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Effects on Man of Prolonged Exposure to Oxygen at a Total Pressure of 190 mm. Hg

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THE DEVELOPMENT of rocket flight and the prospect of prolonged manned extraterrestrial journeys has stimulated much interest in the choice of the spacecraft atmosphere. Several gaseous environments have been considered which range from sea level conditions to 100 per cent oxygen at an ambient cabin pressure of 190 mm. Hg. The use of low ambient pressure and 100 per cent oxygen at that pressure appears attractive since such an atmosphere makes possible economy of weight, engineering simplification, monitoring ease and reduction of atmospheric gas leak rates. There is available, however, little physiologic data which can be related to prolonged exposure to an atmosphere containing only oxygen at reduced barometric pressure.

The administration of oxygen at high partial pressures is known to produce the syndrome of "oxygen toxicity."[1, 3] The experimental work of Becker-Freyseng and Clamann[2] and Ohlsson[11] amply documents the clinical syndrome of oxygen toxicity and the pathological changes which occur on exposure to oxygen pressures of more than 600 mm. Hg. However, there is a paucity of information concerning the effect of oxygen at partial pressures less than 600 mm. Hg. Therefore, the possible use of oxygen atmospheres in the absence of inert gases and at ambient partial pressures greater than that encountered at sea level (Po_2 159 mm. Hg) led us to undertake the experimental studies described in this report.

METHODS

Four 17-day experiments were conducted on healthy male pilots in the two-man space cabin simulator at the USAF School of Aerospace Medicine. Essentially, the simulator is an altitude chamber which contains facilities for the maintenance of two men under carefully controlled conditions for prolonged periods. The general outline of the experiments has been described previously.[9, 14] Volunteer subjects were examined extensively by the Aeromedical Evaluation Service of the USAF School of Aerospace Medicine and baseline studies were conducted at ground level (average barometric pressure 750 mm. Hg, Po_2 156 mm. Hg). Subjects giving a history of dysbarism were excluded. The subjects were then exposed to the experimental environment (Table I). Following 17 days exposure to the experimental environment, physical examinations were repeated and post-experiment studies were obtained at ground level. All subjects completed the experiments without interruption. In three subjects, however, dys-

TABLE I. EXPERIMENTAL CONDITIONS

Duration	17 days
Number of Subjects	8
Equivalent Altitude	33,500 feet
Ambient Pressure	192 ± 15 mm. Hg
pO_2	174 ± 15 mm. Hg
pCO_2	3.2 ± 3 mm. Hg
Temperature	20.7 ± 1° C.
Relative Humidity	58 ± 20%

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barisms occurred despite oxygen pre-breathing (100 per cent O_2 at 750 mm. Hg pressure from 2 to 3 hrs.) before ascent to altitude. In these cases, the experimental plan was altered during the first 24 hours so that both subjects were exposed to higher oxygen tensions for periods up to 14 hours (total pressure 250 mm. Hg, Po_2 237 in one case and total pressure 380 mm. Hg, Po_2 365 in the others).

Several measures of pulmonary function were studied serially, using the methods previously reported.[9] Primary emphasis was placed upon vital capacity and timed expiratory volume studies which were carried out as described by Comroe.[4] All volume measurements were converted to body temperature and ambient pressure, saturated with vapor (BTPS), using the following formula:

$$V_{BTPS} = V_{OBS} \frac{(273 + 37)(P_B - P_{H2O})}{(273 + t)(P_B - 47)}$$

where V_{OBS} is the volume measured; t is the ambient temperature of the gas in °C.; P_{H2O}, the water vapor pressure in mm. Hg at temperature t°C.; P_B, the ambient pressure and 47 the vapor pressure of water at body temperature. The ground level altitude of the laboratory was 577 feet and average station pressure was 750 mm. Hg.

