on this work unit. It was submitted for review on 30 November 1972, approved for publication on 19 January 1973 and designated as NavSubMedRschLab Report No. 736.

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ABSTRACT

The contributions of cutaneous diffusion of atmospheric nitrogen to pulmonary nitrogen elimination was determined by mass spectrometric analysis. In short term experiments, subjects were enclosed in gas-tight bags containing helium, O_2 , N_2 or air while breathing room air. Moreover 24 hour studies of nitrogen elimination were carried out in a pressure chamber in which the ambient gas composition as well as the total pressure was varied. A linear relationship between ambient PN_2 and nitrogen elimination through the lungs was established. At zero PN_2 ambient nitrogen elimination was present after 18 hours and amounted to 0.5 ml/min. This is considered the metabolic component of gaseous nitrogen excretion. Although this amount appears very small, it can account for the frequency found deficit between nitrogen intake (in food) and nitrogen elimination via urine and faeces. Mass spectrometric analysis of ambient and expired air samples collected during three saturation excursion diving experiments showed in all seven subjects cyclic variations in the ratio of expired/inspired nitrogen while the simultaneously measured respiratory quotient remained constant. Whether these delayed nitrogen excretions are due to release of nitrogen from pools in poorly perfused tissues or altered metabolic processes cannot be stated at this time.

One example of the development of large differences between expired and inspired nitrogen was found during decompression of a diver following an air dive to 198 feet. Breath-by-breath monitoring with a mass spectrometer demonstrated a sudden increase in the differences of expired and inspired nitrogen following a normal nitrogen washout curve while breathing oxygen. This occurred at the same time the diver experienced skin bends. The latter lasted for about 1 hour and 40 minutes as did the increase in PN_{2E}/PN_{2I} . In this case the development of bends appears to be associated with inability to eliminate nitrogen properly.



DIFFUSIONAL AND METABOLIC COMPONENTS OF NITROGEN ELIMINATION THROUGH THE LUNGS: EFFECT OF PRESSURE

INTRODUCTION

The question of whether or not free nitrogen is eliminated from the body via the lungs has presented an intriguing challenge to the biological sciences for more than a century. The difficulties did not lie solely in the extraordinary accuracy and sensitivity of the methods required to obtain valid data, but perhaps more importantly in formulating satisfactory concepts. Without recounting a historical survey, it seems appropriate to mention a few critical points in the development of the present status of this problem.

August Krogh, one of the pioneers of modern physiology, made a major contribution to this field and won the Seegan prize of the Imperial Academy of Vienna for his investigations of a possible participation of free nitrogen in metabolism.¹⁵ He characterized the existing situation by describing two camps engaged in battle with each other. On the one side were investigators who used respiration experiments and who agreed that excretion of gaseous nitrogen takes place, e.g. Regnault and Reiset.²⁴ On the other side were the proponents of nitrogen balance studies such as Pettenkofer and Voit²² who contended that all nitrogen ingested in food appears again in the urine and faeces. Krogh noted, that "neither side can convince the other, but each points to the numerous sources of errors which beset the methods not adopted by themselves and I would venture to say that both parties are right in so doing."¹⁵ Krogh decided

to use the closed respiration apparatus of Regnault and for better accuracy immersed it in a constant temperature bath. Regnault and Reiset had observed a rather substantial variable production of nitrogen equal in volume to one and a half percent of the oxygen volume absorbed. Krogh demonstrated that this was partly explained by the erroneous assumption of the authors that the temperature of the animal chamber must be equal to that of the water bath. Krogh stated "my three series of respiration experiments, with chysalides, eggs and mice, show an extremely slight production of gaseous nitrogen, amounting in the case of eggs to 1.5 cc. during the whole period of incubation and in mice up to 0.01 percent of the absorbed volume of oxygen."¹⁵ Krogh's critical experiments, carried out with extraordinary care and accuracy, gained him international renown. They were considered as proof that nitrogen does not participate in the respiratory metabolism as stated by Rehberg²³, and seemed to have answered Benedict's query³, that such a proof was still lacking in spite of the assumption of physiologists that no excretion of nitrogen takes place. From then on, the assumption of equality of inhaled and exhaled nitrogen was firmly established and found its expression in the relevant formulas for calculation of oxygen consumption and carbon dioxide excretion.

As a matter of fact, Krogh found some gaseous nitrogen excretion in all his experiments, albeit an extremely small amount. However, he found it

difficult to interpret such a small amount of nitrogen excretion, since no pathway for liberation of gaseous nitrogen from metabolism had been demonstrated in higher animals.

Rather than leave the issue unresolved until further data came along, the observed difference between inhaled and exhaled nitrogen was simply discarded as being practically within the limits of error of the methods. The matter rested thus for about fifty years. A good review of nitrogen balance studies has been given by Duncan⁸. Systematic discrepancies between nitrogen balance values and nitrogen retention determined by carcass analysis in rats were reported by Nehring²⁰, Müller, Wilmes and Knappen¹⁷, and Neubert²¹.

Cumulative nitrogen balance measurements suggested higher retention of nitrogen than were found by carcass analysis. The "loss" of nitrogen was particularly marked by feeding of rat diets with higher protein levels. Costa⁶ compared nitrogen balances with live-weight changes in dogs, rats and mice and found that positive nitrogen balances indicating retention of nitrogen was not reflected in weight gain of animals. To explain this discrepancy, Costa suggested a hypothetical pathway of nitrogen metabolism by which a small amount of nitrogen gas is eliminated through respiration. In further studies of mice in closed metabolic systems using mass spectrometric determinations, Costa et al⁷ concluded "that some food could be converted into nitrogen gas" in quantities which would balance the nitrogen equation. Similar results were obtained in human subjects. Nitrogen concentra-

tion in the chamber which had a volume of 950 liters and which had been made nitrogen-free increased during the first 6 hours corresponding to a nitrogen excretion from the body of about 300-400 milliliters. Muysers¹⁸ found in 1969, analyzing inspired and expired air with the mass spectrometer and with volumetric methods, that nitrogen was excreted through the lungs. In resting conditions, it averaged 3.2 ml/min for women and 5.9 ml/min. for men. Assuming an average oxygen consumption of about 200 ml/min for men, the nitrogen elimination through the lungs would amount to about 2.1% of the oxygen intake.

More recently, Cissik and Johnson⁵ investigated nitrogen production values in steady state conditions using standard open circuit methods with two Tissot spirometers. They reported values of gaseous nitrogen excretion as high as 208 ml/min. amounting to 66% of the oxygen consumption under conditions of high protein intake. These values are quite out of line with all previous findings obtained in investigations covering more than a century; therefore the burden should be placed on these investigators to explain their results.

