Oxygen Bends

K. W. DONALD[1]. *From the Admiralty Experimental Diving Unit, H.M.S. Vernon, Portsmouth, England*

IT IS REMARKABLE that there is no serious mention of the possibility of bubble formation in the body after exposure to increased tensions of oxygen in any of the modern reviews or articles on decompression sickness. Paul Bert, and many workers since, assumed that, even when there is considerable supersaturation of the body with oxygen, the excess oxygen will be so rapidly used by the tissue metabolism that there is no danger of bubble formation on return to air breathing at atmospheric pressure. Yet perusal of the early literature shows that not all investigators were of the same opinion. Leonard Hill (1) described bubbles of oxygen in the cortex of mice after exposure to 8 atm. of oxygen. These mice convulsed for a long time after decompression. A number that were not killed for examination recovered completely without therapeutic recompression. Hill also demonstrated oxygen bubbles in the heart and many other organs of toads, rats and guinea pigs, following rapid decompression from between 10 and 20 atm. of oxygen. Finally, Hill pointed out "that in only one dog out of many experiments did Bert record 's'agitant demi-convulsivement' while under compression. In all other cases the convulsions only came on after rapid decompression. Rapid decompression from air, on the other hand, did not produce convulsions, but embarrassed respiration, paralysis or death." He concluded that "the convulsions which Bert details as occurring in dogs are clearly decompression results and due to the effervescence of oxygen gas in the central nervous system." Although it is now known that sudden decompression from high tensions of oxygen may precipitate the convulsions of oxygen poisoning (2, 3), this is an infrequent occurrence and Hill's observations concerning Bert's experiments are still pertinent.

Received for publication November 24, 1954.

[1] Present address: Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Birmingham, England.

The experiments so far discussed were under conditions little related to those encountered in diving and submarine escape. However, in the report of the Royal Naval Deep Diving Committee in 1933 (4), a number of instances of severe paralyses in goats after simulated submarine escapes from pressures corresponding to 200 feet of seawater were reported. These animals were breathing 70% oxygen for 20 minutes at an average depth of 135 feet, and for another 5 minutes at 200 feet; they were then brought to atmospheric pressure in 100 seconds. In view of the relatively small percentage of nitrogen present, these paralyses were presumed to be due to oxygen bubbles. Recompression cured only a very few of these goats, and in no case was bends (flexion of leg due to pain in joint) seen. Lennox (5) reported a possible instance of mild decompression sickness in a human subject after breathing 2–3 atm. of oxygen, consisting of bend-like pains in the shoulder which passed off in a short period. Stadie (6) ventured to state that decompression from 2 to 5 atm. of oxygen would not cause the formation of bubbles.

In the author's personal experience, divers have surfaced immediately after an exposure of 2 hours to oxygen at 2.5 atm. absolute, and after 30 minutes exposure to oxygen at 3.4 atm. absolute, without symptoms. In the case of self-contained oxygen-nitrogen mixture divers, who go to depths of 140 feet of sea water or more, the risk of decompression sickness is assessed by calculating the depth at which an air diver would be breathing a similar tension of nitrogen (equivalent air depth). The rate of decompression is controlled by the ordinary 'air tables' according to the time at the equivalent air depth. The risk of oxygen poisoning is similarly determined by calculating the depth at which a diver on pure oxygen would be breathing a similar tension of oxygen (equivalent oxygen depth). As the breathing of oxygen at more than 2 atm. is known to be dangerous (3), divers are instructed not to go

below the depth where this oxygen tension is exceeded. It is assumed that oxygen need not be considered in relation to decompression sickness and it is even suggested that its presence will help in the elimination of nitrogen from the tissues. During the recent war many experimental dives, while breathing oxygen-nitrogen mixtures, were carried out by Donald and J. B. S. Haldane at equivalent oxygen depths up to 2 atm. combined with equivalent air depths up to 100 feet of sea water. Routine decompression, according to the equivalent air depth, caused no untoward symptoms apart from some itching and a very occasional mild bend. However, as higher tensions of oxygen were occasionally hazarded while breathing mixtures on certain urgent operational occasions, the author felt that the hypothesis that oxygen could not contribute to bubble formation on decompression should be more severely tested. Further the problem was of importance in relation to experiments concerning the possibility of submarine escape while breathing air or artificial oxygen-nitrogen mixtures (7). The time spent at high pressure under these conditions is of sufficient brevity to allow exposure to tensions of oxygen greatly in excess of the normal limit of 2 atm.