Medical appraisal was carried out twice daily at 7:00 a. m. and 7:00 p. m. by systematic review. Symptoms obtained were noted but not discussed and leading questions were avoided wherever possible. Daily blood pressure, pulse rectal temperature and electrocardiogram were recorded and performance on a psychomotor apparatus monitored continuously from each subject for 10 hours each day. The work-rest schedule and schedule of test periods was that described previously.[7] The psychomotor apparatus was designed to test functions of the peripheral and central nervous system and motor responses at various levels of behavior.[5]

During these studies, pre- and post-experimental brachial or femoral artery punctures were performed on subjects breathing 100 per cent oxygen by face mask for 10 minutes, and oxygen content and capacity was determined by the method of Van Slyke.[13] Postero-anterior and lateral chest x-ray films were obtained during the baseline studies and post-experiment immediately following the arterial puncture studies.

RESULTS

During the course of the experiment, all subjects reported symptoms which previous workers have attributed to oxygen toxicity. These symptoms were of varying intensity and are tabulated in Table II. At 33,500 feet, a single subject had unequivocal burning substernal pain (subject 2); this pain occurred at the ninth day and persisted for a period of about 24 hours. As a trial, oxygen partial pressure was increased for several hours (increased total pressure) and the subject reported amelioration of the symptoms which did not then recur on returning to 190 mm. Hg total pressure Po_2, 175, equivalent altitude 33,500 ft.). The experiment was completed uneventfully. Nasal congestion and eye irritation was an almost universal complaint, the coryza and irritation being especially severe during the early days of exposure. Nasal dryness, congestion and rhinorrhea all occurred, sometimes in the same subject. Mild cough was noted in half the subjects. All subjects noted that they were forced to clear their ears by Valsalva maneuver or swallowing, especially after arising from sleep; in five subjects there was actual ear discomfort at some time during the experiment with difficulty in clearing the blocked ears. Transient parasthesiae (cold sensations, flushing, tingling of extremities) were noted in 50 per cent of the subjects. Two subjects had postural dizziness which was transient and did not interfere with the conduct of the experiment. Aching in the teeth was noted in one subject who had had an episode of barodontalgia in the same tooth several years previously. This pain was probably not due to oxygen, *per se*. Joint pain, as reported by Comroe,[3] occurred frequently in our experiments, however, in only one instance might the pain have been due to oxygen toxicity. In this case, mild, aching, left thigh pain occurred on the sixth day and diminished without therapy by the eighth day. In the remaining four cases, bends of up to grade 2 severity were encountered at the beginning of the experiment as a result of the change in total barometric pressure. These bends were relieved by appropriate temporary adjustment of cabin pressure.

TABLE II. MANIFESTATIONS OF OXYGEN TOXICITY

Symptom	Occurrence (Number of Subjects)
Substernal pain	1
Lower respiratory tract:	
Reduced vital capacity *	8
Upper respiratory tract:	
Cough	4
Nasal congestion	6
Sore throat	1
Ear discomfort (Aural atelectasis)	5
Fatigue	–
Eye irritation	7
Other:	
Paresthesiae	4
Dizziness	2
Aching teeth *	1
Joint or muscle pain **	1

* Probably related to reduced barometric pressure. See Discussion.
** Four other cases were noted and were probably related to reduced barometric pressure. See Discussion.

Ausculation of the lungs was performed by medical observers at 750 mm. Hg ambient pressure immediately following the conclusion of the experiment. In six of the eight subjects, definite crepitant rales were heard on inspiration at both lung bases posteriorly; these cleared on repeated deep inspiration. As noted previously,[9, 12] vital capacity was uniformly reduced in subjects exposed to altitude. This reduction in vital capacity cannot be separated from any possible reduction due to the atmospheric composition (Table III). Vital capacity was reduced in all subjects, the average experimental value being 7.6 per cent less than the pre-experimental baseline control values. This reduction occurred in the first measurements made after reaching altitude. Values returned to the pre-experiment level promptly on return to ground level pres-