The problem of gaseous nitrogen excretion through the lungs is a complex one. At least two processes seem to be involved: (1) transcutaneous diffusion of atmospheric nitrogen through the skin; and (2) metabolic production of gaseous nitrogen. The skin diffusion of nitrogen and argon was determined by Klocke et al¹⁴ at the lower arm. Extrapolating the data obtained on the arm to the total body surface, it was calculated that under the given conditions

with a skin surface area of 2 m², 0.07 ml/min. of nitrogen and 0.002 ml/min. of argon were taken up. Based on these data only 1.2% of the 5.8 ml/min. nitrogen excretion found in the current study could be explained by skin diffusion. Skin diffusion of N₂ may explain the findings of Lundin¹⁶, who observed that nitrogen was still eliminated through the lungs after 24 hours of oxygen breathing. Groom and Farhi¹⁰ have demonstrated in nitrogen washout curves in dogs, using O₂ breathing, that after 3 hours, the venous-arterial N₂ difference remains constant and that under these conditions the rate of skin diffusion of nitrogen equals the rate of removal of nitrogen from the lungs.

Critical experiments to be carried out appeared to be prolonged nitrogen washout curves, while eliminating nitrogen diffusion by enclosing the body in a nitrogen-free atmosphere. Such studies were performed and are described in this report. An attempt was made to differentiate the diffusional from the metabolic components of nitrogen excretion. Moreover, more information was obtained about nitrogen elimination under increased pressure.

METHODS

If the Respiratory Quotient (R) is not equal to 1, then the nitrogen tension of partial pressure in the inspired air is not equal to the nitrogen pressure in the expired air. An increase in the nitrogen of the expired air on its own does not prove the existence of nitrogen elimination. For a state of equilibrium to exist, it is generally held that the quantity of inhaled and exhaled nitrogen

will be equal. The same conditions apply for argon, which is at a level of 0.93% in the atmosphere.

If these assumptions are correct, the expiratory and inspiratory concentration relationships of argon $\frac{FEAr}{FIAr}$ must be equal to or a reasonable average of the same ratio of inspired and expired nitrogen $\frac{FEN_2}{FIN_2}$. The respiratory quotient or momentary quotient and the resulting intrathoracic volume changes would have the same significance for those two expressions. Using a mass spectrometric analysis of inspired and expired air, with four different types of mass spectrometers, it was found that the quotient of $\frac{FEAr}{FIAr}$ behaves differently from the quotients $\frac{FEN_2}{FIN_1}$ or

$$\frac{FEAr \cdot FIN_2}{FIAr} - FEN_2 \neq 0$$

Technique

If U represents the voltage of the mass spectrometer proportional to the argon and nitrogen concentrations and if the ion currents are amplified in such a form that for room air or any dilutions of room air by oxygen, helium or any other gas do not affect the measurements of N₂, and if U_{Ar} equals U_{N₂}, then the voltage of argon equals the voltage of nitrogen, or the quotient of U_{IN₂}/U_{IAr} equals 1. The difference between U_{EAr} and U_{EN₂} could be read directly at the digital voltmeter.

If, for expired gas, these differences are not zero, but negative, this could mean either a nitrogen elimination from

the lungs, or an argon uptake by the lungs or both.

For such investigations, a very high degree of accuracy is necessary. In the instruments used, the accuracy for UN_2 and UAr was such that a difference of 5 parts per million between two samples could be clearly detected. The drift of the instrument was below 0.5% of full scale per hour.

Experimental procedures

In order to arrive at the quantitative measurement of nitrogen which is taken up via the skin, studies were done with eight subjects.

The men were encased in gas-proof bags. These bags were filled with an atmosphere consisting of either pure oxygen, nitrogen, or helium. During their stay in these bags, the subjects were breathing ordinary room air through a mouth-piece protruding through their gas-filled bag. Previous tests had made sure that these bags were sufficiently sealed so that no nitrogen or argon could escape.

By adding 0.93% argon, the atmosphere surrounding the subjects was made comparable to that of the room air they were breathing, in regard to concentration of argon. In this way the previously described requirements for mass spectrometric analysis were fulfilled.

In a second series of studies, the duration of the experiments was extended to approximately 24 hours to determine the influence of different gas

compositions of the ambient air and of increased pressure on the nitrogen elimination through the lungs as a function of time. Each of six subjects was exposed to the following atmospheres: (1) 2 ATA-air; (2) ATA-air plus 1 ATA-helium, and (3) 0.2 ATA oxygen and 0.8 ATA helium in a pressure chamber.

The main chamber had a volume of 8 cubic meters and the antechamber of 2 cubic meters. The main chamber was first filled with a mixture of 0.8 ATA helium and 0.2 ATA O_2 . The subjects entered the antechamber which contained air, and started to breathe oxygen. The antechamber was then decompressed to the equivalent of 25,000 feet in altitude and flushed with helium. This procedure was carried out 3 times within a period of 45 minutes, while the subjects continued to breathe oxygen. After this period, the O_2 content of the antechamber was raised to 0.2 ATA. The subjects then entered the main chamber.

With this procedures, the N_2 partial pressure of the ambient atmosphere in the chamber was kept below 1 mm Hg (actually about 0.75 mm Hg). Nitrogen exhaled by the subject into the chamber during the 24-hour period was estimated to raise the nitrogen concentration in the 10 cubic meter volume of the chambers by 0.005%, or an increase in the partial pressure of nitrogen in the chambers from 0.75 to 0.76 mm Hg. No special procedures were required in the other two 24-hour experiments with 2 ATA air, 1 ATA air, and 1 ATA helium.

This report also includes studies which were carried out during saturation-excursion dives to 800 and 1000

feet while breathing helium-oxygen atmospheres, and during a 12-day saturation exposure at 200 feet.

During these experiments, samples of mixed expired gas and alveolar gas were collected, together with samples of the chamber atmosphere in evacuated steel cylinders and later analyzed with a mass spectrometer at the Naval Research Laboratory, Washington, D.C.

Data of respiratory O₂ and CO₂ gas exchange obtained during these experiments has been published elsewhere^{25,26}.

Moreover, additional data are presented from a recent investigation carried out during a 200-foot air dive in which continuous breath-by-breath analysis of inhaled and exhaled nitrogen, oxygen, carbon dioxide, and argon was carried out.

RESULTS

I. Nitrogen elimination under normal conditions.

Nitrogen elimination under normal conditions, breathing air, (Figure 1) shows a characteristic example of a mass spectrometric analysis of partial pressure of respiratory gases during expiration. The straight line shows, for comparison, a corresponding increase of PN₂ and PAr by increasing the total pressure of room air at the capillary tip. In the expiration curve, one can see that the nitrogen and argon partial pressures behave in a significantly different manner. At the beginning of the expiration, the nitrogen partial pressure increases rapidly while

the argon partial pressure remains nearly unchanged and only slowly rises later. The mean excess of PN₂ amounts to 3.5 mm Hg. For a mean breathing volume of 8L/min this means a N₂/excretion of 4 ml/min.

