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Nitrogen elimination during steady-state hyperbaric exposures

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Vorosmarti, J., Jr., E. E. P. Barnard, J. Williams, and R. de G. Hanson. 1978. Nitrogen elimination during steady-state hyperbaric exposures. Undersea Biomed. Res. 5(3):243–252.—Nitrogen elimination was measured in six divers during steady-state exposures in an oxygen-nitrogen atmosphere at 1, 2, and 3 ATA using both oxy-helium and pure O_2 as washout gases. This was accomplished by using mass spectrometry to measure the expired N_2 concentration breath-by-breath over periods of 120 min in all experimental conditions except for O_2 breathing at 3 ATA, which was limited to 30-min periods. In all cases the area under the elimination curve increased with pressure. Total area under the curve was also greater when breathing O_2 than when breathing oxy-helium, but this difference decreased with depth and washout time. Nitrogen elimination on a semilogarithmic plot falls rapidly during the first four minutes and then shows a slow linear fall for the remainder of the measurement period. Effective elimination of nitrogen decreased with depth and oxygen was more effective than oxy-helium in washing out nitrogen at all depths studied. Possible causes of the different variations noted in the washout curves during the experiment are discussed.

inert gas elimination	oxygen
washout curves	oxygen-helium
hyperbaric	mass spectrometry

Returning safely to one atmosphere after exposure for some time to increased pressure has been a major problem in diving since the 19th century.

Several theories of inert gas exchange have been developed and used to compute diving schedules, but unfortunately such calculations are so unreliable that safe diving depends almost entirely upon empirical data unrelated to gas exchange data.

Measurements of the gas taken up by the body at raised pressure have been made in man for nitrogen (Campbell and Hill 1931; Behnke and Willmon 1941; Willmon and Behnke 1941; Kindwall 1975), helium (Behnke and Willmon 1941; Krekeler, von Nieding, Muysers, Cabarrou, and Fust 1973; Kindwall 1975), and argon (Krekeler et al. 1973). The usual technique consists of collection and analysis of volumes of gas eliminated during successive time intervals. This method gives an accurate integration of the expired volumes of gas but gives no detailed account of the way in which the concentration of inert gas falls during washout.

Barnard, Hanson, Reid, and Williams (1973) measured expired gas concentration by mass spectrometry at atmospheric pressure, a method which showed the rate at which the concentration of gas fell, breath-by-breath, but which gave no estimate of the total volume eliminated. A similar method was used by Krekeler and co-workers (1973), who studied helium and argon washout 15 min after surfacing from 4-h exposures at pressure.

This study was undertaken to measure nitrogen washout in men at pressure during a steady-state exposure; that is, one in which the partial pressure of inert gas in the body is in equilibrium with the partial pressure of inert gas in the hyperbaric atmosphere. The main purpose of the experiment was to discover if there was any difference in nitrogen washout at depth compared to that at one atmosphere.

METHODS

Six subjects were used in this study; all were qualified divers from the Royal Naval Saturation Diving Team at *HMS VERNON* experienced in physiological testing, both at atmospheric and raised pressures. After initial experiments in which washout was performed using pure oxygen or a 20-80% oxy-helium mixture at atmospheric pressure, washout was performed at 2 and 3 ATA (Table 1). Washout with oxygen at 3 ATA was restricted to 30 min to avoid oxygen poisoning. Chamber atmosphere was oxygen-nitrogen, with the oxygen partial pressure held at 0.22 bar throughout the exposure.

The method of performing these experiments was to compress three divers at a time to 3 ATA and to maintain them at this pressure for at least 24 h. Washouts were performed on each diver using oxygen or oxy-helium (Table 1). The washout was then performed 24 h later using whichever gas had not been used initially (Fig. 1). The divers were then decompressed to 2 ATA and after 24 h at this pressure the experiments were repeated as described above. Decompression to the surface was accomplished the day after all experiments were completed. All washouts for a particular diver were performed at the same time of day to avoid any circadian variability.

