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# STUDIES ON THE RESPONSE TO ACUTE ALTITUDE EXPOSURE WITH SPECIAL REFERENCE TO THE POSSIBILITY OF EARLY DETECTION OF HIGH ALTITUDE PULMONARY EDEMA

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## SUMMARY PAGE

### THE PROBLEM

The pathogenesis of acute pulmonary edema of high altitude remains unknown. The present study was designed to evaluate the baseline and acute cardiorespiratory acclimation data of a group of young males selected to construct and maintain a scientific station on the Antarctic Plateau (pressure altitude 13,500 feet). Should serious altitude sickness or pulmonary edema develop in any of these subjects, it might be possible to determine which investigations, if any, could be used to screen potentially susceptible subjects and to identify avenues for more extensive studies.

### FINDINGS

The baseline studies revealed the subjects to be in good health. The acute cardiorespiratory changes, both in the altitude chamber at 14,000 feet after 36 hours and following return to sea level, were similar to those described by other authors. No evidence of overt or insipient pulmonary edema was detected. However, there was an unexpectedly high incidence of protracted nausea and vomiting, necessitating the removal of two of the subjects from the chamber.

## INTRODUCTION

This investigation represents an attempt to define predisposing and precipitating factors in pulmonary edema of high altitude in a group of men who were first exposed to simulated altitude in a low pressure chamber and then later observed on the Antarctic Plateau at a pressure altitude of 13,500 feet. Although pulmonary edema was not demonstrated in any subject under either circumstance, the findings have, nevertheless, advanced our knowledge in two respects: First, they demonstrated the absence of edema under a constellation of factors generally regarded as favoring its occurrence; second, lines of approach for future investigations have been indicated.

Although mountain sickness and the process of acclimatization to altitude have attracted attention since Mosso's (1) description of mountain sickness in 1899, the study of high altitude pulmonary edema is a relatively recent one. Since 1900 several reports in mountaineering journals* have documented sudden respiratory distress in apparently healthy young people after rapid ascent to high altitudes. These attacks, frequently fatal, were first attributed to a fulminant pneumonia. In 1937 Hurtado (2) was the first to identify the attacks as those of acute pulmonary edema, and since that time several groups from Peru have published clinical, pathological, and physiological reports of the syndrome (3-5). In the United States Houston (6), Hultgren et al. (7,8), and Fred et al. (9) have reported physiological measurements on pulmonary edema and have speculated as to possible etiologies. Since Singh et al. (10) reported a series of 332 incidences of pulmonary edema which occurred while the Indian Army was engaged in defending their Northern Frontier, there has been a resurgence of interest in the problem. An additional report by Menon(11) of the Indian Army placed the incidence at 5.7 per thousand among a group who had been flown to a mountainous territory with altitudes ranging from 11,000 to 18,000 feet.

## PROCEDURE

### SUBJECTS

Twelve men ranging in age from 20 to 30 years were selected from two groups: Eight men were part of a Navy Mobile Construction Battalion and were the technicians responsible for the erection of a scientific station on the Antarctic Plateau; the other four were chosen from the Naval Antarctic Support Force assigned to maintain the Base during the wintering-over period of seven to ten months. The construction team was expected to remain at the Plateau station only for about one month and then return to sea level. Since the subjects were available for a strictly limited period of testing, emphasis was placed upon obtaining maximum time at simulated altitude in the low pressure chamber. This allowed one day for obtaining baseline data, followed by a thirty-six-hour exposure to altitude.

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*Personal communication

The subject's health record and completed questionnaires covering family history, social history, and system review were carefully reviewed. Following a complete physical examination which included anthropometric measurements, each subject was interviewed and questioned closely for any history of recurrent pulmonary disease, allergies, heat or cold intolerance, and cardiovascular symptomatology either in himself or his family. He was further questioned about prior acclimatization and/or altitude exposure and use of supplementary oxygen. The families of all subjects were contacted to rule out neonatal respiratory problems or any history of malabsorption or autonomic disturbances.

## BASELINE GROUND-LEVEL STUDIES

The baseline studies performed in the laboratory included routine urinalysis with microscopic examination, and postero-anterior and right lateral x-rays of the chest. Venous blood was drawn for the determination of hematocrit, WBC and differential count, reticulocyte count, $CO_2$ content, serum sodium, potassium, and chloride, protein bound iodine, cholesterol, lipoproteins, and atherogenic index (12). Blood sugar determinations were made in the fasting state and two hours following ingestion of 100 grams of carbohydrate.

