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Protective effect of oxygen and heliox breathing during development of spinal decompression sickness

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Hyldegaard O, Møller M, Madsen J. Protective effect of oxygen and heliox breathing during development of spinal decompression sickness. Undersea & Hyperbaric Med 1994; 21(2):115–128.—A rat model of spinal decompression sickness (DCS) allows study of spinal cord function for at least 3 h after decompression to 1 atm abs (101 kPa) after an exposure to air at 3.8 atm abs (385 kPa) for 1 h. During these 3 h, spinal evoked potentials (SEPs) elicited by peroneal nerve stimulation may be reduced or disappear, and histologic lesions in the spinal cord are observed. Three groups of animals were given either air, oxygen, or heliox (80/20) to breathe at 1 atm abs for 3 h after decompression. Both oxygen and heliox breathing impeded the development of DCS significantly as judged by the mortality of the animals and disappearance of the SEPs. The effect of heliox seemed to be superior to that of oxygen. The latency time from stimulation to the first SEP peak increased significantly during both air and oxygen breathing, whereas no significant increase was seen during heliox breathing. Histologic examination of the spinal cords of animals breathing air, oxygen, or heliox (80/20) showed focal lesions in the white and gray matter. In the white matter, degenerated myelin sheaths as well as expanded extracellular spaces compatible with bubble formation were seen. In the gray matter, perikaryal degeneration was observed. The extracellular space in the white matter was increased in all decompressed animals compared with controls ($P < 0.01$). Oxygen and heliox breathing caused a smaller increase in extracellular space as compared with air-breathing animals ($P < 0.05$) and ($0.10 > P > 0.05$), respectively. It is concluded that breathing of oxygen or heliox (80/20) at 1 atm abs has a preventive effect on the development of DCS when compared with air breathing; the effect of heliox seems to be superior to that of oxygen.

evoked potentials, histology, rat, myelin

Recompression with heliox has proved beneficial in spinal cord decompression sickness (DCS) after air dives in a number of cases that did not respond satisfactorily to recompression with oxygen breathing (1–4). Minute air bubbles injected into the posterior funiculus of the spinal cord of decompressed rats will grow during air breathing at 1 atm abs, but will shrink and disappear during heliox breathing (5). During oxygen breathing they will initially grow and then shrink and disappear (5).

Similar effects can be seen on bubbles in adipose tissue (6). The aim of the present work was to study in the rat spinal conductive function by means of spinal evoked potentials (SEPs) as well as changes in morphologic parameters of the spinal cord during the development of DCS. Further, we studied the influence of air, heliox, and oxygen breathing on the spinal conductive function and morphologic parameters.

METHODS

General

The experimental protocol is summarized in Fig. 1. Female rats weighing 300–350 g were anesthetized with sodium thiomebumal i.p. (0.1 g/kg). A cannula was inserted in the trachea. To reduce electric noise from muscle activity, the rats were paralyzed with pancuronium bromide (Pavulon, 2.0 mg/kg) by i.m. injection and ventilated artificially by a rat respirator maintaining a normal arterial CO_2 tension measured with a Radiometer ABL 30 blood gas analyzer. The arterial mean blood pressure was registered continuously during the experiments through a catheter inserted in a carotid artery. To keep the catheter open, isotonic saline was continuously infused at a rate of 1 ml/h. A thermocouple was placed in the vagina for continuous temperature registration. The electrocardiogram (ECG) was monitored continuously. The rat was fixed in a stereotactic device in the ventral position. Ascending spinal cord function was examined by recording SEPs at the cervical level during stimulation of the peroneal nerves.

The rats were compressed in air to 3.8 atm abs (385 kPa) for 1 h followed by decompression over 7.5 min in three stages. Body temperature was maintained constant by suitable heating of the pressure chamber. After decompression the animal was removed from the chamber and placed under a heating lamp controlled by the vaginal thermometer to maintain constant body temperature. Immediately after