It was therefore decided to carry out immediate decompression after exposures to nitrogen-oxygen mixtures containing considerably more than 2 atm. of oxygen.

METHOD

In view of the lack of knowledge concerning the subject, and the possibility of untoward symptoms, it was decided to employ goats, and not men, for these experiments. Goats are excellent experimental animals for the study of decompression sickness and were first employed by Boycott, Damant and Haldane in 1908 (8). These animals have since been used in a number of investigations concerning decompression sickness (7, 9) and the results obtained have been safely applied to the human diver. The development of a 'bend' in the leg can be watched in all its stages. Firstly, the animal will rest its weight very lightly on the affected leg. Soon it lifts it with increasing frequency and vigor. Sometimes the goat paws the ground with the affected limb. When the 'bend' is fully developed, the leg is well flexed, and kept clear of the ground. The animal walks reluctantly with a severe limp. If myelitis occurs, owing to bubbles in the spinal cord, the animal first shows slight unsteadiness, and is inclined to lean against the side of the chamber. Next, the affected legs (usually rear legs) begin to straddle. In a few minutes the animal is unable to stand.

When working with goats, in high tensions of oxygen under pressure, scrupulous care must be taken that no 'live' electric wires are left inside the chamber lest the bold and never failing search of these animals for new dietetic sensations causes a 'short' with sparking.

A 100 cubic foot compression chamber was employed. The goat was submitted to a pressure of 2.52 atm. absolute (50 ft. of seawater) by means of compressed air. Pure oxygen was then run in from high pressure cylinders, until a total pressure of 5.54 atm. absolute was reached (150 ft.). The goat was now breathing 36% nitrogen and 64% oxygen and was exposed to the same tension of nitrogen as a diver on air at 50 feet of sea water (2.52 atm. absolute), and to the same tension of oxygen as a diver on pure oxygen at 84 feet of sea water (3.56 atm. absolute). The animal remained at this pressure for 60 minutes. It was carefully observed throughout for any signs of oxygen poisoning. A sample of the chamber gas was taken at 30 minutes and analyzed by the Haldane volumetric method. Carbon dioxide tensions were never in excess of 5 mm Hg. At the end of the hour, the pressure was released at the rate of 1.25 ft/sec., and the animal watched closely for the development of decompression sickness.

Separate control experiments were carried out on each animal at similar tensions of nitrogen (air, 50 feet) and oxygen (80% oxygen, 110 feet), respectively, for the same period. An interval of at least 48 hours was allowed to elapse between experiments on the same animal.

RESULTS

The results of a typical experiment were as follows. The goat surfaced apparently normal. In about 5 minutes, the animal began to develop a bend in the right foreleg. Three minutes later, a bend appeared in the right hindleg and the animal began to pant vigorously, with loud râles in the chest. Three minutes later, multiple bends had developed and the goat was unable to stand. Motor power was lost in the hindlegs. The râles in the chest and respiratory embarrassment became even more marked, the goat being restless and apparently in pain. Five minutes later, the animal was resting peacefully with quiet respirations. Twenty minutes later the goat was led away with no bends, paralysis, or signs of any kind. To anyone associated with work on compressed air illness, this series of events flavored of the miraculous.

In the two separate control experiments which were carried out on each animal in similar tensions of air and oxygen respectively, for the same period (60 min.), no animal developed any signs of any kind to indicate bubble formation, although in the exposures to oxygen, certain signs of oxygen poisoning were noted.

The results of the experiments are detailed below. Pressures are stated throughout as feet of sea water (D). The absolute pressure in atmospheres equals 1 + D/33.

