THE CARDIOVASCULAR RESPONSE TO EXERCISE, WITH AND WITHOUT ATROPINE, IN AIR AT 8.5 ATMOSPHERES

IP Unsworth, BM, FFARCS
Director, Hyperbaric Medicine, Prince Henry Hospital
University of New South Wales, Sydney
First published at RNPL, 1968

ABSTRACT

In 5 subjects exposed to a pressure equivalent of 250 feet on air, the peak exercise heart rate was reduced by 38% of that attained before pressure, while with atropine the reduction was 24%. It is suggested that the bradycardia of increased oxygen pressure synergises with that of increased nitrogen pressure, to produce this reduction. The relative increases in conduction time within the heart structure may be due to nitrogen absorption and the ventricular myocardium may be relatively more affected in conditions of atropinisation.

INTRODUCTION

Evidence has been accumulating that, at increased pressures of nitrogen and inert gases, the pulse rates of subjects in both resting and exercising conditions have been depressed.[1, 3, 4, 11] Some inert gases such as xenon, exert this effect even at atmospheric pressure[2]. The exact mechanism of this action has not been fully explained and the use of the electrocardiogram may be able to clarify the position. It is well established that oxygen breathed at one or more atmosphere's pressure will exert a depressant effect on heart rate,[5,6] that is vagal in origin.[7] It was the present intention to carry out an investigation of the pulse rates of resting and exercising subjects at 8.5 atmospheres absolute in Air and to obtund the effect of the increased partial pressure of oxygen, by the administration of Atropine. The results from five subjects provide the basis for this preliminary report.

METHOD

The subjects were healthy unconditioned civilian volunteers aged from 24-34. The experimental conditions were as near as possible identical for each of the runs made by the 5 subjects and any undue apprehension was overcome by the men diving as attendants for other subjects in the experiment.

The Electrocardiograms of the subjects were monitored from four MRC silver disc electrodes fixed to the limbs, giving 6 clinical leads by direct recording on a Sanborn multichannel UV recorder. Pulse rates were recorded from a Devices R-R wave instantaneous rate meter, and exercise pulses counted from the paper record of lead II.

A 500 cubic foot chamber was used for the runs, the depth being 250 feet gauge pressure and rate of descent 63 feet per minute. Time at pressure was 20 minutes and decompression time 1 hour 41 minutes, oxygen by mask was given for the last 10 foot stop of 25 minutes. Exercise consisted of a minutes' toe touching from the supine position at the rate of 40 per minute by metronome. This may be classified as severe exercise. This was selected in preference to a bicycle ergostat or gemini rubber cord exercises, as it also involved a positional change from supine to past the vertical of the trunk and enabled a quicker transition from exercising to complete relaxation.

The exercise sequence was rest for 15 minutes, exercise for one minute, followed by a further period of rest of 7 minutes before the start of compression. At 13 minutes from start of compression (ie. after 9 minutes at depth) a further minute's exercise was followed by complete rest till 13 minutes after reaching surface. Complete 6

lead tracings were taken, at rest before exercise. Immediately post exercise, and 2 minutes, 4 and 6 minutes post exercises. At all other times, slow speed lead II monitored the ECG. Pulse rates during rest were taken every minute, and every 15 seconds post exercise for 2 minutes.

The main task of the attendant who accompanied every subject was to ensure the subject was adequately covered with warm clothing before decompression and to fix the BIBS mask on the subject at the 10 foot stop. The attendant otherwise was at liberty to move and occupy himself as he wished. The significance of this will be discussed later.

The second section of the experiment required the subjects to repeat the dives after receiving 0.6 mg atropine sulphate intravenously immediately prior to the initial rest period.

RESULTS

The results indicate primarily pulse rate values before exercise, at the peak of exercise and at 2 minutes post exercise, on the surface, at 250 feet and on return to surface. Without atropine, the mean resting value pre dive was 56 beats per minute with an exercise peak of 197.