The subjects then underwent tilt table studies in which baseline blood pressure and pulse recordings were obtained for twenty minutes in the horizontal position. They were then quickly tilted to 70 degrees from the horizontal and blood pressure and pulse rate recorded every minute through the fifth minute and at 10, 15, and 20 minutes.

They then performed the Harvard step test (13), using a 20-inch step, in the following sequence with appropriate intervals for rest: 1) four minutes of exercise at 30 steps per minute; 2) five minutes of exercise at 30 steps per minute; and 3) one minute of exercise at 20 steps per minute. Before and after each of the three exercise tests, serial electrocardiograms were recorded.

The electrocardiograms were analyzed for rate and rhythm; P wave; QRS and T wave configuration, duration, and amplitude; ST configuration, mean frontal QRS angle; mean frontal T angle; and the frontal QRS-T angle. The precordial R to S transition zone was noted and the ratio of R to S amplitude in $V_4$ computed.

In the Harvard step tests, the heart rate immediately following exercise, the delta rate (basal to maximum rate with exercise), and the rate of pulse recovery were determined. The mean frontal QRS angle, the QRS-T angle, and the T angle were then compared with pre-exercise values. An abnormal S-T depression was defined as a horizontal depression of one millimeter or greater in any lead with exercise.

Special electrocardiographic studies included the recording of lead II during inspiration, expiration, standing, Mullier maneuver, Valsalva maneuver, carotid compression, and with response to one milligram of intravenous atropine sulfate.

Pulmonary function studies included measurement of vital capacity (VC), inspiratory capacity (IC), and expiratory reserve volume (ERV) during closed circuit spirometry. Functional residual capacity (FRC) was determined by the helium dilution method and the diffusion capacity ($D_{LCO}$) by the single-breath carbon monoxide method. Helium concentrations were measured by means of a Collins helium catharometer and carbon monoxide concentrations by a Beckman Model IR-L5A infra-red analyzer. Forced expiratory volumes at one second and at three seconds ($FEV_{1\ sec}$, $FEV_{3\ sec}$), and maximum mid-expiratory flow rates (MMFR) were calculated from forced vital capacity (FVC) maneuvers; the $CO_2$ absorber was bypassed in the circuit and the recirculation motor switched off. All measurements were made in triplicate, and the results read as the means of each set of three values. Volumes, corrected to body temperature, ambient pressure, and saturated with water vapor (BTPS), were also recorded. Diffusion capacities are expressed at standard temperature and pressure, dry (STPD).

The volumes of VC, FVC, $FEV_{1\ sec}$, $FEV_{3\ sec}$, and MMFR were subjected to a statistical analysis of variance for each set of values, excluding those obtained immediately upon reaching altitude. In addition VC, FVC, and $FEV_{1\ sec}$ volumes were subjected to a simultaneous significance test (Newman-Keuls).

Brachial arterial blood was drawn from the subjects at rest for determinations of $pO_2$, $pCO_2$, and pH by means of an Epsco blood parameter analyzer and associated electrode systems.

## SIMULATED ALTITUDE STUDIES

After completion of the ground-level studies all of the subjects, except Subject 2, were exposed to a simulated ascent to 14,000 feet altitude in a low pressure chamber. Maximum altitude was reached in approximately thirty minutes. The men remained at this altitude for thirty-six hours during which time temperature of the chamber was maintained at between 50° and 75° F. Immediately on arrival at 14,000 feet, FVC was determined in eight of the eleven subjects. Then after 12, 24, and 36 hours at altitude the following tests were carried out: Harvard step test for one minute at 20 steps per minute, followed by post-exercise electrocardiographic monitoring, VC, FVC, $FEV_{1\ sec}$, $FEV_{3\ sec}$, and MMFR. In addition, after 12 and 36 hours brachial arterial blood was drawn for determination of $pO_2$, $pCO_2$, and pH.

## POST HYPOXIC EXPOSURE TESTS

After completion of the low pressure chamber exposure all pulmonary function tests except arterial blood gas determinations were repeated. All subjects were re-interviewed, and follow-up electrocardiograms and chest x-rays obtained from those subjects who had manifested unexpected changes during the ground-level or chamber studies.

# RESULTS

## BASELINE

All subjects were found to be in good health. Subject 7 gave a history of asthma up to age 10 and at the time of the physical examination was recovering from a mild, upper respiratory infection. Rhonchi were scattered throughout both lungs but cleared with coughing. Seven subjects had been smoking an average of one pack of cigarettes per day for the past seven years. Two others had stopped smoking no less than one year previously, and two others had never smoked.