Subj. 1. ♀, *29.6 kg, dive to 150 ft. for 1 hr.*
Analysis, 63.04% O_2. Equiv. O_2 depth 82.3 ft.
Equiv. air depth 52.3 ft.

	hr.
At 150 ft.	1000
Restless, no convulsant signs	1040
Left 150 ft.	1100
At surface	1101½
Bend in right foreleg	1107
Bend in right hindleg and severe respiratory embarrassment	1110
In pain, moving continuously	1112
Sitting down, unable to stand	1112½
Lying down, unable to stand, loud râles in chest	1114
In severe pain with multiple bends	1117
Lying peacefully, respirations normal	1126
Animal completely normal	1150

Control dive in oxygen, depth 110 ft.
Analysis, 82.2% O_2. Equiv. O_2 depth 84.7 ft.

	hr.
At 110 ft.	1015
Lip twitching	1100
Convulsive tremors	1108
Sustained lip twitching	1114
Left 110 ft.	1115
Surfaced	1117

No signs of decompression sickness after dive

Subj. 2. ♀, *37.8 kg, dive to 150 ft. for 1 hr.*
Analysis, 63.13% O_2. Equiv. O_2 depth 82.3 ft.
Equiv. air depth 51.4 ft.
At 150 ft. for 1 hr., no signs during, or after, the exposure.
Control dive in oxygen, depth 110 ft.
Analysis, 81.2% O_2. Equiv. O_2 depth 82.8 ft.

	hr.
At 110 ft.	1408
Lip twitching	1433
Left 110 ft.	1508
At surface	1510

No signs after decompression

Subj. 3. ♂, *37.7 kg, dive to 150 ft. for 1 hr.*
Analysis, 62.08% O_2. Equiv. O_2 depth 82 ft.
Equiv. air depth 54.8 ft.

	hr.
At 150 ft.	1008
Moving uneasily	1052
Twitching of lips	1053
Sustained lip twitching	1058
Restless, but no convulsant symptoms	1106
Left 150 ft.	1108
Arrived at surface	1110
Bend in left hindleg	1113
Lying down, in pain	1115
Standing appears to have bend in both hindlegs	1122
Greatly improved, still has slight bend in right hindleg	1128
Animal completely normal	1200

Control dive in oxygen, depth 110 ft.
Analysis, 85.3% O_2. Equiv. O_2 depth 90 ft.
At 110 ft. for 1 hr.
No signs during exposure or on decompression

Subj. 4. ♂, *40 kg, dive to 150 ft.*
Analysis, 61.78% O_2. Equiv. O_2 depth 80 ft.
Equiv. air depth 55.4 ft.
At 150 ft. for 25 min. *convulsed*

Subj. 5. ♀, *30.8 kg, dive to 150 ft. for 1 hr.*
Analysis, 64.05% O_2. Equiv. O_2 depth 84 ft.
Equiv. air depth 50.1 ft.

	hr.
At 150 ft.	1033
Animal somnolent and 'dopey' towards end	
Left 150 ft.	1133
Arrived surface	1135
Bends in both hindlegs	1140
In severe pain, restless, multiple bends	1145
Lying down, loud râles and panting	1148
Lying down with bends in all legs	1152
Stood up	1157
Normal	1200

Control dive in oxygen, depth 110 ft.
Analysis, 83.3% O_2. Equiv. O_2 depth 81.8 ft.

	hr.
At 110 ft.	1002
Convulsant respiration	1042
Eyelids ptosed, appears stupified	1047
Multiple tremors	1049
Appears very sleepy	1101
Surfaced in 90 sec. Arrived surface	1103½

No signs on decompression

Subj. 6. ♀, *36.3 kg, dive to 150 ft. for 1 hr.*
Analysis, 63.04% O_2. Equiv. O_2 depth 82.3 ft.
Equiv. air depth 52.3 ft.

	hr.
150 ft.	1005
No symptoms at depth. Surfaced in 130 sec. Arrived surface	1107
Bend in left hindleg	1110
Bend in right foreleg	1117
Bends in both hindlegs and in severe pain	1125
Lying down, unable to stand, restless, panting heavily	1130
Lying quietly	1136
Animal completely normal	1155

