

Physiologic Response to Increased Oxygen Partial Pressure II. Respiratory Studies

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ABSTRACT

The respiratory effects of a 30-day exposure to an alveolar partial pressure of 171 mm. Hg have been studied in 4 subjects at a total pressure of 700 mm. Hg (33.3 per cent O₂) and 4 subjects at 258 mm. Hg (100 per cent oxygen). Vital capacities decreased on ascent to the 258 mm. Hg pressure altitude and returned to normal immediately upon descent to ground level. Maximum breathing capacities increased concomitantly. No changes were seen in the 700 mm. Hg exposure. There was no evidence of changes in the oxygen carrying capacity of the blood.

The lack of any persistent, unaccountable effects of an alveolar partial pressure of 171 mm. Hg in the presence or absence of nitrogen indicates that as far as pulmonary function is concerned, man appears to be able to tolerate either environment equally well.

PREVIOUS REPORTS of respiratory effects of chronic exposures of man to decreased pressures and at higher than normal alveolar oxygen tensions have been restricted to exposures of 17 days or less.^{7, 9, 10, 14} Changes in respiratory function noted in these experiments appear completely innocuous for these periods of exposure. However, it is difficult to predict possible changes in respiratory function for longer periods of time. In addition, the role of the

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presence or absence of inert gas when the alveolar oxygen tension is increased is not clearly defined.

The Air Force atmospheric selection program requires that adequate information be available on the effects of "space equivalent" atmospheres on all physiological systems. This report deals with respiratory function studies undertaken in conjunction with other studies, to elucidate the question of physiologic effects of a 30-day exposure to higher than ambient oxygen partial pressures in the presence or absence of inert gas.

METHODS

The experimental altitude chamber, atmospheric monitoring and control system, the life support system, and basic experimental design have been described elsewhere.⁸ The atmospheric conditions used in each experiment were given in Table I of that paper. The oxygen concentration in the ambient atmosphere at 700 mm. Hg was calculated by the alveolar equation¹¹ so that the alveolar oxygen tension would be equivalent to breathing pure oxygen at 258 mm.

TABLE I. PRE AND POST-EXPERIMENTAL RESIDUAL VOLUMES AND CARBON MONOXIDE DIFFUSING CAPACITIES (DLCO) (SINGLE OBSERVATIONS)

Subject #	Residual Volume liters BTFS		D _L CO ml/min/mm. Hg	
	Pre-Experimental	Post-Experimental	Pre-Experimental	Post-Experimental
Experiment 63-3				
38	1.70	1.71	16.3	14.8
39	1.74	1.76	18.4	20.1
40	1.42	1.40	15.2	17.3
41	1.60	1.56	20.2	20.1
42*	1.75	1.78	18.3	14.1
43*	1.68	1.67	16.8	14.3
Experiment 63-4				
44	1.45	1.47	21.3	18.1
45	1.52	1.55	16.4	18.3
46	1.62	1.62	15.6	19.8
47	1.32	1.36	23.4	20.1
48*	1.60	1.57	18.3	16.4
49*	1.45	1.48	20.2	22.0

* Control subjects for each group

Hg. The small amount of carbon dioxide in the air was neglected in this calculation. The alveolar equation in the absence of carbon dioxide is:

$$P_{A_{O_2}} = (P_B - 47)F_{I_{O_2}} - \frac{P_{A_{CO_2}} + P_{ACO_2}}{R} \frac{(1-R)F_{I_{O_2}}}{R} \quad (\text{equation 1})$$

where $P_{A_{O_2}}$ = alveolar oxygen tension, P_B = barometric pressure, $F_{I_{O_2}}$ = fraction of oxygen in the inspired air, $P_{A_{CO_2}}$ = alveolar carbon dioxide tension, and R = respiratory exchange ratio of $\dot{V}_{CO_2 (STPD)}$ divided by $\dot{V}_{O_2 (STPD)}$. When pure oxygen is the inspired mixture, the respiratory exchange ratio (R) is equal to 1 and equation 1 becomes:

$$P_{A_{O_2}} = P_B - 47 - P_{A_{CO_2}} \quad (\text{equation 2})$$

At 258 mm. Hg, assuming a normal $P_{A_{CO_2}}$ of 40 mm. Hg, the $P_{A_{O_2}}$ would be equal to 258-47-40, or 171 mm. Hg. Then using equation 1 and assuming an R of 0.8, the $F_{I_{O_2}}$ required for an equivalent $P_{A_{O_2}}$ was calculated to be 0.33. The average measured alveolar oxygen tension was 177 mm. Hg. This difference was due to the presence of carbon dioxide and the R values of greater than the assumed 0.8.