Samples were measured with a magnetic mass spectrometer (Model MS 10, Associated Electrical Industries, England). This instrument had a range from mass 2 to mass 200. Within the range 12–40 it was possible to select the peak response for a particular mass and to tune the instrument to record this mass continuously. Nitrogen was measured in these experiments at mass 28. Checks were made before and after each recording to ensure that no drift had occurred from the chosen mass. Base-line drift was checked by an electrical zero at intervals throughout the recording. The MS 10 was easily able to measure the nitrogen contained in

TABLE 1
WASHOUT GAS MIXTURES AND WASHOUT TIMES USED AT 1, 2, AND 3 ATA

Exposure Pressure, O_2/N_2	Washout Gas	Washout Time, min
1 ATA (0.21/0.79)	20% O_2/80% He	120
1 ATA (0.21/0.79)	100% O_2	120
2 ATA (0.22/1.78)	11% O_2/89% He	120
2 ATA (0.22/1.78)	100% O_2	120
3 ATA (0.22/2.78)	7% O_2/93% He	120
3 ATA (0.22/2.78)	100% O_2	30

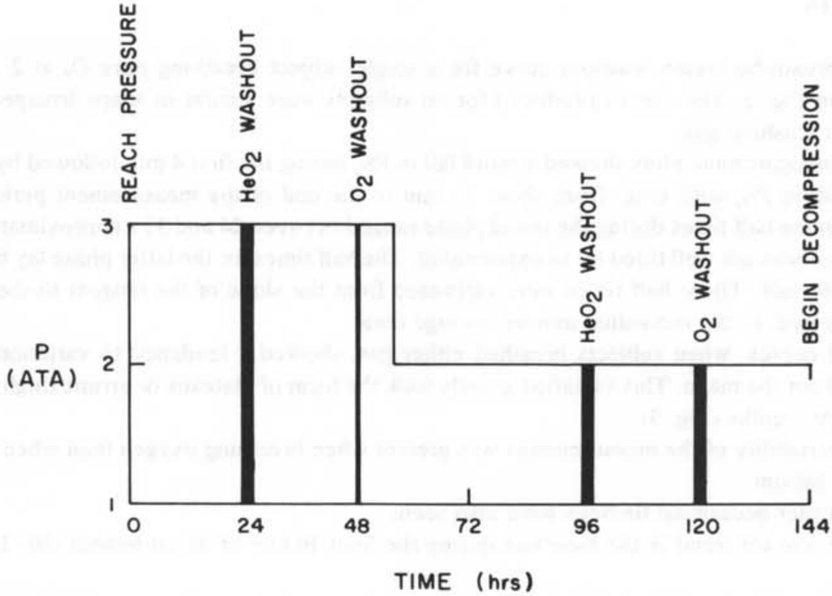

Fig. 1. Diagrammatic representation of experimental protocol for an individual subject.

breathing oxygen (0.39–0.44% N_2) and in oxy-helium mixtures (0.25–0.35% N_2). For any one experiment the inspired nitrogen level was constant in the range given above. The constancy of the inspired nitrogen level could be used to ensure that no leaks occurred or at least to guarantee that they could be individually recognized. Initial calibration involved adjusting the output to an arbitrary level (5000 units) for the ambient P_{N_2} to which the divers were exposed (exposure pressure, Table 1).

Sampling took place via one meter of 0.33-mm i.d. stainless steel capillary tubing sealed at one end into the oronasal mask. The other end penetrated the chamber wall and ended in a T-piece through which excess gas could vent to atmosphere. The sidearm of the T-piece was connected by a short length of capillary tubing. This final capillary was heated to a temperature of 40–60°C to prevent condensation within the sample line. This arrangement facilitated sampling at atmospheric pressure regardless of the pressure within the chamber.

The output from the MS 10 was taken to a Telsec (700 series) potentiometric recorder and recorded on paper by hot stylus.

All measurements were made with the subjects resting comfortably in a semisupine position. To begin an experiment, the subject took a deep breath of the ambient gas and held it until the mask was fitted. He then exhaled and this was taken as the first breath of the measurement period. The subject then continued to breathe for the remainder of the two hours' washout time.

Data were analyzed by measuring the difference between the inspired P_{N_2} and the peak of the expired P_{N_2} for each breath. The resulting washout curve was then plotted for individuals on both linear and semilogarithmic axes, and the same data were also described as minute-average curves for the six subjects and as mean-minute-average curves for each depth. Further analysis involved integrating the mean-minute-average curves with respect to time (Fig. 5) and scaling with respect to depth (Fig. 6). This data-reduction involved using a computer program developed by CI Data Centre of Farnborough, England.