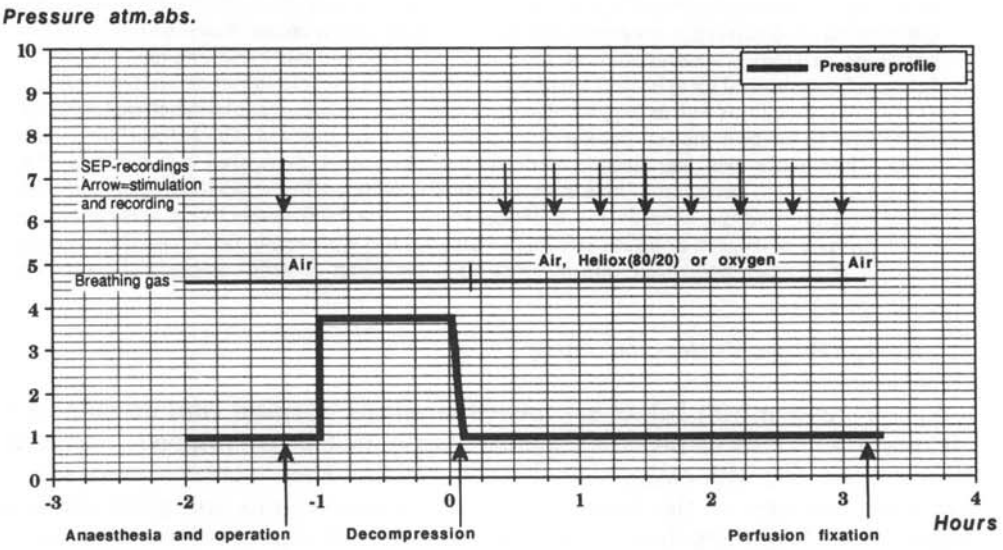

FIG. 1—Experimental protocol.

decompression the breathing gas would be either air, heliox (80/20), or oxygen. Stimulation of the peroneal nerves and SEP recordings were started 25–30 min after decompression. From then on stimulations were done at about 20-min intervals. Three hours after decompression, the rats were disconnected from the SEP registration and fixed in vivo by perfusion with either 4% paraformaldehyde or 4% glutaraldehyde in 0.1 *M* phosphate buffer (pH 7.6). The time interval from disconnecting the animal from the SEP instrumentation to the initiation of perfusion fixation was approximately 10–15 min, during which period all animals were ventilated with air. For histologic examination, two air-breathing animals were fixed 1 h and two others 2 h after decompression.

In an attempt to increase the volume of bubbles (5–8) and thus visualize a possible separated gas phase in the spinal cord, two air-breathing animals were shifted to a breathing mixture of N_2O–O_2 (80/20) when their SEPs began to deteriorate.

Recording of spinal evoked potentials

Through a dorsal midline incision, the cervical vertebral column was exposed and two silver electrodes placed on the dura mater through drillholes in the 2d and 5th cervical vertebra. Vents were left open to the vertebral canal by cutting openings in the ligamentum flavum adjacent to the 2d and 5th cervical vertebra to allow the escape of gas accidentally introduced. A polyethylene tube was placed in the operation field as a drain, and the incision closed. Both peroneal nerves were exposed and placed on stimulating electrodes, and the incisions closed. SEPs were registered from the cervical electrodes (i.e., over the surface of the dorsal funiculus) through a Nicolet signal averaging system during alternate stimulation of the right and left peroneal nerves. The averaging was done over 512 consecutive stimulations each time. The nerves were stimulated with a Grass model S4 stimulator with a stimulus duration of 0.1 ms. Stimulation intensity was chosen to give maximal amplitude of the evoked potential. The averaged curves where drawn with a x,y-printer (Fig.2). To reduce electric noise from the heart, the stimulator was triggered by the R-peak

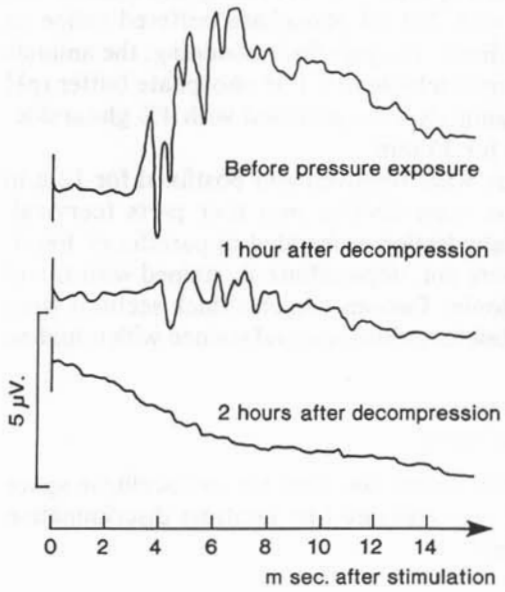

FIG. 2—Spinal evoked potentials recorded from cervical spinal medulla after maximal stimulation of peroneal nerve in an air breathing animal before pressure exposure and 1 and 2 h after decompression.

of the ECG with a delay to place the stimulus and SEP in the isolectric phase of the ECG. The whole animal set-up was placed in a Faraday cage to prevent noise from surrounding alternating current sources.