The respiratory studies were divided into 3 phases corresponding to the experimental periods: 1) pre-experimental control with the subjects confined in the chamber at ground-level pressure and composition; 2) experimental with the subjects and chamber at test conditions, and 3) post-experiment control with the subjects again confined in the chamber at ground level pressure and composition. Carbon monoxide diffusing capacities and residual volumes were measured 2-3 days prior to the pre-experimental period. Resting carbon monoxide diffusing capacities were measured by the steady-state method of Filley.⁶ The inspired gas mixture for this test was approximately 1000 parts per million carbon monoxide in air. Residual volumes were measured by the 3-breath method of Rahn¹² during this same period. These measurements were repeated during the post-experimental control period and were performed within one hour of the subjects being returned to ground-level pressure following the experimental period.

Basal metabolic rates were measured during each period. These studies were performed with the subjects fasting and recumbent after they had awakened from a 7 hour sleep period. The subjects inspired from a Tissot spirometer through a set of 1-way valves and expired into a Douglas bag. A differential pressure transducer (Statham— ± 2.5 psid) was attached to the vestibule of the 1-way valve and used to indicate the pattern of pressure changes corresponding to respiratory movements. The output of the transducer was recorded on a Sanborn 150 and the tracing used to calculate the total time of breathing on the system and the number of breaths taken. The volume of exhaled air in the Douglas bag was measured in the Tissot spirometer. From these values, inspiratory minute volume (\dot{V}_I) and expiratory minute volume (\dot{V}_E) were calculated for body temperature, pressure, and saturated with water vapor (BTPS). Alveolar air was

collected by the Rahn sampler technique¹³ with the subject recumbent immediately following the \dot{V}_I and \dot{V}_E collections. Samples of alveolar air, expired air, and cabin atmosphere were collected in syringes lubricated with saturated lithium chloride and then analyzed. Oxygen content was measured by a rapid response Beckman E-2 paramagnetic oxygen analyzer and carbon dioxide determined with Beckman LB-1 infrared CO_2 analyzer. From these results, CO_2 production (\dot{V}_{CO_2}) and oxygen consumption (\dot{V}_{O_2}) were calculated by equations given by Rahn.¹¹

Forced vital capacities and maximum breathing capacities were measured with a Servo-Spirometer which was calibrated against a Tissot spirometer at ground-level and at 258 mm. Hg. The spirometer head was located inside the chamber and the amplifier and recorder were outside. Measurements were carried out through coordination between the subjects and spirometer operator via interphones.

Alveolar-arterial (A-a) oxygen gradients were determined using anaerobic brachial arterial samples and end tidal alveolar samples drawn at the same time. Arterial oxygen tensions ($P_{a_{O_2}}$), arterial carbon dioxide ($P_{a_{CO_2}}$), and pH were measured using electrodes made by Instrumentation Laboratories, Inc. Alveolar gas tensions were collected and analyzed as noted before and the alveolar-arterial oxygen gradients calculated. Arterial blood samples were analyzed for oxygen content, and oxygen capacity by the Van Slyke technique.¹⁵

RESULTS

Typical alveolar oxygen and carbon dioxide tensions are shown in Figure 1 for subject 41 (700 mm. Hg