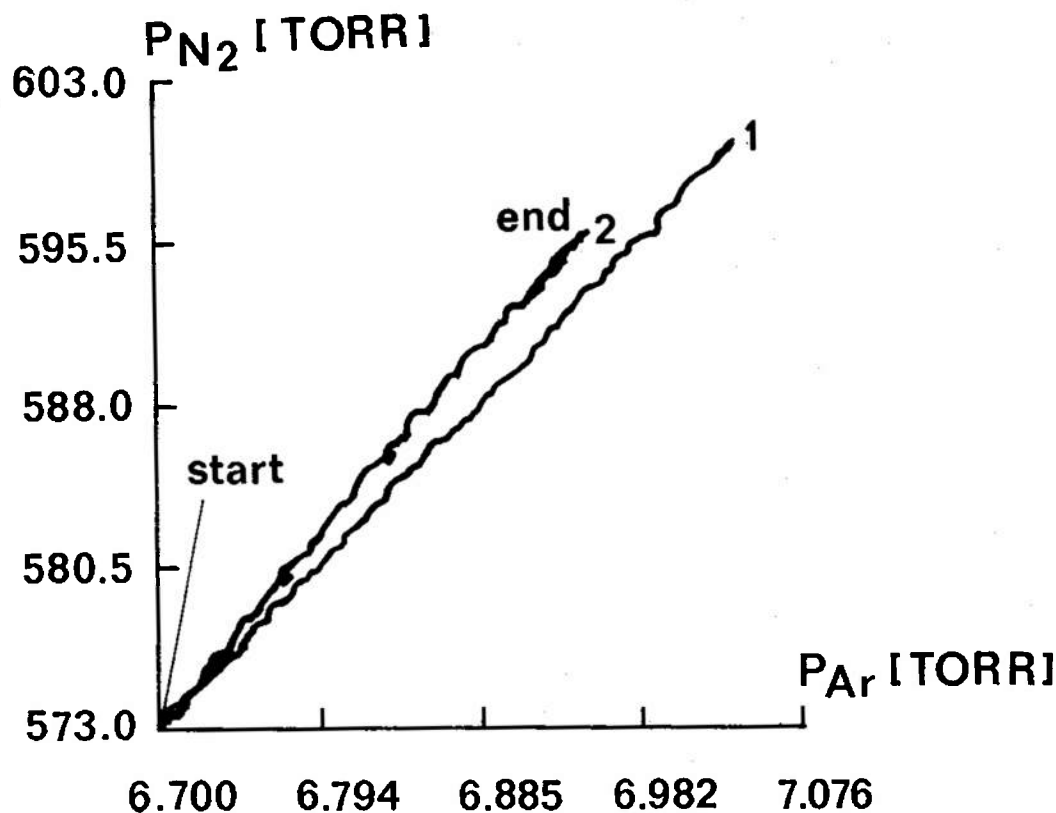
Nitrogen elimination of the lungs measured in 20 subjects under resting conditions was found to be 1.5 to 9.1 milliliters per minute.

II. Nitrogen elimination in subjects surrounded by an environment free of nitrogen or 100% nitrogen.

In the second series of experiments, the nitrogen elimination was measured in subjects surrounded either by an atmosphere made nitrogen-free, or containing 100% nitrogen, while these subjects were simultaneously breathing room air. If the atmosphere surrounding the subject consisted of pure nitrogen, the nitrogen elimination through the lungs during one hour was not influenced in a measurable way, as shown in Table 1. However, nitrogen elimination decreased if the atmosphere enclosing the subject consisted of pure oxygen, or helium-oxygen. In an oxygen atmosphere, the nitrogen elimination fell to 61% of the nitrogen elimination measured under normal conditions (1 ATA). In a helium atmosphere, while the subjects were breathing room air, the nitrogen elimination was reduced to 68% of the original value. According to Table 1, the nitrogen elimination reached a new steady state quickly following the change in the atmosphere surrounding the subject. For a series in which bag air was replaced by helium and by oxygen, respectively,

Table 1. The Effect of an Ambient Nitrogen-Helium and Oxygen Atmosphere on Nitrogen Elimination Through The Lungs in 7 Subjects

CONDITION	TIME	NITROGEN EXCRETION ml/min		
		\bar{x}	$S_{\bar{x}}$	$\bar{x}_{\bar{x}}$
Ambient Gas	Before			
1) 99.1% N ₂ 0.9% Ar		2.41	0.152)	2.41
		2.41	0.128)	
	10'	2.48	0.147)	2.49
	20'	2.43	0.123)	
	30'	2.44	0.136)	
	40'	2.51	0.112)	
	50'	2.51	0.107)	
	60'	2.57	0.234)	
	10'	2.70	0.293)	
after 20'		2.34		2.52
2) 99.1% He 0.9% Ar	TIME Before	2.49 2.37	0.165) 0.181)	2.43
	10'	1.66	0.129)	1.65
	20'	1.67	0.104)	
	30'	1.50	0.093)	
	40'	1.73	0.182)	
	50'	1.76	0.151)	
	60'	1.56	0.092)	
	10'	2.30	0.177	
after 20'		2.31	0.181)	2.255
3) 99.1% O ₂ 0.9% Ar	TIME Before	2.16 2.09	0.139) 0.197)	2.125
	10'	1.45	0.185)	1.29
	20'	1.24	0.234)	
	30'	1.13	0.153)	
	40'	1.23	0.168)	
	50'	1.41	0.116)	
	60'	1.20	0.091)	
	10'	2.33	0.236)	
after 20'		2.26	0.206)	2.295



1 slope for proportional pressure increase of P_{N_2} and P_{Ar}

2 course of a prolonged expiration

Fig. 1. X-Y plot of proportional pressure increase of nitrogen P_{N_2} and argon P_{Ar} obtained by increasing the total pressure of room air at the tip of the capillary tip of the mass spectrometer is presented in curve 1. X-Y plot of P_{N_2} and P_{Ar} during the course of a prolonged expiration differs from control curve 1 showing an excess of nitrogen.

the control values were 2.49 milliliters per min. and decreased to 1.66 ml/min after 10 min in the helium atmosphere and to 1.24 ml/min after 20 min in the oxygen atmosphere. At the same time, the nitrogen content of the bag surrounding the body increased by 8

ml/min in the oxygen atmosphere and 5 ml/min. in the helium atmosphere. According to these figures, the nitrogen elimination through the lungs was somewhat higher when the surrounding atmosphere was helium as compared to oxygen.

III. Nitrogen elimination during the exposure to different gas mixtures at different pressure.

In this series of experiments, the ambient atmosphere and the breathing gas were the same.

The results of these experiments are shown in Figure 2. At a pressure of 2 ATA-air the nitrogen elimination was increased by a factor of 2, as a mean. However, during the 24-hour period in

which the nitrogen elimination was observed, considerable variations occurred.