RESULTS

The breath-by-breath washout curve for a single subject breathing pure O_2 at 2 ATA is shown in Fig. 2. The curves produced for all subjects were similar in shape irrespective of depth or washout gas:

1) Semilogarithmic plots showed a rapid fall in P_{N_2} during the first 4 min followed by a slow linear fall in P_{N_2} with time, from about 14 min to the end of the measurement period. The approximate half times during the initial phase ranged between 24 and 31 s approximate, since this phase was not well fitted by an exponential. The half times for the latter phase lay between 62 and 69 min. These half times were estimated from the slope of the tangent to the curve, fitted by eye, to the individual minute-average data.

2) All curves, when subjects breathed either gas, showed a tendency to variation in P_{N_2} levels about the mean. This variation usually took the form of plateaus or erratic (high) values for single breaths (Fig. 3).

The variability of the measurements was greater when breathing oxygen than when breathing oxy-helium.

Two other occasional findings were also seen:

1) An upward trend in the base line during the final 30 min of measurement (90–120 min) (Fig. 3).

2) Spikes of increased P_{N_2} followed by a decay towards the base line over about 2 min (Fig. 4).

To present the results of the experiments in a more familiar fashion the (mean-minute-average) P_{N_2} curves of all subjects were integrated with respect to time. The resultant curves are shown in Fig. 5. Although not quantitative, these curves are analagous to the expired volume curves commonly used to express gas washout. The reasons and assumptions concerning this are discussed below. These curves show that when breathing pure oxygen at 1 and

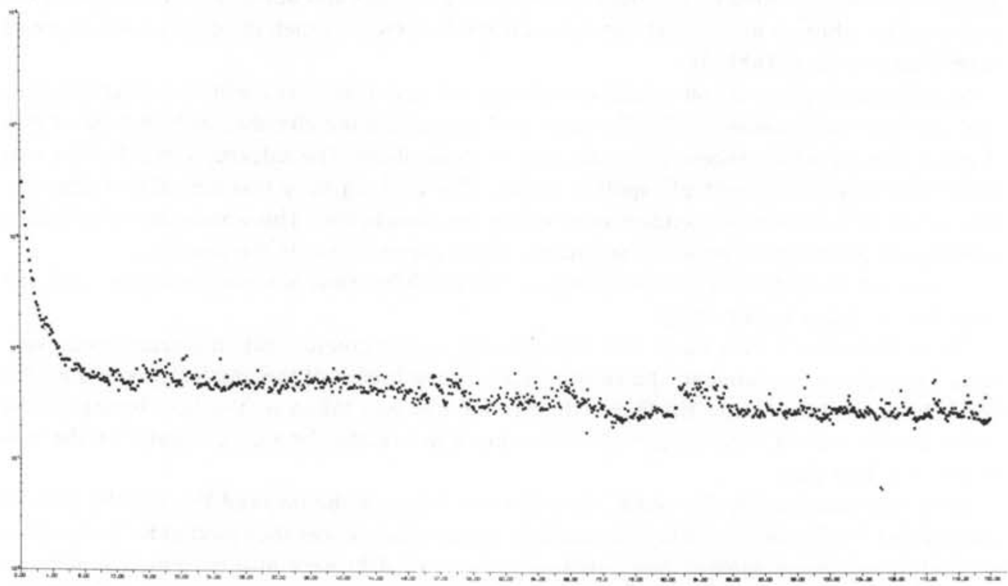

Fig. 2. Semilogarithmic plot of typical individual washout curve showing breath-by-breath fall in expired N_2 with time (*abscissa*, time in min; *ordinate*, arbitrary units of N_2; see RESULTS). This curve was produced while breathing O_2 at 2 ATA.