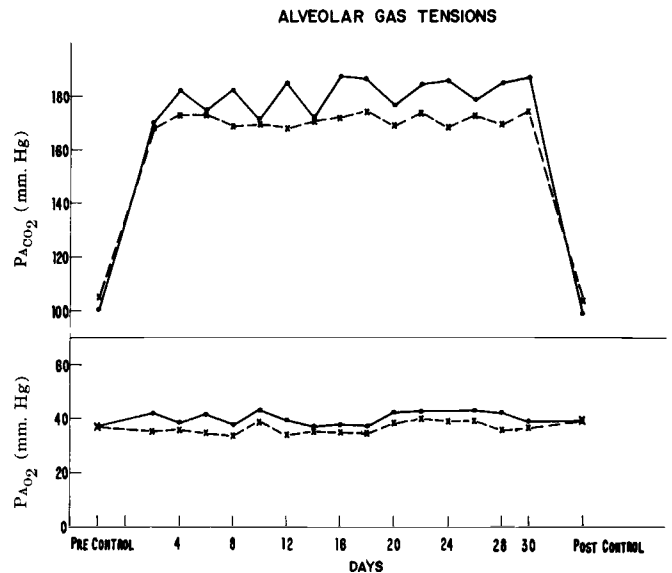


Fig. 1. Alveolar Oxygen ($P_{A_{O_2}}$) and Carbon Dioxide ($P_{A_{CO_2}}$) partial pressures for Subject 41 (solid line) of the 700 mm. Hg exposure and Subject 44 (dashed line) of the 258 mm. Hg exposure.

experiment), and subject 44 (258 mm. Hg experiment). All the subjects at each exposure had similar alveolar gas tensions which indicated that the alveolar oxygen

tensions in both experiments were comparable and, in fact, the alveolar oxygen partial pressure averaged slightly higher (approximately 7 mm. Hg) in the 700 mm. Hg exposure. Alveolar oxygen tensions remained relatively constant through each altitude exposure indicating that the chamber atmospheric control system functioned throughout and essentially the same inspired oxygen tensions were maintained.

Pre and post-experimental control values of carbon monoxide diffusing capacity and residual volumes are presented in Table I. There were no significant changes for any subject and the values shown are typical of healthy normal males of this age group.

Oxygen consumption (\dot{V}_{O_2}) and carbon dioxide production (\dot{V}_{CO_2}) are shown in Table II for each period

TABLE II. OXYGEN CONSUMPTION (\dot{V}_{O_2} AND CO_2) PRODUCTION (\dot{V}_{CO_2}) FOR EXPERIMENT 63-3, 700 mm. Hg PRESSURE ATMOSPHERE AND EXPERIMENT 63-4, 258 mm. Hg PRESSURE ATMOSPHERE

Subject #	\dot{V}_{O_2} ml/minSTPD			\dot{V}_{CO_2} ml/minSTPD		
	Pre-Experimental	Experimental	Post-Experimental	Pre-Experimental	Experimental	Post-Experimental
Experiment 63-3						
38	396.5 ± 124.7	359.9 ± 92.3	294.7 ± 34.3	391.8 ± 49.9	328.4 ± 38.7	260.8 ± 12.6
39	341.3 ± 24.1	350.3 ± 70.6	322.0 ± 72.5	290.4 ± 34.8	302.6 ± 30.3	342.7 ± 25.9
40	299.7 ± 17.3	299.7 ± 78.1	234.4 ± 38.7	419.2 ± 49.4	292.0 ± 82.1	250.9 ± 29.6
41	251.2 ± 32.5	273.5 ± 47.9	326.6 ± 67.7	306.8 ± 26.3	271.4 ± 27.7	265.7 ± 32.5
42*	355.2 ± 79.0	420.7 ± 103.1	266.8 ± 28.8	364.5 ± 57.5	349.6 ± 77.3	251.7 ± 20.1
43*	375.8 ± 140.2	302.1 ± 80.8	255.0 ± 34.1	371.4 ± 142.3	302.4 ± 91.1	250.3 ± 23.3
Experiment 63-4						
44	234.9 ± 40.8	279.8 ± 47.0	311.0 ± 40.7	239.7 ± 51.2	197.9 ± 17.5	261.9 ± 17.0
45	222.2 ± 61.6	279.3 ± 62.3	294.8 ± 7.5	208.9 ± 24.4	199.5 ± 16.8	227.8 ± 4.1
46	232.5 ± 28.1	303.7 ± 92.9	353.8 ± 34.0	238.9 ± 46.2	198.0 ± 46.9	256.8 ± 29.4
47	215.2 ± 42.5	299.3 ± 84.0	269.6 ± 30.4	205.4 ± 26.9	190.5 ± 18.4	243.7 ± 20.1
48*	262.3 ± 16.0	266.2 ± 78.3	283.4 ± 10.5	234.7 ± 4.3	229.1 ± 26.6	248.2 ± 24.8
49*	209.8 ± 20.5	211.3 ± 41.5	255.8 ± 23.0	225.1 ± 19.1	207.6 ± 32.4	223.7 ± 10.4