Control dive in oxygen, depth 110 ft.
Analysis, 82.27% O_2. Equiv. O_2 depth 84.7 ft.
At depth 1 hr.
Lip twitching after 35 min.
Sleepy and bemused last 20 min.
No signs after decompression

Subj. 7. ♀, *22.8 kg, dive to 150 ft. for 1 hr.*
Analysis, 59.5% O_2. Equiv. O_2 depth 75.9 ft.
Equiv. air depth 61 ft.

	hr.
At 150 ft.	1040
No symptoms of oxygen poisoning	
Left 150 ft.	1140
Arrived surface	1142
Bends in left foreleg and right hindleg	
Multiple loud râles in chest, dyspneic	1145
Bend in left foreleg disappeared	1150
Increasing weakness of legs, could not stand	
In pain and distress	1156
No relief. Therapeutic recompression carried out	1206½
Complete recovery	

Control dive in O_2, depth, 110 ft.
Analysis, 80.5% O_2. Equiv. O_2 depth 82.8 ft.
At depth 1 hr.
No signs during exposure or after decompression

Subj. 8. ♀, *45.6 kg, dive to 150 ft. for 1 hr.*
Analysis, 62.95% O_2. Equiv. O_2 depth 82 ft.
Equiv. air depth 52.8 ft.

	hr.
At 150 ft.	0957
No symptoms at depth	
Left 150 ft.	1057
Surfaced	1059
Bend in right foreleg	1101
Bend gone	1112
Bend recurred in right foreleg	1115
Goat sat down, lassitude, râles in chest and dyspneic	
Appeared to be in pain	1118
Goat normal	1130

Control dive in oxygen, depth 110 ft.
Analysis, 77.7% O_2. Equiv. O_2 depth 78 ft.
1 hr. at depth
No signs during or after exposure
Control dives in air carried out on all animals for 1 hr. at 50 ft.
No signs of decompression sickness after surfacing in any animal.

It will be noted that *goat 7* was recompressed after 25 minutes. The animal was paralyzed, in pain and, as there appeared to be no improvement, therapeutic recompression was carried out for humanitarian reasons. Analysis of the chamber gas showed an unusually high percentage of nitrogen, and an equivalent air depth of over 60 feet during the exposure.

DISCUSSION

The signs developed by these animals were undoubtedly those of severe decompression sickness, caused by the presence of bubbles in the body. As these signs were only transient it is reasonable to conclude that the bubbles were largely reabsorbed in this short interval. It is common experience that decompression sickness of this severity, due to bubbles mainly composed of nitrogen, does not pass off rapidly in this dramatic fashion without recompression, owing to the lack of solubility and resistance to metabolism of this gas. There is no reason to inculpate carbon dioxide in the formation of these bubbles and it is reasonably certain that oxygen was responsible. Further the use of this gas in body metabolism would account for the remarkable relief of these animals.

This is the first time severe transient decompression sickness, which was almost certainly mainly due to oxygen, has been demonstrated in conditions not far removed from those of extreme mixture dives. They were obtained in the most favorable conditions for bubble formation that could be devised, i.e., in a maximum air tension that did not of itself cause bends, combined with a maximum oxygen tension that did not cause severe oxygen poisoning in the majority of animals. Release from the total pressure (5.5 atm. absolute) to 1 atm., in 120 seconds, was too rapid for the harmless elimination of the total excess of gases, although the body could eliminate either gas without untoward signs after separate exposures to similar nitrogen or oxygen tensions.

It is of interest to consider the probable oxygen tensions that occurred in these animals. The ambient oxygen tension during the exposure was of the order of 2500 mm Hg. Lambertsen *et al.* (10) found arterial oxygen tensions of 2100 mm Hg in human subjects breathing oxygen at 3.5 atm. The oxygen pressure in the present experiments was 0.16 atm. less and the arterial pO_2 was probably of the order of 2000 mm Hg. Such arterial blood would contain 6.0 vol. % of dissolved oxygen. Lambertsen and co-workers (10) have shown that, at these tensions of oxygen, there is considerable cerebral vasoconstriction and that the cerebral arterio-venous oxygen content difference is therefore increased so that sufficient dissolved oxygen is used to cause some of the oxygen combined with hemoglobin to be utilized with a fall of jugular venous oxygen tension to about 70 mm Hg. Using a modification of Barcroft's approximate method of calculation, he suggested that the mean cerebral

capillary oxygen tension was probably of the order of 850 mm Hg during his experiments.