The nitrogen elimination remained elevated continuously when compared to the values obtained under normal atmospheric pressures, with the exception of some measurements during the night. In the second series of experiments, in which one ATA helium was added to one atmosphere of air there appeared to be no significant influence

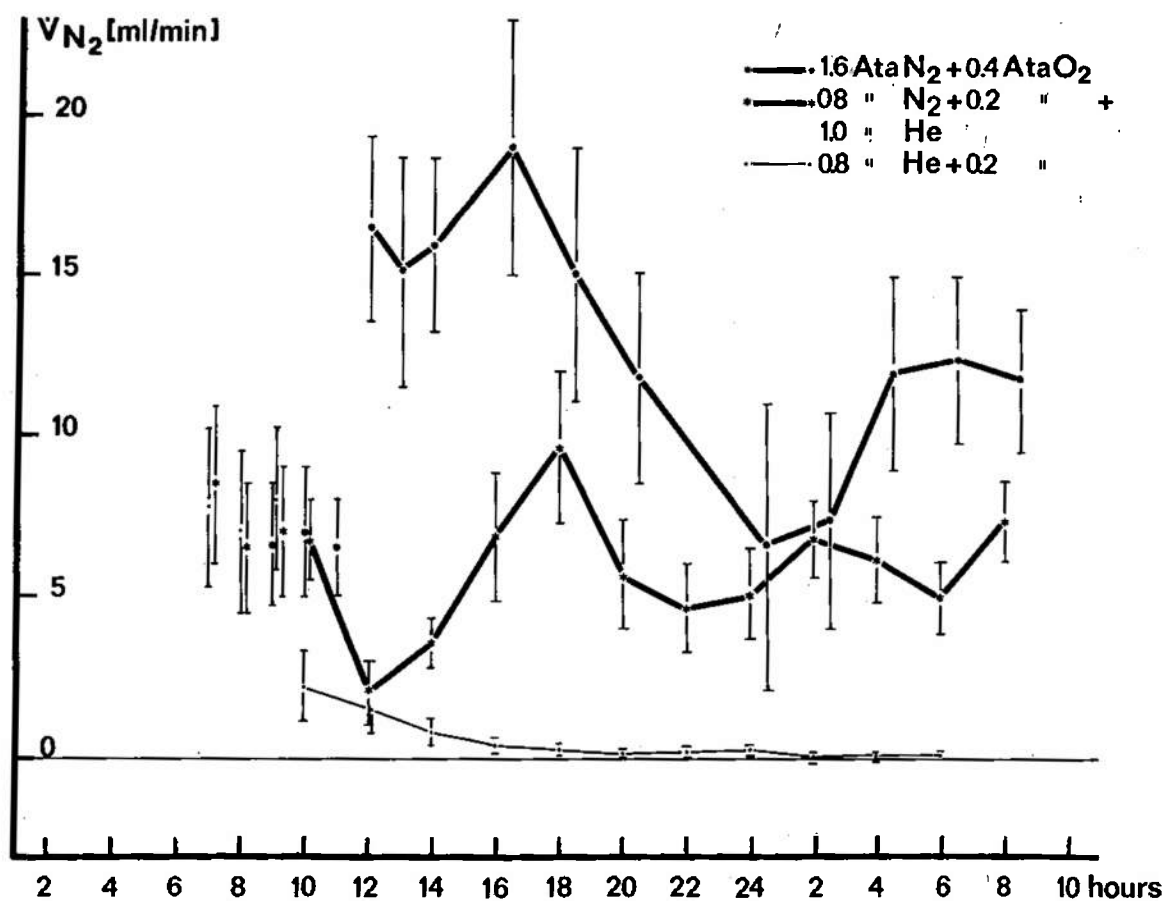


Fig. 2. Nitrogen elimination during 20-24 hour exposure to a) 2 ATA air, b) 1 ATA Helium + 1 ATA Air and c) 0.8 ATA Helium-0.2 ATA oxygen. Marked reduction of nitrogen elimination in helium-oxygen atmosphere.

on the nitrogen elimination. However, in this case too, a larger variation in the elimination of nitrogen was observed. In the oxygen-helium atmosphere, there is a significant reduction of nitrogen elimination below control values. The nitrogen elimination decreased in an exponential manner during the first ten hours without reaching zero values during the entire 18-hour experiment.

In Figure 3, average nitrogen excretion values obtained after 18-24 hour exposure to different gas mixtures are plotted against partial pressures of inspired nitrogen. There is a nearly straight-line relationship between the partial pressure of nitrogen in the ambient air and the amount of nitrogen excreted through the lungs. The line crosses the abscissa at 0.5 ml of nitrogen excreted when the ambient par-