* Control subjects for each group

of each experiment. There were no significant changes for any subject. There was a slight progressive decrease in oxygen consumption for each subject with time of exposure. This trend is believed to be a function of the inactivity resulting from confinement in the chamber and not an effect of the gaseous environment. In addition, as the experiments progressed, the subjects slept better and were probably in a more basal state when the measurements were taken.

Pre-experimental control values for vital capacity and maximum breathing capacity are shown in Table III.

TABLE III. PRE-EXPERIMENTAL CONTROL FORCED VITAL CAPACITY (FVC) AND MAXIMUM BREATHING CAPACITY (MBC)

Subject	Age yrs	Weight kgm	Height cm	Surface Area m ²	FVC (l _{BTPS})			MBC (l/min _{BTPS})		
					Pre-dicted	Observed	SD	Pre-dicted	Observed	SD
Experiment 63-3										
38	20	82.7	198.1	2.07	5.03	6.52	0.07	157.4	152.5	1.8
39	19	86.6	190.5	2.07	4.86	6.79	0.09	158.5	144.9	0.5
40	21	62.0	172.1	1.67	4.37	4.70	0.09	126.1	150.0	18.0
41	24	72.4	174.0	1.81	4.34	6.47	0.10	133.9	127.7	1.0
Experiment 63-4										
44	18	61.2	172.7	1.67	4.42	5.84	0.07	128.8	143.0	20.5
45	17	68.2	175.3	1.85	4.31	4.30	0.06	143.6	145.5	6.9
46	18	71.3	182.9	1.85	4.68	6.27	0.09	142.6	134.3	6.2
47	19	66.7	167.6	1.73	4.27	4.43	0.08	132.5	129.3	12.0

Predicted values were calculated on the basis of the following equations:
 FVC (Predicted) = (27.63 - (0.112 x Age)) height (cm) (Ref. 3, p.8)
 MBC (Predicted) = (86.5 - (0.522 x Age)) x surface area (m²) (Ref. 3, p.131)

Vital capacities were decreased by 3 per cent upon immediate ascent to 258 mm. Hg. As shown in Figure 2, the values did not return to normal throughout the

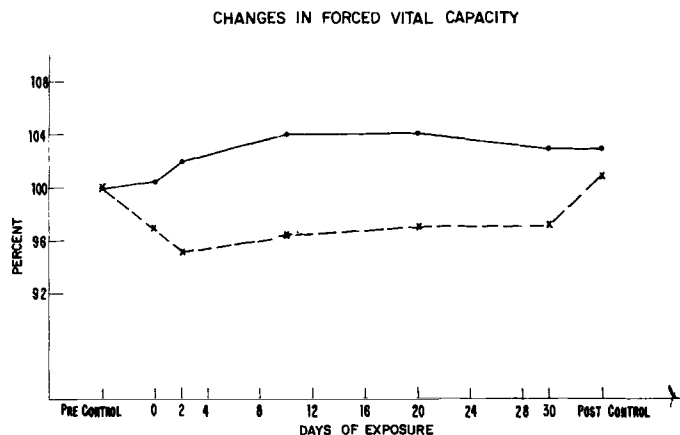


Fig. 2. Changes in forced vital capacity expressed as per cent of normal. Each point represents the average of 4 subjects. Standard deviations were too small to depict. The solid line represents values for the 700 mm. Hg exposure, the dashed line, the 258 mm. Hg exposure.