However, the whole body cannot be similarly protected by widespread vasoconstriction and, as no significant change of oxygen uptake has been shown under these conditions, the only way in which the arterial-mixed venous blood oxygen content difference could be increased would be by a fall of cardiac output. There is no evidence that such a fall occurs.

Behnke *et al.* (11) measured the arterial and mixed venous blood pO_2 of anesthetized dogs breathing 3.8–3.9 atm. of oxygen and obtained mean figures (6 expers.) of arterial pO_2 of 2840 mm Hg and mixed venous blood pO_2 of 630 mm Hg (range 90–1440). Those animals with small arterio-venous oxygen content differences, and presumably a raised cardiac output, showed, as would be expected, the highest venous oxygen tensions. In all these experiments but one, the mixed venous blood oxygen tensions were well above the levels in which significant dissociation of oxy-hemoglobin occurs. Assuming that oxygen demands and transfer are the same along each unit length of each capillary, then the fall in oxygen tension in most of these animals capillaries would be 'linear in space' and the mean capillary oxygen tension would be the mathematical mean of the arterial and mixed venous blood pO_2, that is, 1735 mm Hg.

Under the conditions of this experiment it is not possible to be certain of the arterio-venous oxygen content differences, the mixed venous blood pO_2, or the tissue tensions. However it would appear most likely that the mean capillary tension lay between 1000 and 1500, except in those animals with a very high arterio-venous blood oxygen content difference. The mean tissue tension would be but little below this after 1 hour's exposure. For the sake of simplicity, let it be assumed that all tissues have an oxygen solubility coefficient of the same order as blood. Then in 1 kg of tissue the amount of oxygen dissolved would be of the order of 36 ml. If the tissue contained any fatty substance, in which oxygen is approximately five times more soluble, this figure will be a considerable underestimate (12). When air breathing at atmospheric pressure is resumed, although there will be considerable supersaturation of the tissues with oxygen, this will be immediately reduced by metabolism. However this will only be at the approximate mean rate of 3.4 ml/min/kg, varying greatly in different tissues, and thus about 10 minutes will be necessary to reach normal levels of tissue oxygen tension. It would appear that the commonly accepted view that significant supersaturation with oxygen for any period will be prevented by metabolism is not well founded.

If these considerations are valid then the absence of signs of bubble formation in the control 'high oxygen' exposures with 80% oxygen is worthy of further investigation. Nims' contention (5) that "it is only an accident of nature that nitrogen is the chief factor in decompression sickness" may be an over simplification.

The occurrence of violent bubble formation and decompression sickness when the animals were exposed to the same oxygen supersaturation but with added nitrogen supersaturation, which, by itself, caused no signs, could be explained in the following manner. It would appear very likely that, in the control air experiments, small nitrogen bubbles causing no appreciable signs ('silent bubbles') occurred. If such bubbles also occurred in the body after the combined exposure then, in view of the very considerable supersaturation with oxygen and its greater solubility and apparent speed of diffusion, this gas would enter these 'silent bubbles' in large quantities. In the case of the animals which recovered so rapidly, it is difficult to see how bubbles which were almost a third of nitrogen could disappear completely in this time. This would suggest that the absorption of oxygen to normal tensions rendered these bubbles 'silent' again as in the control air experiment. The goat which was exposed to the highest nitrogen tensions in the combined exposure did not obtain relief without therapeutic recompression and it is probable that it had genuine 'nitrogen' bends as well as the short lived exacerbation of its decompression sickness by oxygen supersaturation. After the control 'high oxygen' exposures with 20% nitrogen at 4.33 atm. absolute, when 'silent bubbles' would hardly be expected to occur with such a trivial nitrogen supersaturation, there were no signs of bubble formation or decompression sickness.