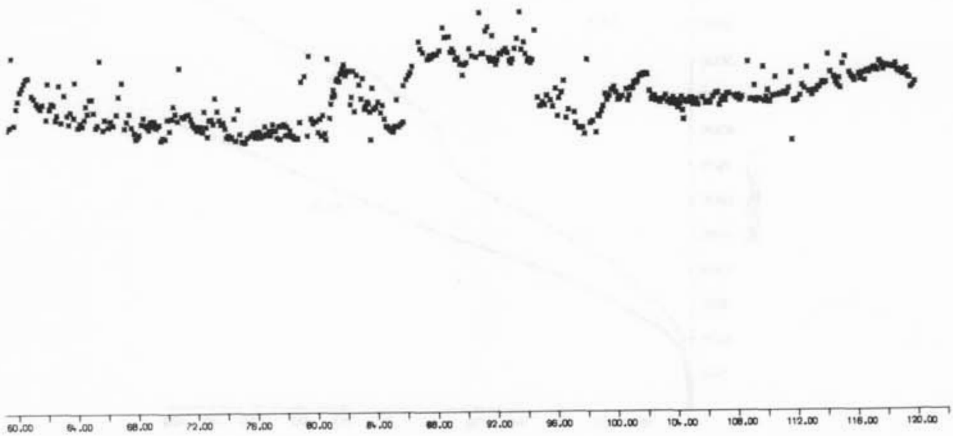

Fig. 3. Portion of semilogarithmic plot of an individual washout curve illustrating irregular peak (82–86 min), plateau (86–98 min), and upward trend of base line during final portion of measurement period. (1 ATA, washout gas 20-80 O_2–He). (Axes same as Fig. 2).

2 ATA, the "volume" of nitrogen washed out is greater than when breathing oxy-helium. At 3 ATA the curves produced during the first 30 min of breathing oxygen or oxy-helium were almost identical.

If the oxy-helium curves in Fig. 5 are compared, it can be seen that the "volume" of nitrogen washed out increases with depth for any time. A comparison of the "volume" eliminated when breathing oxygen shows no such change with pressure. Although the "volume" of nitrogen eliminated when breathing oxygen at 1 and 2 ATA was greater than that eliminated breathing oxy-helium, this difference decreased with depth so that at 3 ATA there was no obvious difference between the effects of the two washout gases.

The comparison of "volume" just discussed takes no account of the differences in the quantity of gas dissolved at different depths. Figure 6 shows the data of Fig. 5 scaled by the method discussed below. This seems to show that oxygen at 1 ATA is the most effective washout gas, but its effectiveness becomes less at increasing pressure. Oxy-helium mixtures are less effective than oxygen at 1 and 2 ATA but of comparable effectiveness at 3 ATA.

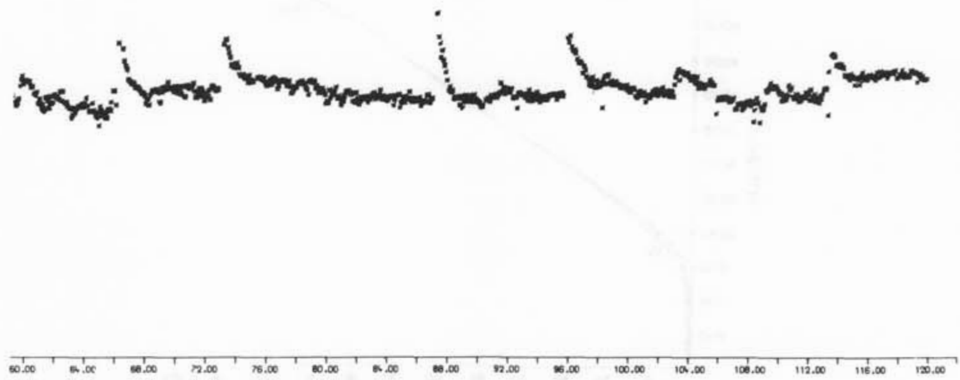

Fig. 4. Portion of semilogarithmic plot of an individual washout curve illustrating sudden spikes of P_{N_2} followed by regular decay to base line (1 ATA, washout gas 20-80 O_2–He). (Axes same as Fig. 2).