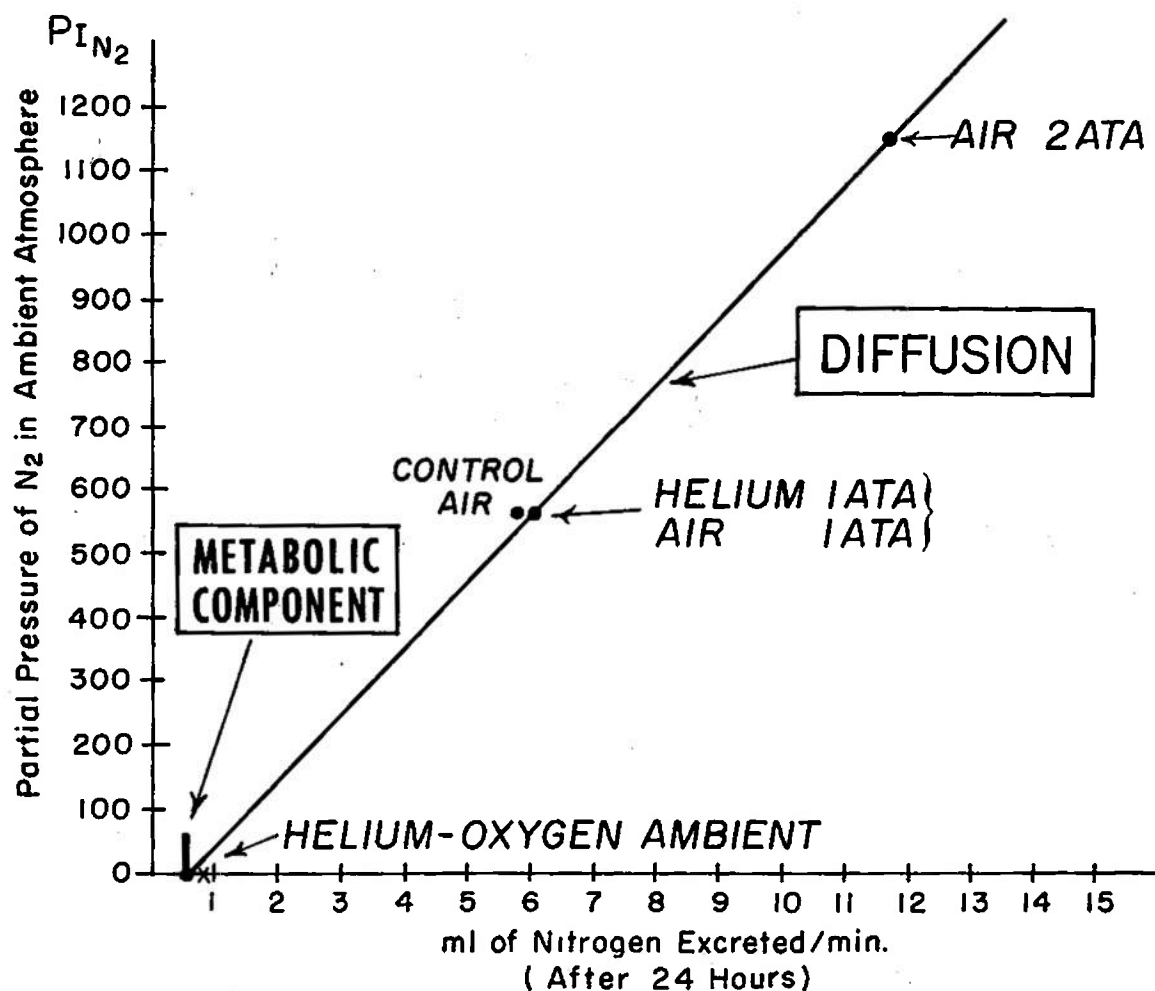


Fig. 3. Plot of partial pressure of nitrogen in ambient atmosphere against nitrogen elimination measured after 18-24 hours of exposure to different atmospheres. Values from Figure 2 are used. (x) data obtained by Herron et al¹² after exposure to a helium-oxygen atmosphere for 13 hours.

tial pressure of nitrogen is zero, which is the metabolic component of nitrogen excretion through the lungs under resting conditions. The cross marks the value of 0.86 ml/min obtained by Heron et al.¹² after 13 hours in a He-O₂ atmosphere.

IV. Nitrogen elimination during saturation dives to 200 feet and saturation-excursion dives to 800 and 1,000 feet.

Mass spectrometric analysis was carried out in three saturation-excursion dives on inspired and expired air samples obtained at various time intervals. The respiratory exchange ratio (R) was determined using the standard formula:

$$R = \frac{FECO_2 - FICO_2}{(1 - FEO_2 - FICO_2)} \cdot \frac{FIO_2}{(1 - FIO_2 - FICO_2) - FEO_2}$$

The ratio of the measured expired to inspired nitrogen partial pressure was also calculated.

Since the R values remained constant at about 1.00 throughout the diving experiments, with the exception of slightly higher values at the beginning and end of the experiments, one would expect that the ratio of expired to inspired nitrogen would also remain constant. However, there was a marked transitory increase during the dives followed by a decline and a secondary rise and decrease. These cyclic variations of the ratio of expired to inspired nitrogen were found in every one of the three dives involving a total of seven subjects (Figure 4, 5 and 6).

The level of inspired nitrogen was markedly reduced in all dives and re-

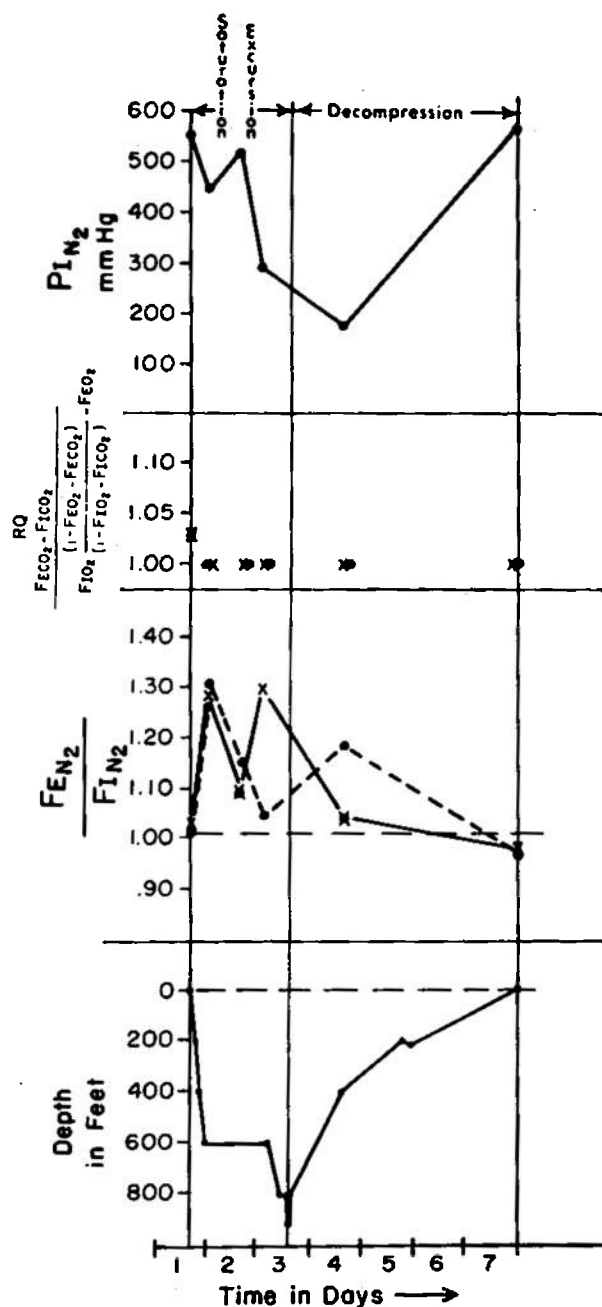


Fig. 4. Saturation-excursion dive to 800 feet of sea water (FSW) on 2 subjects. Time courses of partial pressure of nitrogen in ambient atmosphere. R.Q., values, ratio of exhaled nitrogen fraction to fraction of inhaled nitrogen and depth profile are plotted.