After 9 minutes at 250 feet, the mean resting pulse rate was 55 with an exercise peak of 121, showing a mean decrease of 38.5%. On returning to the surface, the mean resting rate was 51 beats per minute and on exercise, 183 beats/minute. Pulse rate values taken 2 minutes after cessation of exercise were 75 beats/minute pre dive, 59 beats/minute at 250 feet, and 62 beats/minute on return to surface.

After an intravenous dose of 0.6 mgs atropine prior to diving, the mean pulse values changed; resting on the surface was 69 beats/minute, exercise on the surface 182 beats/minute. At depth, the resting pulse was 67 with a mean exercise value of 137 beats/minute, and a mean percentage decrease of 25% over that on surface. The post dive resting level was 54 while this rose to 175 beats/minute with exercise. Two minute post exercise rates were 89 beats/ minute on the surface, 78 beats/minute at 250 feet and 81 beats/minute post dive. The figures are expanded more fully in Tables I and II.

The ECG recordings were examined and the PR intervals and QT computed and tabulated. The QT intervals were corrected for heart rate by the formula of

$$QT_C = \frac{QT}{\text{cycle length}}$$

The mean PR interval for all the subjects ranged from 0.152 seconds pre exercise on the surface, to 0.168 pre exercise on bottom. After exercising, the mean interval further increased in length to 0.171 seconds, while after return to surface and exercise, the mean fell to 0.148 seconds.

After administration of atropine the mean pre exercise surface PR figure was 0.150, shortening to 0.132 seconds after exercise. At depth the resting PR was 0.148 seconds but after exercise this shortened to 0.138 seconds. Post dive mean value for the PR interval were resting 0.162 and post exercise 0.149 seconds.

The mean corrected QT on the surface pre exercise was 0.368 seconds extending to 0.395 seconds after exercise. At depth the mean resting QT_C was 0.380 seconds and 0.388 after exercise. On return to surface, the mean QT_C resting and post exercise were 0.372 and 0.379 seconds respectively. With atropine the pre dive resting mean was

0.374, extending to 0.399 seconds after exercise. At 8.5 atmospheres, the resting mean was 0.393 increasing to 0.408 seconds post exercise. On return to surface, the mean corrected QT was 0.366 seconds resting and 0.376 seconds post exercise.

Apart from measurement of PR and QT intervals the ECG tracings were examined for any irregularity of rhythm. In no subject was any arrhythmia detected, except sinus arrhymia and this was noted to be abolished by atropine. Wave amplitude showed no change of any significance.

During the actual periods of compression lasting 4 minutes, the pulse rates of three subjects fell in a marked linear fashion from a mean pulse rate precisely at the start of compression, of 112 beats to a mean of 62 beats/minute on reaching depth 4 minutes later. It was subsequently noted that this compression-associated fall did not appear after atropine had been administered.

DISCUSSION

From several sources[1,2,3,11] it is becoming apparent that nitrogen at pressure and other inert gases at normal and raised pressures do have an inhibitory effect on the pulse rate and cause a resting bradycardia and decrease in exercise peak.

Shilling (1936) found in his subjects a drop in both pulse rate and blood pressure at 10 atmospheres of air. Pittinger (1953) while using xenon at atmospheric pressure as an anaesthetic agent for man reported a bradycardia and hypotension despite premedication with atropine. He also found that at 3% ATA, xenon gave quite marked bradycardia in monkeys. Unsworth, in published work, has found a definite depression of both the resting and exercising pulse of men in a 19/81% mixture of oxygen/argon at 4 ATA.

Helium has also been reported as having a pulse depressant effect by Hamilton (1966). He noted a slowing of the resting pulse and a depression of the exercise peak in oxy-helium at 650 feet. However, oxygen has been known to have this depressant effect, both at normal (Daly and Bondurant 1962) and increased pressure (Salzano 1966), causing a reduction of cardiac output of 10-12%, primarily associated with bradycardia rather than reduced stroke volume. This may be abolished by atropine as used by Daly and Bondurant or by vagotomy as shown by Whitehorn and Bean (1952). But this oxygen effect was largely overcome in the experiment of Hamilton by using a gas mixture containing 1.5% oxygen at pressure, equivalent to 35% at sea level. Pittinger, when using xenon as an anaesthetic agent at atmospheric pressure, employed an 80:20 mixture of xenon and oxygen.