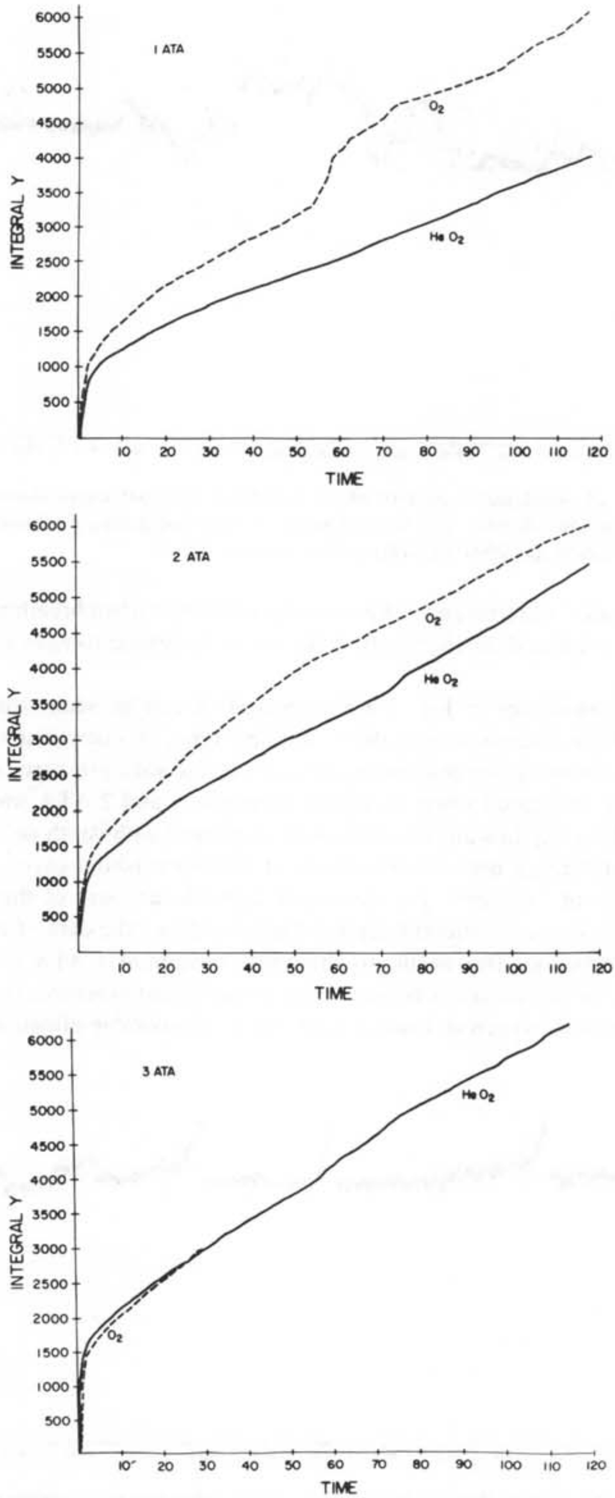

Fig. 5. Comparison of areas under average washout curves while breathing O_2 or O_2–He at 1, 2, and 3 ATA.

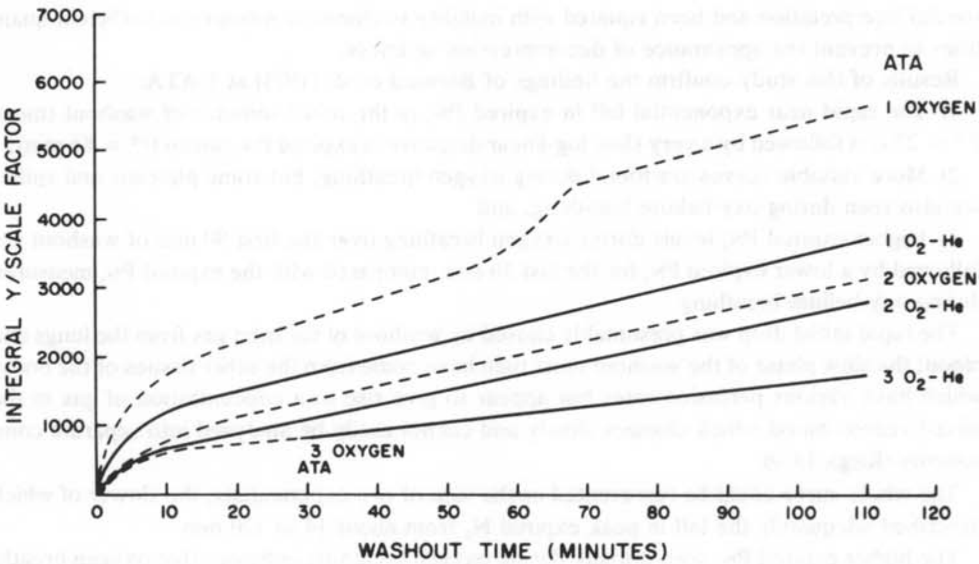

Fig. 6. Diagrammatic comparison of effectiveness of O_2 and oxy-helium mixtures in effecting N_2 elimination at 1, 2, and 3 ATA.