In a control experiment, stimulations and recordings were done in both directions (i.e., peripheral stimulation with central recording and central stimulation with peripheral recording at a frequency of 1.0/s) to characterize the neuronal path involved. It was found that action potentials traveled in both directions with the same latency time = 3.7 ms (i.e., delay from stimulation to the peak of the first wave), corresponding to a conduction velocity of 40.5 m/s. This is similar to the nerve conduction velocity measured with rat tibial nerve stimulation by Gross-Sampson et al. (9, 10) and does not allow for a synaptic delay. In the 74 nerves that were stimulated (i.e., 37 animals each with stimulations of the two peroneal nerves) the mean latency time before pressure exposure was 3.26 ms (SEM ± 0.030).

Increased stimulation frequency (25.0/s) caused no reduction of the peak amplitude of the first wave in contrast to the polysynaptic waves observed later in the recorded SEP. These findings further indicate that the peak of the first wave is caused by direct ascending primary neuron fibers.

Evaluation of spinal evoked potentials

Since the baselines usually were unsteady, an exact measurement of the amplitudes could not be made. Instead they were characterized as unaffected, reduced, or disappeared by comparison with the preexposure curve. Latency time was measured as the time from stimulation to the peak of the first wave. Analysis of latency times were only done on the 37 animals that were killed 3 h after decompression.

Histologic examination

Control animals (n = 9, 5 paraffin embedded and 4 plastic embedded) as well as pressure-exposed animals were fixed by vascular perfusion through the left ventricle of the heart with a venous opening in the right atrium. Preceding the fixative the vascular system was flushed for 2 min with 200 ml phosphate buffered saline to which heparin had been added (15,000 IU/liter). For paraffin embedding, the animals were perfused for 15 min with 4% paraformaldehyde in 0.1 *M* phosphate buffer (pH 7.6). For plastic (Epon) embedding, the animals were perfused with 4% glutaraldehyde in 0.1 *M* phosphate buffer (pH 7.6) for 15 min.

After perfusion fixation the spinal cords were removed and postfixed for 12 h in the same fixative. The spinal cords were then divided into four parts (cervical, thoracic, lumbar, and sacral) and after dehydration embedded in paraffin or Epon. Ten-micrometer-thick paraffin sections were cut, deparaffinized, stained with Luxol fast blue (11), and counterstained with thionin. Two-micrometer-thick sections were cut from the Epon-embedded tissues in a Reichert ultratome and stained with toluidine blue (12).

Morphologic quantitation of extracellular space

In the 10-μm-thick sections stained with Luxol fast blue the extracellular space (the unstained area) in the white matter was measured by contrast discrimination using an IBAS 2000 image analysis system.

The measurements were done in two areas (each 240 × 240 μm) in each of the posterior, lateral, and anterior columns. The measurements were performed on horizontal sections of the spinal cord from the cervical, thoracic, lumbar, and sacral parts of the cord, eight sections from each part (Fig. 3).

In the 2-μm-thick, toluidine blue-stained, Epon-embedded sections the extent of the lesions in both the gray and white matter was clearly visible (Figs. 4 and 5). Therefore, the outline of the lesions in both the gray and white matter was drawn in a camera lucida, transferred via a video camera to a QuickCapture data translation frame grabber card on a Macintosh Quadra 700 computer, and the area of the lesion (in μm^2) determined and expressed as percent of total section area.