TABLE III. FORCED VITAL CAPACITY

Subject	Pre-Experiment (l.)	Experiment (l.)	Post-Experiment (l.)	% Change Pre-Exp. vs. Exp.
1	5.55 ± 0.25 *	4.79 ± 0.21	5.29 ± 0.10	− 13.7
2	5.47 ± 0.07	5.36 ± 0.18	5.54 ± 0.09	− 2.0
3	5.86 ± 0.18	5.52 ± 0.23	5.75 ± 0.13	− 5.8
4	5.82 ± 0.12	5.39 ± 0.18	5.79 ± 0.13	− 7.4
5	4.60 ± 0.08	4.43 ± 0.20	4.60 ± 0.22	− 3.7
6	6.32 ± 0.14	5.54 ± 0.27	6.18 ± 0.17	− 12.3
9	4.64 ± 0.10	4.05 ± 0.20	4.59 ± 0.11	− 12.7
10	5.73 ± 0.11	5.53 ± 0 17	6.02 ± 0.16	− 3.5
Average	5.50	5.08	5.47	− 7.6

* Standard deviation.

sures. Chest x-ray films taken at the close of the experimental period revealed no abnormalities but the subjects had been breathing a normal sea level atmosphere for 10 to 40 minutes prior to these studies.

Post-experiment arterial oxygen saturations determined while the subjects were breathing 100 per cent oxygen at 750 mm. Hg pressure were normal in five subjects (Table IV). In two subjects, there was definite evidence of arterial unsaturation. Veno-arterial shunts were estimated * to be 30 per cent of pulmonary blood flow in subject 2, and 21 per cent in subject 6. In a third subject, arterial unsaturation of borderline degree was present but in the absence of baseline data, no conclusions can be drawn as to the degree of arterial unsaturation resulting from exposure to the experimental conditions.

TABLE IV. ARTERIAL OXYGEN SATURATION DATA

Subject	Pre-Experiment (%)	Post-Experiment (%)
1	*	94.9
2	91.8	88.2
3	96.0	100.0
4	97.0	99.0
5	97.3	100.7
6	99.9	90.0
9	97.3	100.0
10	98.4	101.0

* No pre-experiment data.

Serial electrocardiograms consisting of standards leads, aVF, aVL, and a chest lead (usually V_2) selected so as to show QRS transition in the frontal plane were normal at all times during the experiments. Asymptomatic sinus bradycardia and sinus arhythmia of marked degree was noted on several resting electrocardiograms. This is reflected by the decline in pulse seen in several subjects (Table V) but it should be noted that systolic and diastolic blood pressures were well-maintained and pulse pressure essentially unaltered.

TABLE V. BLOOD PRESSURE AND PULSE RATES (PRE-EXPERIMENT AND EXPERIMENT)

Subject	Pre-Experiment Blood Pressure	Pre-Experiment Pulse	Experiment Blood Pressure	Experiment Pulse	Comments
1	No Data		92/63	59	BP decreased transiently to 70/50 without symptom while asleep on May 3.
2	No Data		109/68	61	
3	117/83	67	114/79	65	
4	104/66	71	118/76	60	Subject had two episodes of transient, narrowed vision, cold sweat, tachycardia and BP 90/55 on days 6 & 15. Probably hyperventilation.
5	110/62	68	108/62	49	
6	106/58	58	104/62	50	
9	110/65	62	107/57	56	
10	111/62	60	126/65	55	

DISCUSSION

The experimental atmosphere employed in this study represents one approach to a solution of the multiple problems of the design of spacecraft atmospheres. Engineering requirements (gas leak rates, weight, ease of monitoring and control, etc.) are of sufficient interest to require the examination of the physiologic response of man to prolonged exposure to atmospheres chiefly composed of oxygen at reduced barometric pressure.