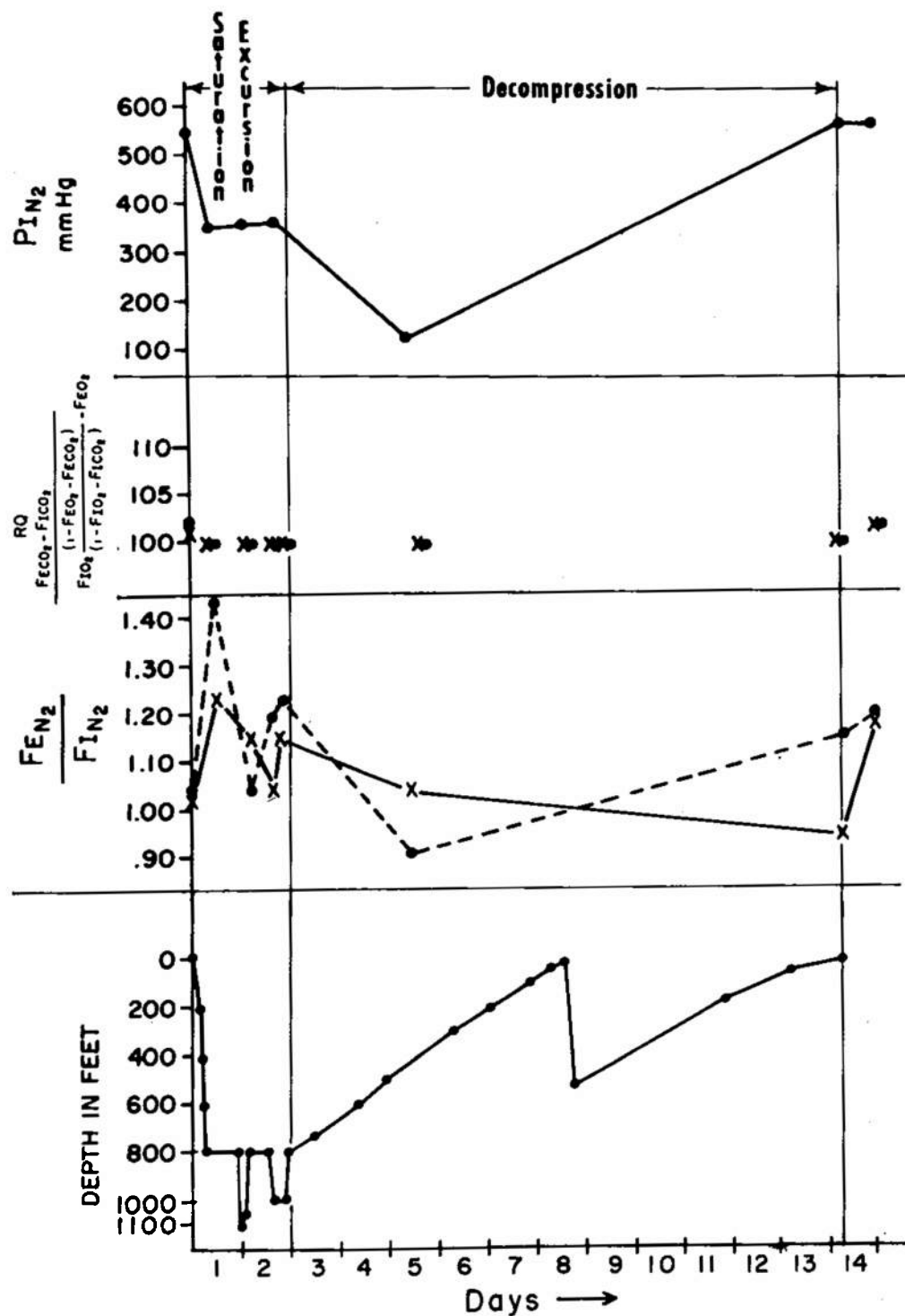


Fig. 5. Saturation-excursion dive to depth equivalent to 1000 feet of seawater (2 subjects). From top to bottom. Time course of partial pressure of nitrogen in ambient atmosphere, R.Q. values, ratio of fraction of expired nitrogen to fraction of inspired nitrogen and depth profile. Note the cycles in F_{EN_2}/F_{IN_2} while R.Q. values remain constant.

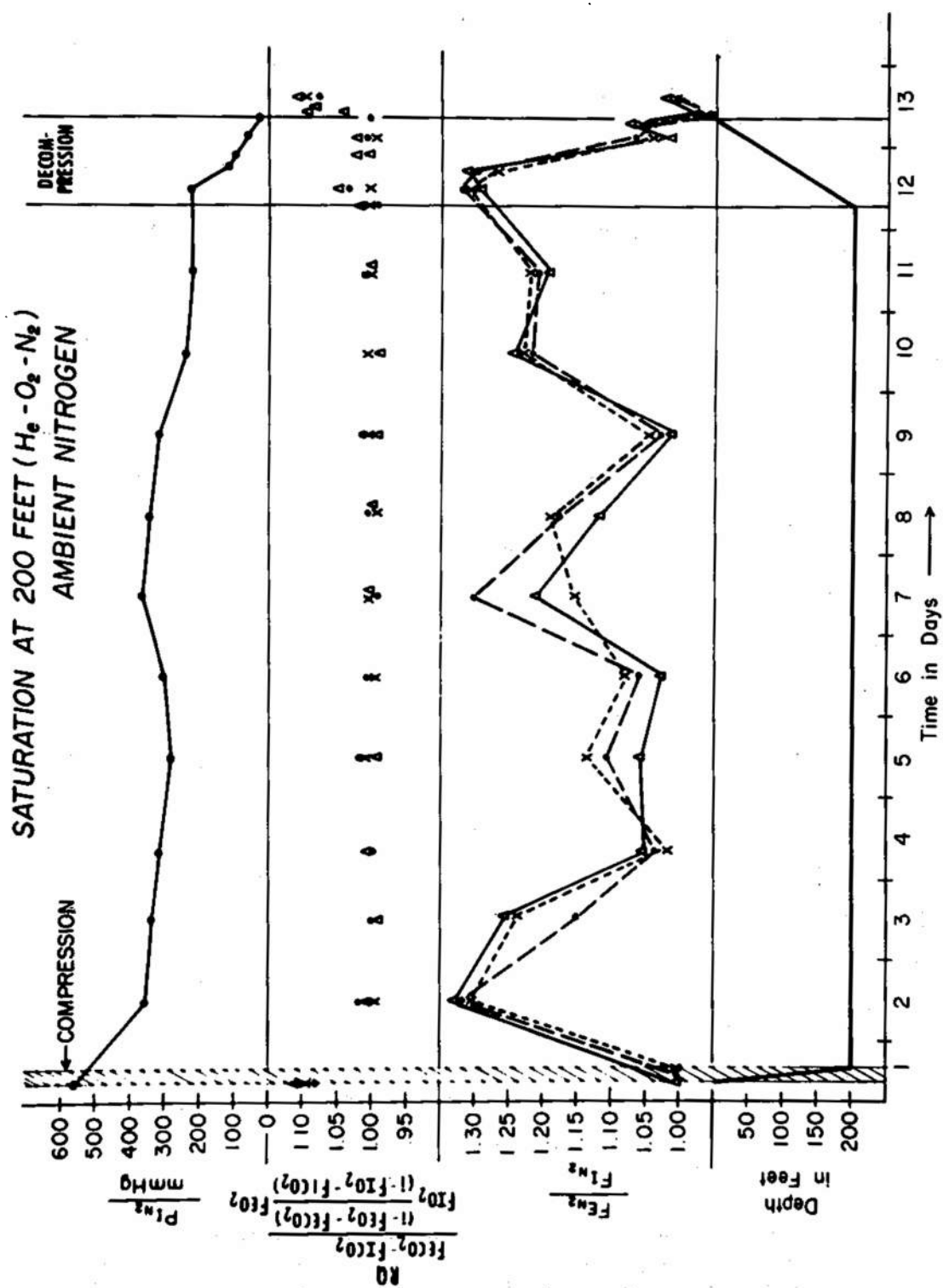


Fig. 6. Saturation due to 200 FSW breathing helium-oxygen lasting for 12 days (3 subjects). Cycles of ratio of expired nitrogen/inspired nitrogen appear in intervals of approximately 3 days without corresponding changes in R.Q. values.

mained in most cases practically constant at the time these increases in the ratio of expired to inspired nitrogen occurred. This circumstance indicates that the observed increase in nitrogen excretion was independent of the level of inspired nitrogen.