Statistics

Spinal evoked potentials in the different treatment groups were compared with 4-fold χ^2 tests (13). Student's *t* test (paired) was done to see whether the mean change in latency time was different from a mean of zero in those animals where the SEPs had not disappeared completely. To examine whether the difference between two mean values of lesion size (in Epon- and paraffin-embedded sections) was different

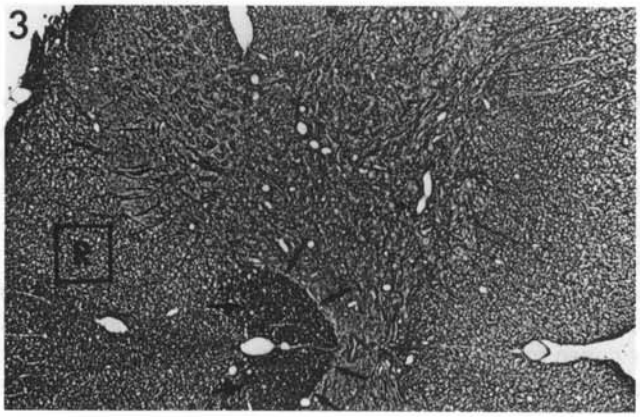

FIG. 3—Ten-micrometer-thick Luxol fast blue stained section of the spinal cord on which contrast computer analysis of the extracellular space was performed. *Arrows* show a normal area in the posterior funiculus. *Rectangle* (*R*) shows the size of the area (240 × 240 μm) of which two were measured in each funiculus.

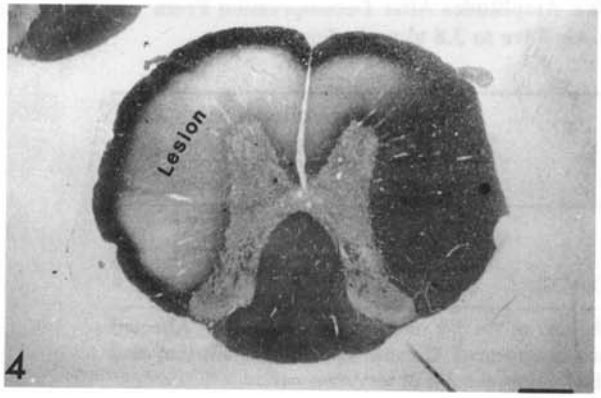

FIG. 4—Two-micrometer-thick plastic embedded section showing DCS lesion in the ventral and lateral funiculi thoracic level. Toluidine blue staining. *Bar* = 400 μm.

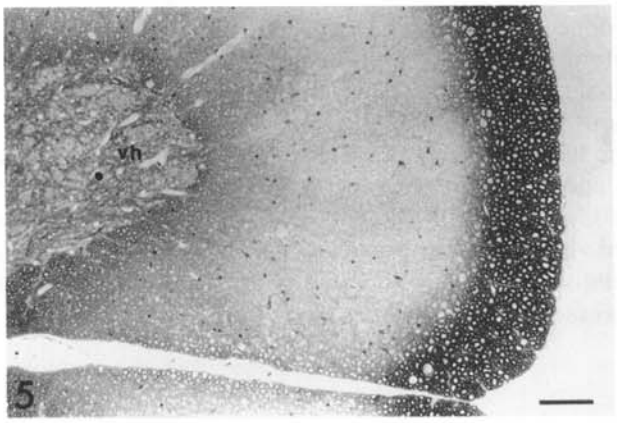

FIG. 5—Higher magnification of Fig. 4 showing the lesion in the ventral funiculus of the spinal cord. *vh* = ventral horn. Toluidine blue staining. *Bar* = 100 μm.

from zero, analysis of variance (ANOVA) followed by the Newmann-Keuls procedure for multiple comparison of several groups was performed on the differences between mean values in the different treatment groups and controls (13–16).

RESULTS

General condition of decompressed rats

The animals were observed for up to 3 h post-decompression. Eleven of 23 air-breathing animals died of decompression sickness during the observation period. Two of 14 oxygen-breathing and 3 of 16 animals breathing heliox died before completion of the observation period. In the animals that died, bradycardia and a pronounced fall in blood pressure preceded death, and at autopsies, performed immediately postmortem, the abdominal veins contained ample bubbles. However, one heliox-breathing animal died spontaneously 2 h 45 min after decompression with no reduction in SEP amplitude before death. On autopsy no bubbles were seen in the abdominal or thoracic veins and no other cause for death could be detected. This animal is not included in Table 1, but figures as dead in Table 2. When the abdominal and thoracic

Table 1: Effect of Air, Oxygen, and Heliox Breathing on Changes in SEP Amplitudes After Decompression From an Air Dive to 3.8 atm abs for 1 h

	Number of Animals With Spinal Evoked Potential Amplitude	
Breathing Gas	Unaffected[a]	Affected[b]
Air, n = 27	0	27
Oxygen, n = 14	1	13
Heliox, n = 15 (80/20)	7	8

[a]Unaffected at the end of the 3-h observation period. [b]Affected includes reduced and disappeared. Column includes animals that died of DCS or were killed during the 3-h observation period.