At a total pressure of 190 mm. Hg and in an oxygen atmosphere, ambient oxygen partial pressure is increased 20 mm. Hg above that prevailing at sea level when partial pressures due to water vapor and carbon dioxide have been subtracted. This 20 mm. Hg increase in P_{O_2} is progressively diminished by increased P_{H_2O} and P_{CO_2} at the lower levels of the respiratory tract, until, at the alveolar level, only very slightly increased P_{O_2} prevails. Nevertheless, a variety of symptoms occurred (Table II) which were very similar to those described for oxygen toxicity.[3] These symptoms were generally mild but some were persistent and reproducible and we cannot exclude the possibility that the symptoms noted in this study were due to the oxygen-rich, nitrogen-poor atmosphere. It is also possible that they were related to increased insensible water loss from the mucous membranes due to the reduced pressure involved. The possibility also exists that those irritative effects were induced by the dehydrating effect of dry oxygen used during pre-breathing and at the beginning of the experiment. Since normal relative humidity was quickly established and maintained continuously at 35 to 65 per cent, we do not feel that dehydration was a significant factor. The substernal pain which occurred in one subject on the ninth day was of the type noted by Comroe,[3] but improved on increasing the oxygen partial pressure. Thus, it seems likely that this pain was related to factors other than increased ambient P_{O_2}.

Although reduced vital capacity may be caused by oxygen toxicity at high partial pressures of oxygen,[2,3] it is more likely that the reduction in these experiments

* Per cent shunt $= \frac{Q_S}{Q} = \frac{\text{arterial oxygen content}}{\text{venous oxygen content}} \cdot 100$

Note: Arterial-venous oxygen difference was assumed to be 5 volumes per cent.

was due to the poorly understood effect of reduced pressure on vital capacity.[9, 12] There remains, however, the possibility that the near absence of nitrogen can produce pulmonary atelectasis by a combination of physical and chemical effects (in much the same manner as aural atelectasis is produced under these conditions). Such atelectasis would be expected to manifest itself by reduced vital capacity, x-ray evidence of linear or coalescent densities and reduced arterial oxygen saturation due to veno-arterial shunting through unaerated pulmonary tissue. The first two manifestations have been noted at oxygen partial pressures of 760 mm. Hg[2] and 418 mm. Hg[8] after 2 and 7 days exposure, respectively, but none of these findings were expected in the present experiment. Thus, the finding of arterial oxygen unsaturation in two (possible 3) subjects (Table IV) was surprising. This finding suggests that occasional subjects will respond to oxygen-rich atmospheres in a one-gravity environment in a manner similar to that reported more frequently in oxygen-rich, multiple-gravity environments.[6, 10] The causes of this condition are not well-understood and are being studied further.

A potential hazard of exposure to reduce barometric pressure was the production of decompression symptoms. Subjects were screened for history of previous altitude reaction ("bends," "chokes," etc.) and denitrogenation was carried out by pre-breathing the subjects for a minimum of two hours on 100 per cent O_2 at 750 mm pressure by well-fitting aviator's masks. Nevertheless, there was a very high incidence of bends (more than 50 per cent) in our subjects, suggesting that a reappraisal of the criteria for denitrogenation and crew selection be made when prolonged exposure to cabin altitudes similar to the pressure utilized here is anticipated.

SUMMARY

Four 17-day experiments were conducted on healthy male pilots in the two-man space cabin simulator. Total pressure during these studies averaged 192 mm. Hg; partial pressure of oxygen 174 mm. Hg.

This atmosphere was reasonably well-tolerated by all test subjects. Symptoms encountered during the course of these studies that were attributable to the "single-gas" atmosphere, were not of sufficient magnitude to warrant termination of the tests. These consisted of upper respiratory tract irritation, aural atelectasis and eye irritation.

Two, and possibly three, of the eight subjects demonstrated reduced arterial oxygen saturation immediately post-experiment. No x-ray evidence of pulmonary atelectasis was evident at that time.

The consequences of reduced pressure caused as much concern as the effect of the "single-gas" atmosphere. The incidence of baropathies following decompression from 750 mm. Hg to 190 mm. Hg exceeded 50 per cent (5 of 8 subjects), even following 2-3 hours of pre-oxygenation.

The utilization of an atmosphere consisting of oxygen, carbon dioxide and water vapor at a total pressure of 190 mm. Hg appears to be physiologically feasible, at least for 17 days. Care must be taken to overcome the problem of bends during the initial decompression and to insure that engineering gains are sufficiently great to offset the symptoms noted in these studies.

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