In the presented series of dives to 8.5 ATA with air, oxygen partial pressure reached 1379.6 mm. Hg or (1.76 ATA) and this may be expected to exert an effect on the pulse rate both resting and at exercise. With a view to eliminating this, atropine, by intravenous injection, for speed of onset, was used. Exercise before and after pressure in both atropinised and non-atropinised subjects, showed the heart could respond to exercise by attaining high peak values but at depth, there was a mean exercise peak reduction in the non-atropinised subjects of 38.5%, with atropine the mean reduction of exercise peak was 24.96%. This reduction in exercise peak at depth, on initial observation, would appear unexpected. Many factors operate at chamber pressure that should increase the exercising heart rate above that attained on the surface. Such factors (Table III) include:

1. Increased air density resulting in
   a) increased resistance to body movement ;
   b) reduction of MVV by approximately 68%; leading to
   c) CO_2 retention with raised alveolar pCO_2 (Lamphier 1963, Jarrett 1966).

2. Increased thermal stress. (Maximum temperature at end of compression 45°C) especially with atropine.
3. Increased humidity.
4. Increased involuntary exertion caused by muscular inco-ordination attributable to nitrogen narcosis.

To produce a peak reduction, the agents that must be responsible are an increased partial pressure of nitrogen and an increased partial pressure of oxygen. That the reduction in peak is greater without atropine, than with atropine, is suggestive of the oxygen effect being synergistic with the depressant effect of the nitrogen. Both non-atropinised and atropinised exercise peaks returned to the pre-dive level after decompression in all but one case.

From analysis of the ECG, the PR interval and the QT interval (corrected for heart rate) appear to be affected at depth, being prolonged in the non-atropinised dives by a mean 12.58% and 5.56% respectively. However, the atropinised dives produced a mean reduction of PR interval at depth of 7.55% yet an increase in the QT_C of 9.1%. This difference between the non-atropinised and atropinised PR at depth is extremely difficult to explain but may be related to the increased atrial conduction associated with atropine. The increase in the lengthening of the QT_C with atropine is also difficult to explain but it may be due to the effect of an increased inert gas uptake at the greatest heart rate, both resting and exercising, during pressure, attributed to the use of atropine. The increased pulse rate results in a higher pulmonary uptake and similarly in a greater myocardial uptake particularly by the larger ventricular tissue mass. It would seem that impulse transmission between individual cardiac muscle fibres of the ventricular myocardium is more susceptible to interference from nitrogen under pressure than the more highly organised neuro-conduction system, between atria and ventricles. Continuing work on these lines using other inert gases is being conducted.

The observed fall in pulse rates of three subjects from a mean peak immediately on compression of 112 beats/minute to a mean level on reaching bottom of 62 beats/minute, is, I believe, the retention in the subjects of some element of the mammalian diving reflex, which in these cases would appear to act in the absence of water contact with the face, but in the presence of increasing air pressure. That it is a vagal reflex is well-demonstrated by its abolition with atropine. No complications or undue side effects were noted with the use of atropine. All subjects reported dry mouth and absence of sweating, and all were seen to have moderately dilated pupils. Two noted that the exercise plus the lack of sweating in the high temperature of the chamber (average temperature at time of exercise 35°C) resulted in their feeling pyrexic but body temperatures were not taken in this series. Exercise at depth produced a pronounced peri-oral pallor in 3 of the 5 subjects but no abnormal feelings were reported. On questioning at surface, the divers stated that with atropine, they felt ‘more alert’, ‘less sleepy’ and ‘more energetic’, an effect that may be of interest for further study.