Table 2: Effect of Air, Oxygen, and Heliox Breathing On the Occurrence of DCS Presenting as Death or SEP Changes 3 h After Decompression From an Air Dive to 3.8 atm abs for 1 h

Breathing Gas	Spinal Evoked Potential Amplitude After 3 h			Dead From DCS
	Unaffected[a]	Reduced[b]	Disappeared[c]	
Air, $n = 23$	0	3	9	11
Oxygen (100%) $n = 14$	1	6	5	2
Heliox (80/20) $n = 16$	7	5	1	3

[a]Number of animals with unaffected SEPs; [b]number of animals with SEPs reduced on one or both, but present on both sides; [c]number of animals with SEPs disappeared on one or both sides.

cavities of the 37 rats that lived through the 3-h observation period were opened for perfusion fixation, no bubbles were visible in the veins. In some rats an occasional extravascular bubble could be seen in the adipose tissue.

Mean arterial blood pressures (MAP)

Before and during the 1-h pressure exposure the MAP was in the range of 120–180 mmHg with 140–160 mmHg as the most frequent interval (average 143 mmHg). During the decompression phase a short transient pressure drop to 80–100 mmHg was seen. In the air-breathing animals MAP fell to a post-decompression level of about 80–110 mmHg (average 103 mmHg) with a decreasing tendency in the post-decompression period. During oxygen breathing the pressure fell only slightly to 130–160 mmHg (average 140 mmHg). During heliox breathing the pressure fell to 120-140 mmHg (average 125 mmHg).

Spinal evoked potentials and decompression sickness

Fifty seven rats were decompressed and subjected to either air, oxygen, or heliox (80/20) breathing. Of these, 16 died within the 3-h observation period. Five of them died before nerve stimulation and SEP recording could be resumed; four animals were killed 1–2 h after decompression and after SEP recording. To obtain maximum information the observations were analyzed in two rounds.

Spinal evoked potential changes

This analysis (Table 1) takes in all animals from which SEPs were obtained after decompression including those who died from DCS or were killed before the end of the 3-h observation period if the SEPs were affected. SEPs were only pronounced unaffected at the end of the 3-h observation period (Table 1). Chi^2 test shows that heliox breathing impeded the development of spinal DCS as compared to air breathing when unaffected SEPs are compared to affected SEPs ($P < 0.001$). The effect of oxygen breathing as compared to air breathing was not significant ($P > 0.1$). The

effect of heliox breathing was significantly better than that of oxygen breathing ($P < 0.05$).

Decompression sickness defined by SEP changes or death

This analysis (Table 2) comprises all animals that died of DCS after decompression whether SEPs were obtained or not. Animals that died are listed as such without regard to their SEP changes. The four animals that were killed 1 and 2 h after decompression are not included because they are not comparable with the others (which were evaluated after 3 h) in this grading of DCS. Table 2 shows the results from animals given the three breathing gas mixtures after decompression divided into four groups: a) those whose SEP amplitudes were unaffected on both sides; b) those in which the SEP amplitude on one or both sides was reduced but had not disappeared; c) those in which the SEPs on one or both sides disappeared; and d) those that died from DCS during the 3-h observation period. Chi^2 tests show that heliox breathing impeded the development of DCS as compared to air breathing, both when the number of unaffected animals is compared with animals with affected SEPs + dead animals ($P < 0.02$) and when animals with unaffected + animals with reduced SEPs are compared with animals with disappeared SEPs + animals that died ($P < 0.001$).

The impeding effect of oxygen as compared to air breathing was significant when unaffected animals + animals with reduced SEPs were compared with animals with disappeared SEPs + the animals that died ($P < 0.02$).