V. Demonstration of large increases in the differences between exhaled and inhaled nitrogen associated with the development of bends.

Figure 7 shows the diving profile, the respiratory rate, the alveolar PCO_2 ,

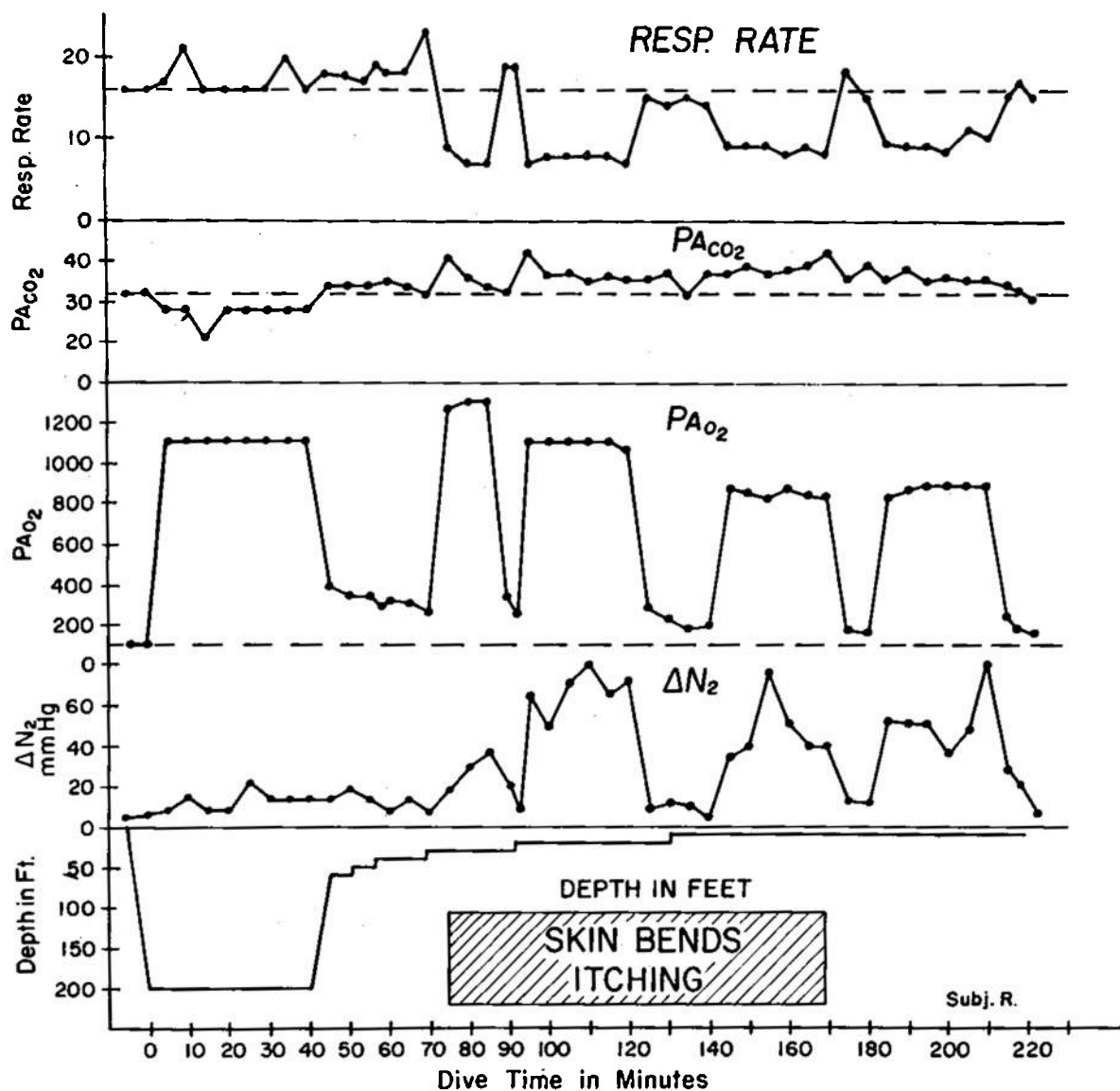


Fig. 7. Dive to depth equivalent to 198 feet of seawater breathing air and subsequent decompression in which the subject was breathing oxygen at 4 stages. Note the marked decrease in respiratory rate and the associated rise of endtidal CO_2 during inhalation of oxygen. Following initial nitrogen washout in oxygen breathing the concentration of exhaled nitrogen rose again and remained elevated during the periods of oxygen breathing. At the same time the diver experienced skin bends.

PO_2 , PN_2 and the difference between alveolar and inspired partial pressure of nitrogen. During the decompression period following the air dive to 198 feet, the subject inhaled pure oxygen on four occasions to hasten nitrogen elimination. Breathing of oxygen from the mask resulted each time in a marked fall of respiratory rate. During the first period of oxygen breathing, there was a typical nitrogen washout curve and the exhaled nitrogen fell to values of 5-9 mm Hg., but the exhaled (alveolar) nitrogen later increased to values between 50-70 mm Hg, while the nitrogen partial pressure of inhaled gas was zero. The period of increased alveolar nitrogen levels coincided with the period in which the subject complained about skin bends (see Figure 7).

DISCUSSION

In previous experiments nitrogen excretion via the lungs had been determined under resting conditions during tests of one-hour duration. The resulting measurements were 1.5-9.1 ml/min with an average of 5.87 ml/min¹⁸. Extrapolating these values to 24 hours, the nitrogen excretion ranges from 2.7 to 15.13 g/day. Assuming a daily protein intake of about 100 g, with a resulting uptake of 16 g N_2 and assuming further that all nitrogen excreted by the lungs is of metabolic origin, 25% to 95% of the nitrogen taken in with the protein of the food would be eliminated as molecular nitrogen via the lungs. This would represent a very large proportion of the nitrogen balance and would have been discovered a long time ago.

The difference between nitrogen content of the food and nitrogen content of

urine for 24 hours is approximately one gm.

As a consequence, nitrogen eliminated via the lungs must have still other sources. The diffusion of molecular nitrogen from the ambient air through the skin into the body followed a partial pressure gradient must be taken into consideration. The contribution of the diffusion component to the nitrogen elimination via the lungs has been demonstrated in these experiments, in which the ambient gases consisted of 2 ATA air and 0.8 He + 0.2 ATA O_2 , respectively. In He- O_2 , the nitrogen elimination was greatly reduced as shown in Figure 2. The values obtained during the first eight hours must be considered as part of the washout process of nitrogen, and they correspond with those previously published for shorter time periods of O_2 or He breathing^{2,13,27}. During the subsequent 12 hours, the level of nitrogen excretion remained fairly constant, averaging about 0.5 ml/min (Figure 2). The diffusion from the ambient air contributed, therefore, about 95% to the nitrogen excretion via the lungs under ambient conditions. The value of 0.5 ml/min is in close agreement with data reported by Herron, Saltzman, Hills and Kylstra¹² who found after 13 hours of exposure to a helium-oxygen atmosphere a nitrogen excretion of between 0.6-0.8 ml/min.