DISCUSSION

As was observed in the introduction to this paper, methods of measuring gas washout which rely upon the collection of expired gas give no detailed information concerning the way in which the expired gas levels fall with time, since mechanical integration of volumes over several breaths cannot give such detailed information as individual measurements. A further disadvantage is that because of the large volume of gas in the lungs relative to that dissolved in the tissues, it is usual to ignore the first few breaths, which are regarded as lung rinsing time. The effect of this practical necessity is to suppress the zero and to begin plotting washout curves at some unknown but relatively consistent starting point. Such a method tends to underestimate the contribution of faster components, including the blood itself, which on a semilogarithmic analysis tends to distort the half times obtained from the remainder of the curve. Results of analysis therefore become dependent upon the details of the method of measurement.

The present method of observing the fall in P_{N_2} breath-by-breath, by comparison, gives no accurate measurement of the volume of inert gas eliminated, but it does allow one to compare two curves if the following assumptions are made: there is a constant relationship between the mean and the peak values of expired nitrogen fraction and the area beneath the curve is therefore proportional to the volume eliminated.

When using volumetric data one must be aware that small fluctuations in expired volumes will not be seen, since they represent variations in an already small addition to a very large volume. The qualitative features of the breath-by-breath curves remarked upon by Barnard et al. (1973) and also described in this paper (plateaus, rises, sudden peaks) are not seen when the volumetric technique is used or when concentration curves are integrated. These are of possible importance in the interpretation of such washout curves, since similar findings during decompression (Muysers, Smidt, von Nieding, Krekeler, and Schaefer 1974) and associated with "skin bends" (cutaneous manifestations of decompression sickness) have been given a special interpretation and been equated with inability to eliminate nitrogen in sufficient quantities to prevent the appearance of decompression sickness.

Results of this study confirm the findings of Barnard et al. (1973) at 1 ATA:

1) The rapid near exponential fall in expired P_{N_2} in the initial minutes of washout (mean $t^{1/2} = 27$ s) is followed by a very slow log-linear decrease in expired P_{N_2} (mean $t^{1/2} = 66$ min);

2) More variable curves are found during oxygen breathing, but some plateaus and spikes are also seen during oxy-helium breathing; and

3) Higher expired P_{N_2} levels during oxygen breathing over the first 90 min of washout are followed by a lower expired P_{N_2} for the last 30 min, compared with the expired P_{N_2} measured during oxy-helium breathing.

The rapid initial drop was presumably caused by washout of the inert gas from the lungs and blood; the slow phase of the washout must then have come from the other tissues of the body, which have various perfusion rates but appear to give rise to a concentration of gas in the mixed venous blood which changes slowly and cannot easily be analyzed into separate components (Riggs 1970).

The whole curve could be represented as the sum of two exponentials, the slower of which described adequately the fall in peak expired N_2 from about 14 to 120 min.

The higher expired P_{N_2} seen initially during oxygen breathing indicates that oxygen breathing increased the washout of nitrogen. However, the difference in the effectiveness of oxygen breathing compared to oxy-helium breathing in washing out inert gas became less with increasing depth and almost disappeared at 3 ATA, the deepest depth at which this comparison has been made.

The various deviations from a smooth base line, no matter which gas is breathed, may have been caused by normal physiologic changes in circulation or changing ventilatory distribution in the lungs. That these variations appeared more often during oxygen breathing accords with the hypothesis that oxygen exaggerates these physiologic changes. An alternative explanation, however, is that they were artifacts associated with the effect of high oxygen levels on the mass spectrometer filament. The sharp, irregular variations which occurred with either washout gas may have been caused by sudden physiologic changes, enteric gas, or leaks into the sampling system from around the mask. The sudden sharp peaks with a smooth fall toward the base line over a period of several minutes could have been caused by any of these factors, but they are important because had these exposures been done during or immediately after decompression, it would be logical to impute these peaks to a sudden delivery of increased amounts of gas to the lungs in the form of a shower of bubbles. In the case of steady-state studies, however, this is not very likely, and another reason must be found to explain the peaks. The occasional rise in the base line during the last 30 min of the washout period is interesting, in that it may be due to diffusion of nitrogen through the skin, reflected as an increasing concentration in the blood. Although these changes all seemed obvious on the records, it must be remembered that they were extremely small; the concentration of nitrogen during the slow phase was less than 0.05 ATA, and for much of the measurement period it was below 0.01 ATA.