When the heliox-breathing animal that died without bubbles or SEP changes is included as dead from DCS, the difference between the effect of heliox breathing as compared to oxygen breathing is not quite significant at the 0.05 level when the number of unaffected animals are compared with animals with affected SEPs + dead animals ($\chi^2 = 3.42$); ($0.1 < P > 0.05$). However, if this animal is omitted from the analysis, the effect of heliox breathing is significantly better than that of oxygen when animals with unaffected SEPs are compared with animals with affected SEPs + the animals that died ($P < 0.05$).

During air breathing the SEPs were affected on both sides in all 12 surviving animals. SEPs were affected bilaterally in 6 of 12 and 2 of 13 animals breathing oxygen and heliox, respectively. Both oxygen and heliox prevented bilateral affection significantly in comparison with air ($P < 0.05$ and $P < 0.001$, respectively). There was no significant difference between the effects of oxygen and heliox breathing.

Latency time from stimulation to first SEP wave

The latency period, measured from stimulation to the peak of the first SEP wave, increased from 3.35 ms (SEM ± 0.092) to 3.78 ms (SEM ± 0.105) ($P = 0.002$) in the air-breathing animals in which the SEP amplitude had not disappeared completely. In oxygen-breathing animals the latency time increased from 3.18 ms (SEM ± 0.065) to 3.33 ms (SEM ± 0.055) ($P = 0.005$). During heliox breathing the latency time did not increase significantly (from 3.25 ms SEM ± 0.039 to 3.28 ms SEM ± 0.053 ($P = 0.454$).

Timing of changes registered in SEPs

In experiments in which the SEP would be reduced or disappear, a reduction could be observed from the beginning of the post-decompression observation period, i.e., 15–30 min after decompression.

Histologic examinations of spinal cord lesions

Ten-micrometer-thick, Luxol fast blue-stained sections

The Luxol fast blue-stained horizontal sections of the spinal cord (Fig.3), exhibited degenerated myelinated fibers in the white matter and an expanded extracellular space. The extracellular space was measured by automated computerized contrast analysis in the white matter. In control animals the extracellular space was (averaged from all sections of the cord) 12.20% ($n = 5$) (SEM $\pm$ 0.662). After decompression and air breathing, this fraction was considerably increased to 23.19% ($n = 3$) (SEM $\pm$ 1.584). The increase was smaller if the animal breathed heliox 18.99% ($n = 3$) (SEM $\pm$ 1.053) or oxygen 17.45% ($n = 3$) (SEM $\pm$ 1.032). Multiple comparison between the groups was performed and showed significant difference between the three treated groups after decompression as compared to undived controls ($P < 0.01$). Oxygen breathing resulted in a significantly smaller increase in extracellular space than air breathing ($P > 0.05$). The effect of heliox (80/20) breathing as compared to air breathing was not significant at the $P = 0.05$ level ($P < 0.10$). There was no significant difference between heliox and oxygen breathing ($P > 0.10$).

Two-micrometer-thick Epon sections

Horizontal sections of the spinal cord showed focal lesions in both the white and gray matter. The lesions were characterized by degenerated, compressed axons with disrupted and weakly stained myelin sheaths (Figs. 4 and 5). In the gray matter, perikarya with various degrees of degeneration was observed (Fig. 5). Lesions were more extensive in thoracic than in cervical and lumbar sections. The white matter was more affected than the gray. No significant difference in the extent of damage was demonstrated between animals that had breathed air, oxygen, or heliox.

Rats killed 1 and 2 h after decompression

Four rats that were perfusion fixed 1 h (two animals) or 2 h (two animals) after decompression and breathing air in the interval showed lesions as described above. Of the four nerves stimulated in the two rats killed 1 h post-decompression, the corresponding SEPs were reduced in three nerves and disappeared in one nerve. In the rats killed 2 h post-decompression, three SEPs were reduced and one disappeared. No significant difference could be demonstrated between the extent of white matter damage in these rats and those that were killed after 3 h air breathing.

Rats breathing N_2O–O_2

Two rats were shifted from air to breathing N_2O–O_2 after their SEPs began to deteriorate. When bradycardia developed (after 90 and 40 min of N_2O–O_2 breathing,

respectively), they were perfusion fixed with glutaraldehyde. In horizontal sections of the spinal cord of these animals, space occupying lesions were observed, especially in the white matter. The lesions consisted of small "bubbles" in the extracellular space (Fig.6).