An incidental finding to emerge from the experimental series was the apparently greater ‘bends’ risk of the attendant as opposed to the subject. Complete relaxation with slowing of circulation during decompression, and vigorous exercise after decompression have been looked upon as providing rather poor conditions for safe bubble-free decompression[10,12] particularly in association with maximal gas uptake just prior to leaving depth. In 6 preliminary dives, oxygen was not used on the last 10 foot stop and from 7 attendants, there occurred one bend and 4 ‘niggles’ but no problems of any kind from the subjects. It is suggestive that exercise at depth prior to decompression, by virtue of increased vasodilatation and blood flow most active during the first few decompression stops, has a protective function. The subjects also, were always made warm and comfortable before decompression, the temperature

during which could fall to 3°C at the first stop. The attendant sometimes neglected their own comfort initially and may have become chilled by the rapid fall in temperature, vasoconstriction prejudicing their chances of a symptoms free decompression.

This effect of pulse reduction at pressure represents the influence of only a short exposure, in this case 13 minutes. Whether in a much longer exposure the heart and cardiovascular mechanisms will compensate for this inhibitory effect is not at present known, but obviously must be investigated, particularly in relation to long term saturation diving that has the express intention of enabling hard work to be performed for long periods at depth.

ACKNOWLEDGEMENTS

The author wishes to thank his colleagues and subjects for their valuable assistance and co-operation.

REFERENCES

1. Shilling, CW, Hawkins JA and Hartsen RA. The influence of increased barometric pressure on the pulse rate and arterial blood pressure. *Navy Med. Bull.*, Washington 1936; 34: 39.

2. Pittinger, CB, Moyers J, Cullen SC, Featherstone RM, Gross EG. Clinicopathologic studies associated with Xenon anaesthesia. *Anaesthesiology* 1953; 14: 10.

3. Hamilton, RW. Physiological responses at rest and in exercise during saturation at 2 atmospheres of He-O_2. *Proceedings of the 3rd Underwater Physiology Symposium. Nat. Acad. Sci.*, Washington. 1966: 361.

4. Unsworth, IP. Effect of argon on pulse rates of men at pressure. Unpublished work, 1968.

5. Daly, WJ and Bondurant S. Effects of oxygen breathing on the heart rate, blood pressure and cardiac index of normal man - resting, with reactive hyperaemia and after atropine. *J. Clin. Invest.* 1962; 41; 126.

6. Salzano, JV, Bell WH, Weglicki WB and Saltzman HA. Metabolic, respiratory and haemodynamic responses to exercise and increased oxygen pressure. *Proceedings of the 3rd Underwater Physiology Symposium. Nat. Acad. Sci., Washington.* 1966; p 351.

7. Whitehorn WV and Bean JW. Cardiac changes induced by 0_2 at high pressure, CO_2 and low 0_2, as manifest by the electrocardiogram. *Amer. J. Physiol.* 1952; 168: 528.

8. Lanphier, EH. Influence of increased ambient pressure upon alveolar ventilation. *Proceedings of 2nd Underwater Physiology Symposium. Nat. Acad. Sci., Washington.* 1963; 1181: 124.

9. Jarrett, AS. Alveolar carbon dioxide tension at increased ambient pressure. *J. Appl. Physiol.* 1966; 21: 158.

10. Cook, SF. Rate of exercise, temperature, drugs and water balance in decompression sickness. In *Decompression Sickness* Fulton, JF ed. Saunders, London. 1951; pp 223-241.

11. Pittinger, CB, Falconer A, Knott JR, Pender JW, Morris LE, Bickford RG. Electro-encephalographic and other observations in monkeys during Xenon anaesthesia at elevated pressures. *Anaesthesiology* 1955; 16: 551.

TABLE I

RESTING AND EXERCISE PEAK PULSE RATES ON SURFACE AND 250 FEET

SUBJECT	Surface		250 feet - air		% Decrease from Surface	Surface	
	Resting	Exercise	Resting	Exercise		Resting	Exercise
JB	50	180	57	100	444	54	110
GC	61	216	53	114	47.2	51	204
TS	54	186	51	114	38.7	47	204
JT	40	210	49	156	25.7	43	204
IU	75	192	65	120	37.5	62	192
MEAN	56	196.8	55	120.8	38.5	51.4	182.8
S.D.	±11.7	13.9	5.7	18.8	7.5	6.5	19.9