Since the volume of gas dissolved in the body is greater at raised pressure, the volume eliminated also increases with depth. To compare the amounts eliminated at different depths it is necessary to scale them. The most satisfactory way to do this is to express all volumes eliminated as a function of the total volume dissolved. Since the total amount dissolved cannot be measured in a 2-h study, one has to approximate this volume in a steady state by using certain assumptions. These are that the alveolar carbon dioxide and water vapor partial pressures remain unaltered with depth, that the inspired nitrogen and oxygen pressures are reduced by the presence of carbon dioxide and water vapor, and that the volume of gas dissolved is proportional to the "corrected" partial pressure of inert gas. The ratios of inert gas dissolved at 1, 2, and 3 ATA for the stated conditions are 1, 2.2, and 3.4, respectively.

It can be seen that effective elimination of nitrogen decreased with depth and that oxygen was more effective than oxy-helium at 1 and 2 ATA (Fig. 6). Not only was elimination reduced in the presence of helium but it was also reduced when breathing oxygen at pressure. Without a measure of variability with which to assess the apparent difference between oxygen and oxy-helium, speculation must be somewhat limited. No independent measurements of carbon monoxide were made; the extent therefore to which the "volume" eliminated might be enhanced by the addition of carbon monoxide (measured at mass 28) liberated from the hemoglobin of blood cannot be judged, but is probably too small to account for the differences. If the differences are real, both the difference at 1 ATA and the lack of difference at 3 ATA must be accounted for; between them these findings suggest that more than one mechanism may be involved in producing the differences reported.

This study was carried out at the Royal Naval Physiological Laboratory, Alverstoke, England and was supported in part by the Naval Medical Research and Development Command, Research Task No. M0099.PN001.1180. The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large. Capt. Vorosmarti and Surg. Capt. Barnard are presently at the Naval Medical Research Institute, Bethesda, MD 20014.—*Manuscript received for publication June 1977; revision received January 1978.*

Vorosmarti, J., Jr., E. E. P. Barnard, J. Williams, and R. de G. Hanson. 1978. Elimination de l'azote au cours d'expositions continues à l'hyperbarie. Undersea Biomed. Res. 5(3):243–252.—Nous avons mesure l'élimination de l'azote chez 6 plongeurs au cours d'expositions continues à une atmosphère oxygène-azote à 1, 2, et 3 ATA. Les gaz d'élimination (washout gases) étaient ou un mélange oxygène-hélium, ou l'oxygène pur. Nous avons utilisé la spectrométrie de masse pour déterminer la concentration en N_2 de chaque expiration pendant 120 min pour chaque ensemble de conditions expérimentales, sauf O_2 à 3 ATA, où la période d'exposition a été limitée à 30 min. Pour tous les cas, l'aire du surface en dessous de la courbe d'élimination a augmenté en fonction de la pression. L'aire totale en dessous de la courbe était aussi plus grande quand les sujets respiraient de l'oxygène, que quand ils respiraient un mélange oxygène-hélium; cette différence a diminué en fonction de la profondeur et du temps d'élimination. En diagramme semilogarithmique l'élimination de l'azote tombe rapidement pendant les premiers 4 min, et présente ensuite une chute linéaire pendant le reste de la période de contrôle. L'efficacité de l'élimination de l'azote a diminué en fonction de la profondeur, et l'oxygène était plus efficace que le mélange oxygène-hélium comme gaz d'élimination à toutes les profondeurs étudiées. Les causes éventuelles des variations des courbes d'élimination au cours de l'expérience sont discutées.

élimination de gaz inertes
courbes d'élimination
hyperbare
oxygène
mélange oxygène-hélium
spectrométrie de masse

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