The range in baseline biochemical data is summarized in Table I. All values were found to be within the normal range except for an elevated atherogenic index (106) in Subject 2 and an elevated reticulocyte count of 13 in Subject 6.

The fasting electrocardiograms of eight subjects showed sinus arrhythmia. In the tracing of Subject 12 there was an S1 S2 S3 pattern, and in that of Subject 9 there was a wandering atrial pacemaker with intervals resembling A-V dissociation. This latter arrhythmia disappeared after exercise and also was abolished by intravenous injection of atropine.

All subjects, except Subject 2, completed the three baseline Harvard step tests. The electrocardiograms of five subjects after exercise showed nonspecific flattening of the T wave on two or three of the tests; one subject's ECG had inverted T waves on the four- and five-minute tests, and one on the five-minute test only (Table II).* There was significant ST depression on the tracings of Subject 3 after the four-and five-minute step tests and of Subjects 1 and 6 on the five-minute test only (Table III).

## SIMULATED ALTITUDE

Subjective symptomatology experienced by the men during exposure to 14,000 feet simulated altitude is listed in Table IV. Eight of the nine subjects who completed the altitude exposure experienced varying degrees of altitude sickness while the remaining subject was symptom free at all times. These eight subjects experienced anorexia, nausea, and headache. The headaches varied in intensity from mild to severe and began about an hour after ascent, lasting for up to thirty hours. Six of the eight subjects

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*For convenience of the reader in comparing the data, the separate pre- and post-altitude findings are presented in the same table.

vomited (Table IV). It can be noted that Subject 9 was removed from the chamber after six hours because of severe nausea and vomiting and that Subject 10 was removed after eighteen hours because of malaise, headache, repeated vomiting, and a pyrexia of 101° F. The latter subject had completed the first altitude step test (1 min. at 20steps/min) prior to his removal, and his electrocardiogram showed inversion of the T waves in $V_{2-4}$ and significant ST depression in $V_4$. These changes reverted after descent to ground level and with administration of 100 per cent oxygen for thirty minutes.

All subjects who remained in the chamber, except Subject 3, completed the step tests at the 12, 24, and 36-hour intervals. This subject's electrocardiogram showed a significant ST depression on the step test given at 12 hours; therefore, he was not tested at 24 or 36 hours. His tracing also showed nonspecific T wave changes. Those subjects completing all the step tests at altitude showed varying degrees of T wave flattening on their ECG's. One of the two subjects whose ECG tracings demonstrated T wave inversion on a ground-level step test also had a record with inverted T waves on the 36-hour altitude step test. One subject's tracings which had shown no ground level T wave changes on exercise now demonstrated inverted T waves on the 24-hour altitude step test (Table II).

In addition to the ST depression already noted in the record of Subject 3, the tracings of another subject which had shown baseline ST depression after exercise now showed no depression at altitude. In that of the third which had shown such change, the ST was depressed after the exercise only at 36 hours. In those with normal tracings at ground level, the ST was depressed in one record at 12 hours, and in two at 36 hours of simulated altitude (Table III).

As compared to the ground-level value at rest, the resting frontal T vector at altitude shifted leftward in six subjects but with exercise the shift varied considerably. In the electrocardiograms recorded at ground level, after exercise there was a leftward shift in five subjects and a rightward shift in six. At altitude the direction of the shift remained the same, but the magnitude lessened (Table V).

There was no change in the mean frontal QRS vector before exercise and subsequent to exercise less rightward shift than at ground level (Table VI). The post-exercise QRS vectors of Subject 5 showed a marked leftward shift.

The mean QRS frontal vector was unaltered at altitude but showed a tendency to shift rightward at ground level with exercise.

The marked variation in the average delta QRS-T angles (Table VII) which ranged from +30° to 3.3° before and after exercise at altitude was not expected. There was a shift in QRS-T angle of 24 degrees or more in the ECG's of four subjects; in the remainder the shift was less than 10 degrees, with a mean of 8.5 degrees (Table VIII).

There was no significant difference between the R-S ratios at ground level and at altitude nor were there significant intragroup differences (Appendix Table A I). All subjects showed the expected clockwise shift secondary to both exercise and exercise during hypoxia.

Resting pulse rates at altitude showed considerable individual differences, the group average resting rate being increased 15 beats per minute over the ground-level average. The average rise in pulse rate immediately following exercise was similar to that for the same level of exercise at ground level, although there was a relative increase at the 24-hour and decrease at the 36-hour step tests (Appendix Table A II).