258 mm. Hg exposure and dropped to as low as 95 per cent of normal. Vital capacities were normal in all subjects immediately upon return to ground level. In contrast, vital capacities were increased above normal control values throughout the 700 mm. Hg exposure. This is attributed to learning. This learning effect was minimized in the 258 mm. Hg experiment by more intensive training prior to the experiment.

Mean values for maximum breathing capacities expressed as per cent of normal values, together with standard deviations are shown in Figure 3. The normal

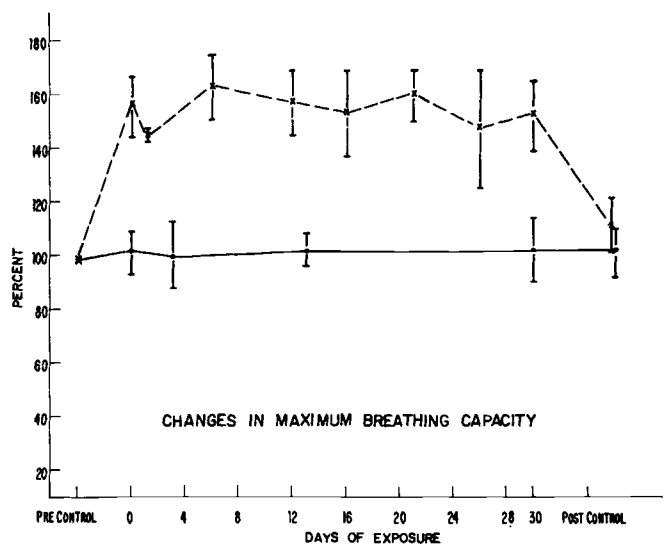


Fig. 3. Maximum breathing capacities expressed as per cent of normal. The solid line depicts results at 258 mm. Hg and the solid line at 700 mm. Hg. Each point shows the mean ± 1 standard deviation for 4 subjects.

value for each subject was calculated from the average of values obtained during the pre-flight control period. Maximum breathing capacities were unchanged

during the 700 mm. Hg exposure and increased on the average of 55 per cent at 258 mm. Hg.

Alveolar-arterial values for the 258 mm. Hg experiment are shown in Table IV. Alveolar-arterial oxygen

TABLE IV. ALVEOLAR-ARTERIAL GRADIENTS (A-a) Δ O₂ WITH APPROXIMATELY 99 PER CENT OXYGEN AT 258 MM. HG

Subject #	P _A O ₂ (mm. Hg)			P _a O ₂ (mm. Hg)			(A-a) Δ O ₂ (mm. Hg)		
	Pre	Exp	Post	Pre	Exp	Post	Pre	Exp	Post
44	101.5 [±] 3.5	171.6 [±] 1.1	104.2	98.1 [±] 6.5	149.6 [±] 9.1	98.2	2.9	22.0	6.0
45	100.6 [±] 2.9	170.5 [±] 1.7	107.1	102.3 [±] 1.3	171.4 [±] 3.5	101.3	5.6	20.0	5.8
46	104.6 [±] 4.5	169.4 [±] 3.5	111.3	105.2 [±] 3.0	146.8 [±] 2.1	103.5	0.5	22.6	7.8
47	107.7 [±] 9.8	169.4 [±] 1.3	115.6	100.7 [±] 8.7	142.0 [±] 1.4	98.1	7.1	27.5	17.5
48*	105.8 [±] 3.4	108.9 [±] 3.3	113.7	102.6 [±] 1.8	101.1 [±] 1.1	103.5 [±] 9.6	6.9	7.1	14.6
49*	113.4 [±] 0.7	110.9 [±] 0.2	104.2	107.9 [±] 1.2	99.4 [±] 1.8	94.9 [±] 5.5	14.4	13.4	12.0

* Subjects #48 and #49 were ground level controls

gradients increased in this experiment when the inspired oxygen tensions increased. This increase is due to the effect of the venous-arterial shunts of the same magnitude (2-4 per cent) resulting in a greater drop in arterial oxygen tension.²