Size of spinal white matter lesion, Epon preparations, and SEP response

There was a tendency toward more extensive lesions in animals with serious functional reduction than in those with SEP unchanged. In animals with unchanged SEPs on both sides, the lesions corresponded to 6.80% (SEM ± 1.145). In animals with reduced SEPs on one or both sides, but present on both sides, the figure was 7.40% (SEM ± 2.022); in animals in which SEPs disappeared on one or both sides, it was 12.45% (SEM ± 2.043). Comparisons by simple *t* test show no significant differences between the groups ($P > 0.1$).

DISCUSSION

The present experiments are in agreement with our direct observations of bubble behavior in the spinal white matter (5). Minute air bubbles were injected into spinal white matter in rats decompressed to atmospheric pressure from an air exposure that would not result in manifest DCS. During air breathing such bubbles would grow for 2 h or more after decompression, but they would shrink during the breathing of heliox. This effect was explained by the higher solubility in blood for nitrogen than for helium in the case of perfusion-limited gas exchange, and by the higher product of the diffusion coefficient and lipid solubility for nitrogen than for helium if the gas exchange were limited by extravascular diffusion in a lipid-rich tissue (6, 17). In the experiments reported here, the same mechanism would explain the effect of heliox if free gas phase is present in the spinal white matter. The better effect of heliox than of oxygen breathing is also in accordance with our previous experiments, in which air bubbles injected into spinal white matter grew for 1–2 h during oxygen breathing before shrinking and disappearing (5).

However, it could be argued that the limiting factors of gas exchange are determined not only by the exchange between blood and bubbles but also between bubbles and

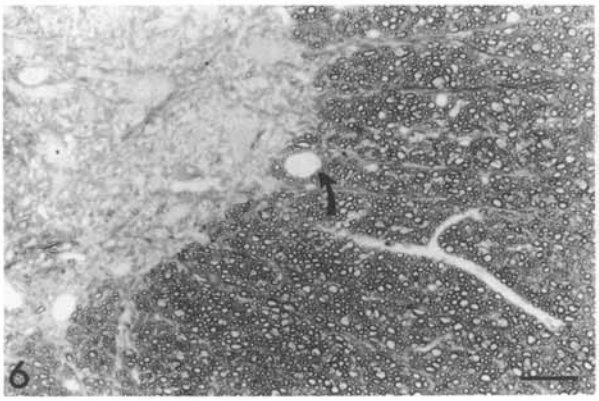

FIG. 6—Photomicrograph of 2-μm-thick, plastic-embedded section showing part of the ventral horn and the anterior funiculus of an animal breathing N_2O-O_2 with small bubble formation (*bent arrow*) in the white matter. Toluidine blue staining. *Bar* = 100 μm.

the surrounding tissue. In our experimental situation a transient increase in tissue-inert gas pressures after a switch of breathing gas from air to heliox (80/20) is possible because the tissue/blood partition coefficient λ is smaller for helium than for nitrogen. This would cause the tissue to saturate with helium faster than it desaturates with nitrogen, leading to a transient increase in inert gas saturation (18–21). This could conceivably result in an increase in bubble volume or a reduced rate of disappearance. Our previous findings of accelerated disappearance of bubbles after switch to heliox (80/20) breathing as well as our present results are consistent with a situation where perfusion-limited gas exchange between bubble and blood is the dominating mechanism (1, 5, 6, 17).

If simple tissue hypoxia and edema, rather than a free gas phase, were significant factors in the DCS in these experiments, then breathing pure oxygen would be expected to give the best result since it provides a 5-fold increase in the arterial oxygen tension. Vasoconstriction (22, 23) may counteract this effect, but may also reduce vascular permeability and tissue hydrostatic pressure. On the other hand, heliox (80/20) would not be expected to be better than air. Our heliox results point toward the existence of a free gas phase in the tissue. In this case, good results of pure oxygen are also to be expected because no inert gas is inspired, and when oxygen is metabolized it contributes little to the gas phase. As the best result was produced by the helium mixture containing only 20% oxygen and the worst result with air containing about the same amount of oxygen, the data suggest that a free gas phase is present.