Respiratory rates and apparent depth of respiration varied considerably in all subjects throughout the altitude exposure. All subjects showed varying degrees of cyanosis and, when asleep, Cheyne-Stokes respiration with periods of apnea lasting several seconds. Since arterial blood samples were drawn prior to spirometry and exercise testing, blood gas tensions reflect values obtained after the subjects had been asleep or inactive for several hours. The 12-hour blood gas values for Subject 12 have been excluded since the procedure triggered an episode of acute excitement and hyperventilation. The mean value of $pO_2$ for the remaining ten men dropped 60 mm Hg and of the $pCO_2$, 10 mm Hg. The mean pH rose from 7.40 to 7.46. There was no significant difference between the 12- and 36-hour values.

Table IX lists the change in VC and FVC expressed as a percentage of the ground-level value for each subject. While VC and FVC values showed the same general trend, the differences between them were almost certainly due to individual subjective effects, in part a learning effect and in part inability to cooperate fully due to malaise. There was a mean reduction of about 4 per cent in VC and FVC but with considerable individual variation. $FEV_{1\ sec}$ volumes and MMFR increased with altitude, also with considerable individual variation (Table X).

The results of the statistical analyses of these parameters are shown in Tables XI and XII. It can be seen that there is a significant difference between values obtained at altitude and those obtained at ground level but no significant difference between values obtained at 12, 24, and 36 hours. Except for the improvement in post-altitude $FEV_{1\ sec}$ there was no significant difference between ground-level values obtained prior to and following the altitude exposure. There was a significant intersubject difference in the magnitude of changes in each set of measurements and a less significant difference among the triplicate values from which the mean was derived for each set of measurements. The differences among the triplicate values indicated that although the majority of subjects performed consistently, others did not. Because of the small size of the sample this inconsistency becomes significant although the same would have applied to maximum values had these been used instead of the mean of each set of three values.

Apart from the $FEV_{1\ sec}$ volumes and MMFR there was no significant difference between postaltitude ground-level values and those obtained prior to the altitude exposure. Although there was no change in the group mean $D_{LCO}$, Subjects 3 and 4 showed a definite fall in postaltitude $D_{LCO}$ but remained above their predicted values. In the absence of other findings, the significance of this change is not clear.

All six subjects whose $FEV_{1\ sec}$ values were measured on descent to ground level showed a loss of the improvement seen at altitude but in one this was still a definite improvement over his prealtitude values. It was not possible to limit smoking prior to the ground-level evaluation, but smoking was prohibited during the altitude study. The improvement resulting from the absence of the acute effects of cigarette smoke on airway conductance (14) and relief of any bronchitis present would have become noticeable because of the high proportion of smokers in the group. This is further suggested by the lack of improvement in the only nonsmoker among six subjects.

## ANTARCTIC FOLLOW-UP STUDY

One of the investigators (HSP) was able to visit the subjects in the Antarctic and to re-test them on the Plateau at a pressure altitude of 13,500 feet and also after their return to sea level. Two of the original group of eight men from the Mobile Construction Battalion Six had been transferred to new assignments. Before reporting to the Plateau Station four of the men had spent eleven days at the South Pole at 9600 feet, the remaining two, seventeen days. Thus, at the time of the visit, four of the subjects had been at the Plateau for twenty-two days and two for twenty-three days.

None of the subjects had any major difficulty adapting at the South Pole station although they all noted slight dyspnea on exertion. Two of the men had slight headache on the first day only, but there was no significant nausea or vomiting. Upon transfer to the Plateau Station all subjects noted a marked increase in dyspnea on exertion and one, Subject 10, had a headache which lasted for twelve hours, accompanied by profound anorexia for seven days. On the tenth day after arriving at Plateau Station, Subject 7, following a sudden prolonged period of exertion, developed a dry but persistent nonproductive cough and noted "chest congestion." He stated that he was unable to stop coughing for two hours and had difficulty sleeping that night due to dyspnea while supine. On the following morning he began to cough again and noted blood tinged sputum. The Base physician noted rhonchi in the left midlung area and prescribed a mucolytic. Following therapy there was a gradual subsidence of this physical finding.

On the last day of their stay at Plateau, Subjects 5 through 10 received a baseline standard 12-lead electrocardiogram; a Harvard step test (1 min at 20 steps/min); pulmonary function studies including VC, FVC, $FEV_{1\ sec}$, $FEV_{3\ sec}$, and MMFR utilizing a 9

liter Collins Spirometer; and a VC and mean expiratory flow rate (MEFR) utilizing a Vitalor Spirometer Model No. VC-25-A. Within six hours after return to sea level repeat baseline electrocardiograms and Harvard step tests were obtained and Vitalor pulmonary function studies made.