Arterial O₂ contents, O₂ capacities, and per cent saturation are shown in Table V. There were no changes

TABLE V. ARTERIAL OXYGEN CONTENTS AND CAPACITIES WITH PER CENT SATURATION

Subject #	Oxygen Content (Vol %)			Oxygen Capacity (Vol %)			% Saturation		
	Pre	Exp	Post	Pre	Exp	Post	Pre	Exp	Post
Experiment 63-3									
38	19.8	19.7	19.2	21.5	20.1	20.3	92.1	96.0	89.7
39	21.3	19.8	19.3	21.5	18.1	20.3	99.1	105.3	95.1
40	20.0	18.8	19.0	22.5	20.1	-	88.9	93.5	-
41	21.3	21.5	18.0	20.7	19.9	17.5	102.8	108.0	102.9
42*	17.7	18.9	19.2	21.5	18.8	18.6	82.3	100.5	103.2
43*	19.4	18.2	19.0	19.2	19.0	-	101.0	95.8	-
Experiment 63-4									
44	18.4	19.2	19.0	18.9	18.7	18.9	97.4	102.7	100.5
45	16.5	18.1	18.0	19.3	17.2	-	85.5	105.2	-
46	17.6	18.6	21.2	18.1	17.7	-	97.2	105.1	-
47	18.0	17.6	18.4	17.9	17.6	17.8	100.6	100.0	103.4
48*	18.1	18.4	19.7	18.5	18.7	19.6	97.8	98.4	100.5
49*	18.9	19.6	18.2	18.9	19.2	19.5	100.0	102.1	93.3

* Control subjects for each group

which would indicate a deficiency in the oxygen carrying capacity of the blood. The slight increase in oxygen content and per cent saturation during the experimental periods represents the increase in dissolved oxygen at the higher alveolar oxygen tensions.

DISCUSSION

The lack of any persistent, unaccountable effects of an alveolar partial pressure of oxygen of 171 mm. Hg in the presence or absence of nitrogen for 30 days indicates that as far as pulmonary function is concerned, man can tolerate either environment tested equally well.

Changes in forced vital capacities with decreased pressure have been reported previously¹⁴ and attributed to a reduction in barometric pressure. Results confirm this finding and it is significant to note that the reduction in vital capacity remained throughout the 258 mm. Hg experiment. The reduction in vital capaci-

ty occurred upon ascent to altitude and disappeared immediately with descent to ground level. Maximum breathing capacities increased at reduced pressure as a function of decreased gas density.¹⁴ The magnitude of the increases measured in these experiments are higher than those reported in that study. A portion of this increase can be explained by learning since post-flight control values were 112 per cent of pre-flight control in the 258 mm. Hg exposure. If percentage increases are calculated based on post-flight values, the increases are comparable to those reported.

Changes in alveolar-arterial oxygen gradients do not reveal any significant change in vein-to-artery shunting of blood. The increases in (A-a) oxygen gradients are attributed to greater dilution effect of the normal 2-4 per cent venous-to-artery shunt. The use of (A-a) oxygen gradients to indicate the presence of atelectasis was suggested by Morgan, *et al.*¹⁰ (A-a) oxygen gradients represent a reasonable index for lung collapse but since blood flow through an atelectatic area ceases with time,¹ the effect of the increased shunt would disappear and (A-a) oxygen gradients would return to normal. In these experiments, no discernible evidence of lung collapse was present. (A-a) oxygen gradients were normal and upon return to the ground level pressure, residual volumes and carbon monoxide diffusing capacities were at pre-experiment levels. These measurements do not rule out the possibility of small diffuse areas of atelectasis.

Ernsting⁵ reported drops in diffusing capacity with pure oxygen breathing at ground level. In these experiments and those reported by DuBois,⁴ no changes were noted between pre and post-experimental values. It would appear that these data are in direct contradiction to those of Ernsting. However, it has been proposed that many of the effects of hyperoxia may be a time-concentration effect¹⁶ and if man is exposed to longer durations of oxygen at decreased pressure, similar results might be obtained.

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