These findings and considerations suggest a

possible new method of demonstrating the presence of 'silent air bubbles' that are thought to occur after certain degrees of decompression in air. Knowledge of their presence is most important in the evolution of safe decompression tables as the occurrence of such bubbles at any stage of decompression, although causing no immediate signs or symptoms, will render decompression to the next stage dangerous as they will increase in size and act as reservoirs into which further gas can diffuse from the supersaturated tissues. The reinforcement of various degrees of symptomless nitrogen supersaturation with oxygen supersaturation may help to solve the difficult problem of the 'silent bubble'.

The fact that these animals developed grave decompression sickness while there was almost certainly a surfeit of oxygen dissolved in the tissues would suggest that loss of function is caused by other factors than immediate tissue anoxia due to interference with local circulation.

In conclusion it must be emphasized that decompression sickness caused by oxygen alone has not been demonstrated. Nevertheless it would appear that, providing a certain degree of supersaturation with nitrogen is present, the initial risk of dangerous bubble formation can be greatly influenced by increased tensions of oxygen in the body. Although the resulting disturbances were only short lived in most of these animals, one continued to be severely embarrassed. It is probable that, if the nitrogen tension during the exposure had been a little greater, not only would more animals have required therapeutic recompression, but some may have been fatally injured. Although oxygen tensions of the order used in these experiments will never be encountered in standard air diving, it would be advisable to review with great care the possibility of oxygen contributing to bubble formation in submarine escape and after oxygen-nitrogen, oxygen-helium and even air diving at considerable depths. The precise risk of decompression sickness, particularly after deeper dives, has so far defied the most elaborate mathematical and physical analyses and the role of oxygen in bubble formation may have contributed to this enigma. Further, oxygen supersaturation may be a useful technique of demonstrating the presence of the elusive 'silent nitrogen bubble'.

SUMMARY

Goats have been exposed to 64% oxygen and 36% nitrogen for 1 hour at 5.54 atm. absolute. On returning to air breathing at atmospheric pressure a number of these animals developed grave decompression sickness which, however, remitted rapidly without recompression. The same animals did not develop any signs of decompression sickness after separate control exposures to equivalent tensions of oxygen (80% oxygen, 20% nitrogen) or nitrogen (in air). The danger of oxygen supersaturation contributing to the occurrence of decompression sickness in the presence of a relatively safe degree of nitrogen supersaturation is discussed.

The author acknowledges with pleasure the help of Surgeon Commander W. M. Davidson, O.B.E., Royal Navy, in these experiments which were carried out in 1945. Chief Petty Officer G. Derrick, Royal Navy, also gave invaluable assistance.

REFERENCES

1. Hill, L. *Caisson Sickness*. London: Arnold, 1912.
2. Bean, J. W. *Physiol. Rev.* 25: 1, 1945.
3. Donald, K. W. *Brit. M. J.* (i) 667 and 712, 1947.
4. Admiralty Deep Diving and Ordinary Diving Committee. R.N. Diving Report, 1933.
5. Fulton, J. F. (L. F. Nims) *Decompression Sickness*. Philadelphia & London: Saunders, 1951.
6. Stadie, W. C., B. C. Riggs, and N. Haugeard. *Am. J. M. Sc.* 207: 84, 1944.
7. Donald, K. W., W. M. Davidson, and W. O. Shelford. *J. Hyg.* 46: 176, 1948.
8. Boycott, A. E., G. C. C. Damant, and J. S. Haldane. *J. Hyg.* 8: 342, 1908.
9. Donald, K. W. and W. M. Davidson. Admiralty Experimental Diving Unit Report No. 17, Surface Decompression, 1945.
10. Lambertsen, C. J., R. H. Kough, D. Y. Cooper, G. L. Emmel, H. H. Loeschcke, and C. F. Schmidt. *J. Appl. Physiol.* 5: 471, 1953.
11. Behnke, A. R., L. A. Shaw, C. W. Shilling, R. M. Thomson and A. C. Messer. *Am. J. Physiol.* 107: 13, 1934.
12. Lawrence, J. H., W. F. Loomis, C. A. Tobias, and F. H. Turpin. *J. Physiol.* 105: 197, 1946.