ATROPINE

Subject	Surface		250 feet - air		% Decrease from Surface	Surface	
	Resting	Exercise	Resting	Exercise		Resting	Exercise
JB	75	180	75	138	23.3	51	162
GC	68	180	69	138	23.3	58	168
TS	65	180	68	134	25.6	56	162
JT	44	168	53	129	23.2	45	168
IU	95	204	72	144	29.4	61	214
MEAN	69.4	182.4	67.4	136.6	24.96	54.2	174.8
S.D.	±16.5	11.8	7.6	4.9	2.29	5.6	19.8

TABLE 11

EFFECTS OF EXERCISE AT 250 FEET

ON COMPONENTS OF THE E.C.G.

	SURFACE		250 FT - AIR		SURFACE	
	PRE-EXERCISE	POST-EXERCISE	PRE-EXERCISE	POST-EXERCISE	PRE-EXERCISE	POST-EXERCISE
PULSE RATE bts/min	56± 11.7	75.1 ± 11.9	55 ± 5.7	58.9 ± 4.9	51.4 ± 6.5	62.1 ± 8.9
P-R Interval (Secs)	0.152±0.003	0.156 ±0.009	0.168±0.009	0.171±0.009	0.168±0.009	0.148±0.009
Q-T (Corrected) "	0.368±0.016	0.395±0.019	0.380±0.022	0.388±0.022	0.372±0.014	0.379±0.018

ATROPINE	SURFACE		250 FT - AIR		SURFACE	
	PRE-EXERCISE	POST EXERCISE	PRE-EXERCISE	POST-EXERCISE	PRE-EXERCISE	POST-EXERCISE
PULSE RATE bts/min	69.4±16.5	89±13.2	67.4±7.6	78±6.2	54.2±5.6	81.8±5.3
P-R Interval (Secs)	0.15±0.008	0.132±0.009	0.148±0.015	0.138±0.013	0.162±0.011	0.149±0.013
Q-T(Corrected)Secs)	0.374±0.016	0.399±0.025	0.393±0.012	0.408±0.017	0.366±0.022	0.376±0.015

± Standard Deviation.

TABLE III

FACTORS AFFECTING PULSE RATE AT INCREASED AIR PRESSURE

1.	Air Density	a. increased effort of movement (inc. respiratory) b. decreased MVV - increased alveolar pCO_2
2.	Temperature	Ambient (∝ rate of compression) body temperature
3.	Acoustic stress	(∝ rate of compression, chamber silencing) up to 130 lbs.
4.	Exercise	CO_2 production, catecholamines, temperature
5.	Psychological	Apprehension (central, catecholamines)
6.	Drugs	agolytics, tranquillisers, etc
7.	Increased gas partial pressure	Nitrogen and oxygen
8.	Nervous	Vagal 'diving mammals' reflex

FIGURE 1

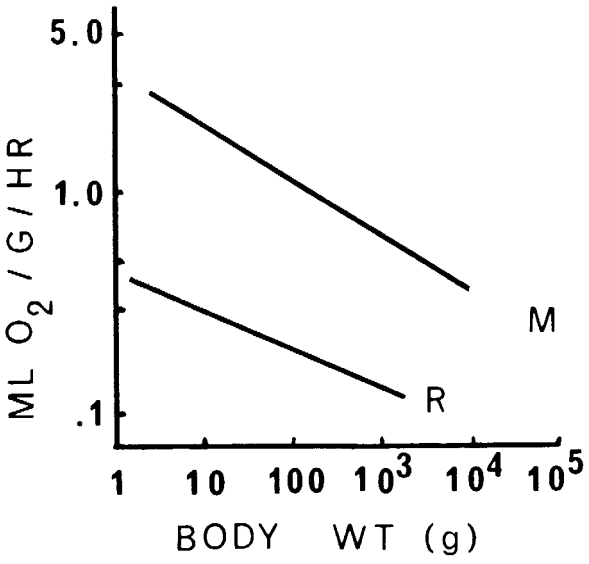

FIGURE 2