The picture of swollen and detached myelin sheaths and space-occupying lesions (Figs. 4–6) could as well be caused by free gas as by interstitial edema. Similar appearances were observed in medullae of decompressed dogs by Sykes and Yaffe (24), who believed that the changes represent a type of autochthonous bubble formation, although no "conventional" bubbles were seen. In dogs with fulminant DCS, Francis et al. (25), using electron microscopy, observed extravascular space-occupying lesions in the spinal white matter, probably caused by gas separation. The present N_2O–O_2 experiments were intended to amplify a possible gas phase (5–8). The observation that breathing of N_2O–O_2 yielded several space-occupying lesions in the white matter suggests that gas separation did occur in our decompressed rats. If bubbles are forming, they are most likely to form in the white matter where the amount of dissolved nitrogen is high and perfusion lower than in the gray matter. The observation that the thoracic segments where the ratio of white matter to gray is the highest (26) seemed most affected could be explained by the greater volumes of nitrogen dissolved in these areas.

Oxygen breathing is recommended during transportation of diving casualties to a recompression facility (27). However, in rat experiments we have observed an initial increase in the volume of bubbles not only in spinal white matter (5) but also in adipose tissue (6) and tendon (28) when oxygen breathing at 1 atm abs was started. This increase in volume was usually followed by shrinking and disappearance of the bubbles. It may therefore be advantageous to administer heliox rather than pure oxygen to a patient with spinal DCS during transportation to a recompression facility. The optimal heliox composition remains to be established.

In the present experiments, oxygen breathing had a beneficial effect in reducing the increase in the extracellular space as compared to air breathing, indicating an anti-edematous effect. This effect could be explained either by the vasoconstriction

and blood flow reduction elicited by the high oxygen tension or by a reduced tendency of leukocytes to block microvessels after exposure to bubbles (22, 23, 29). The process of fixation and paraffin embedding may cause the extracellular space to shrink to a value less than the one that is obtained when the extracellular compartment in brain tissue is measured as chloride or thiocyanate space (30, 31). However, since all groups of animals were exposed to the same preparation procedures comparisons are justified.

Animal experiments have been reported in which no beneficial effect on DCS could be demonstrated with heliox as compared to air. Catron et al. (32) found a small increase in pulmonary artery pressure in dogs when heliox was administered on the surface after an air dive, corresponding to the effect reported after the infusion of air into the pulmonary vasculature (33). Lillo and coworkers (34) found that guinea pigs maintained a higher ventilation rate for a short time on recompression to 200 fsw on heliox than on recompression on air. Comparing the effect to the increased respiratory rate seen after pulmonary microbubble embolism they argued that their finding indicated an adverse effect, resulting from growth of bubbles in the blood because of helium's higher diffusibility product than that of nitrogen. However, this may not be a valid comparison, because in animals struggling to survive a near fatal bout of DCS it may be an advantage to have a higher ventilatory rate and reduced work of breathing to compensate acidosis. It is notable that at the end of 1 h there was good recovery of all the variables (i.e., blood pressure, heart rate, and ventilation) in their heliox-treated group and that none of the 33 animals died, whereas 3 animals died out of the 38 in the air-recompression group.

Pearson et al. (35) reported a trend in favor of air against heliox on recompression from deep air dives. The effect was judged by the extent of recovery of SEPs in a dog model of DCS, where spinal bubbles are known to appear. The animals were compressed to 300 fsw for 15 min followed by a decompression to the surface at 60 ft/min. Nine of the 16 dogs were subjected to a second dive to 300 fsw for 8 min because they did not develop DCS from the first exposure. Unfortunately it was not stated to which treatment group these animals were assigned. This is very important, because comparisons are invalid if the animals are not equally distributed between the two groups.

In the present experiments, heliox breathing seems to give better results than either air or oxygen breathing at the surface. Whether heliox breathing is superior to oxygen or air breathing during recompression is uncertain. Rat studies show less and shorter growth of injected bubbles in spinal white matter (36) and in adipose tissue (37) after shift to oxygen breathing at 2.8 atm abs than at 1 atm abs (5, 6). There are clinical reports of successful treatment of serious cases of DCS with heliox recompression, including cases where oxygen therapy failed (1–4, 38). However, in these cases heliox (50:50) was used. Worsening of symptoms has also been reported despite recompression when oxygen or air was used as breathing gas (1, 39), but no cases of worsening are known to us when heliox has been used.

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