If one calculates the nitrogen excretion for a 24-hour period based on a nitrogen excretion of 0.5 ml, the daily nitrogen elimination via the lungs amounts to 0.86 g/day which corresponds closely with the frequently found

deficit between nitrogen uptake in food and nitrogen elimination through the urine and faeces of approximately one g per day. These observations were made in long-term (156-220 days) nitrogen balance studies in 23 human subjects, who did not gain weight¹⁹.

In the short-term bag experiment, air was the breathing gas. Therefore, a nitrogen gradient from the alveoli to the blood and the skin had to develop in contrast to the 24-hour helium experiments in the chamber, where inhaled and ambient P_{N_2} were the same resulting in a nitrogen gradient from the tissues into blood and alveoli and from the tissues through the skin. The difference between $V_{N_2} - 79.1 \times V_{AR}$ measured in the bag experiments might not represent a nitrogen elimination through the lung, but rather an uptake of argon, because argon in the bag might have been diluted by water vapour and CO_2 excreted from the skin. Since argon has a higher solubility coefficient than nitrogen, the argon uptake might be relatively higher than the nitrogen elimination.

A competition between the two processes of argon uptake and nitrogen elimination could perhaps explain the large variation observed during the experiment with 2 ATA air (Figure 2).

Following the compression to 2 ATA, there is first a large rise in nitrogen excretion. This can be partially explained by an increase in argon uptake until the tissues are saturated. The subsequent fall of nitrogen excretion occurs during the night hours and appears to represent diurnal changes in pulmonary nitrogen excretion, since

parallel decreases also occur during the same time in the experiment with 1 ATA air and one ATA He, perhaps in parallel to the skin perfusion. Moreover, Abernethy et al.¹ observed diurnal changes in urinary nitrogen excretion with a peak during the night hours, showing the opposite trend to the diurnal changes in pulmonary excretion observed in these studies.

The subsequent rise of pulmonary nitrogen excretion in the morning hours in the experiment with 2 ATA to a plateau considerably below the initial values could be interpreted as part of diurnal variation. The lowering of this second increase could be caused by the fact that argon has reached a saturation in the tissue and does not therefore interfere with the nitrogen elimination as measured. The average values of nitrogen excretion obtained after 18-24 hours at different levels of inspired nitrogen pressures (Figure 2) show a nearly linear relationship. At an inspired nitrogen level of 0 ATA it demonstrates an endpoint of 0.5 ml/min of N_2 . This is considered the non-diffusion, or metabolic part of the nitrogen release. In the light of these findings on pulmonary nitrogen excretion, it appears that the blood transport capacity of nitrogen should be examined.

Under normal conditions (0.8 ATA N_2) one liter of blood contains 11.2 ml of nitrogen, based on a solubility coefficient of nitrogen of 0.014. Assuming a cardiac output [minute volume] of 5 liters/min, 56 ml of nitrogen will reach the lungs every minute. A pulmonary nitrogen excretion of 5-10 ml/min would cause a decrease of the partial pressure from 0.72 to 0.65 which is equal

to a decrease from 547 to 494 mm Hg. Such large arterial-venous nitrogen gradients have not yet been measured^{10, 11}. Further investigations of the means of transportation of nitrogen and the transport capacity for nitrogen are planned to clarify this problem.

In the light of these considerations on nitrogen transport of the blood, the recently reported values of Cissik et al⁵ appear questionable. They show nitrogen excretion of between 100-200 ml/min following protein-rich meals. Excretion of such quantities following a protein-rich meal with a nitrogen content of 10 grams would mean that the nitrogen of the total meal would be eliminated via the lungs within 40-80 minutes. The arterio-venous difference would have to be larger than one ATA in this case, if such a quantity of nitrogen had to be transported in physical solution⁹.

Cyclic increases in pulmonary nitrogen excretion were found in all three saturation diving experiments without concomitant changes in the classical respiratory quotient. These findings indicate that, following washout of nitrogen in a helium-oxygen atmosphere at high pressure, delayed excretion of nitrogen occurs, unrelated to carbon dioxide/oxygen exchange. These delayed nitrogen excretions, which varied in time between one and three days might influence decompression events.

It is difficult to interpret these cyclic rises in pulmonary nitrogen elimination. They could be due to release of accumulated nitrogen deriving from the metabolism, or as results of altered metabolic processes. Moreover, insuffi-

cient nitrogen elimination over a period of time, associated with respiratory, and perfusion-ventilation changes, could produce the appearance of larger differences between expired and inspired nitrogen.

In Figure 7, an example of the development of larger differences between expired and inspired nitrogen is presented. This occurred while subjects were breathing oxygen during decompression from an air dive to 198 feet. The oxygen breathing by mask was associated with a dramatic fall of respiration rate and elevated alveolar CO₂ tension. Following a normal nitrogen washout curve in which expired nitrogen decreased within a few minutes to levels between 3-9 mm Hg, sudden increases in the difference between inspired nitrogen (zero) and expired nitrogen (70 mm Hg) occurred at the same time as the diver experienced skin bends. During the two subsequent periods of oxygen breathing, the same phenomenon was observed. During the period of one hour and 40 minutes while the diver experienced skin bends, the concentration of exhaled nitrogen was increased, a condition which indicates that the development of bends in this case was associated with an inability to eliminate nitrogen in sufficient quantities.

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<p>The contribution of cutaneous diffusion of atmospheric nitrogen to pulmonary nitrogen elimination was determined by mass spectrometric analysis. In short-term experiments, subjects were enclosed in gas-tight bags containing helium, O₂, N₂ or air while breathing room air. Moreover, 24-hour studies of nitrogen elimination were carried out in a pressure chamber in which the ambient gas composition as well as the total pressure was varied. A linear relationship between ambient PN₂ and nitrogen elimination through the lungs was established. At zero PN₂ ambient nitrogen elimination was present after 18 hours and amounted to 0.5 ml/min. This is considered the metabolic component of gaseous nitrogen excretion. Although this amount appears very small, it can account for the frequently found deficit between nitrogen intake in food and nitrogen elimination via urine and faeces. Mass spectrometric analysis of ambient and expired air samples collected during three saturation-excursion diving experiments showed in all seven subjects cyclic variations in the ratio of expired/inspired nitrogen while the simultaneously measured respiratory quotient remained constant. Whether these delayed nitrogen excretions are due to release of nitrogen from pools in poorly perfused tissues or altered metabolic processes cannot be stated at this time.</p>			

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