At this time a complete interval history and physical examination were obtained as was a blood count including a differential and reticulocyte count. Thereafter the electrocardiograms and Harvard step test were repeated daily for four days; the reticulocyte counts and posteroanterior and lateral chest roentgenograms were repeated every other day for four days.

The baseline 12-lead standard electrocardiograms at altitude revealed a slight increase in rate over the baseline ground-level studies reported previously. The Harvard step tests revealed no significant change in the mean frontal QRS vectors, T vectors, nor in the delta QRS angles. There were no significant ST or T wave changes at altitude.

However, upon return to sea level the baseline electrocardiogram of Subject 8 revealed a diphasic T wave in $V_1$. In the tracings of Subjects 6 and 10 the T of $V_1$ was inverted whereas it had been previously upright, and in Subjects 5, 7, and 9 the T waves were inverted in $V_1$ and $V_2$ whereas they had been previously upright. The changes were seen both in the standard 12-lead baseline tracings and in the Harvard step test. At the end of four days of serial tracings all T wave changes had reverted to their normal configuration. The chest films revealed no significant changes as compared with a prior series. The serial reticulocyte count utilizing cresyl blue and methyl blue maintained normal levels throughout. There was an initial right shift in the differential count which returned to normal within two weeks after return to sea level (Appendix Table A III).

The pulmonary function data obtained at Plateau revealed the expected increase in flow-dependent measurements whereas volume measurements returned toward ground level values. Unfortunately, sea level values obtained after descent from Plateau were limited by the volume range of the Vitalor spirometer (5 liters) so that useful comparisons could not be made.

## DISCUSSION

The incidence of acute mountain sickness in the unacclimatized subject markedly increases with altitudes in excess of 10,000 feet, particularly when ascent is rapid. The rate of ascent used in this study was designed to simulate flight in a nonpressurized aircraft from sea level to 14,000 feet with ascent taking approximately thirty minutes. While the high incidence of acute mountain sickness was expected, that of nausea and vomiting was not. Barcroft (15) considered headache, nausea, and vomiting to be part of the fully developed syndrome of acute mountain sickness although McFarland (16) and more recently Pugh and Ward (17) have found these symptoms to be uncommon. Armstrong (18) differentiated between acute mountain and acute altitude sickness, and pointed out

that the latter, being associated with flight, was associated with rapid ascent and lack of exercise while at altitude. He listed headache as being the most common symptom above 12,000 feet, in acute altitude sickness. While the distinction between the two types of sickness is tenuous, headache is undoubtedly potentiated by more rapid ascent and when severe is responsible at least in part for the increased incidence of nausea and vomiting.

There is still a wide divergence of opinion about the exact etiologic factors and mechanisms included in producing high altitude pulmonary edema. Most investigators agree that hypoxia plays the central role, but there is considerable speculation concerning other factors. For example, pulmonary hypertension has been noted by many investigators after right-sided catheterization studies in patients with this syndrome; yet, in few patients with pulmonary hypertension does pulmonary edema actually develop. Cournand (19) has stated, "It is interesting to speculate that pulmonary edema at high altitude develops at the end of an exhausting day, especially when people are resting at night. Three factors then may be important to consider: first, that the exhausted climbers are trying to sleep flat on their backs, and that therefore their venous return increases in this position as compared to what it was while standing or standing and at rest; second, that the heart rate at high altitude increases considerably during the night, and third, that oxygen saturation in the arterial system drops markedly during sleep." He then concluded by saying, "One cannot exclude the possibility that left ventricular failure is the initiating factor in pulmonary edema at high altitude and that it is caused by a combination of very rapid heart rate, increased venous return, and hypoventilation, causing more severe hypoxemia." Other authors have suggested additional factors such as hypoxic capillary endothelial damage increasing permeability, deep respirations which lead to large, rhythmic reductions in intrathoracic pressure, pulmonary venous constriction, inadequate reacclimatization following return to high altitude after a stay at a lower level, pulmonary infection and alkalosis which aggravate hypoxia both at the tissue and at the respiratory levels in susceptible people. Houston (6), acting as a moderator on a panel for Pulmonary Edema at High Altitude, noted that "there is a definite predisposition of certain persons to develop this condition repeatedly while others who are exposed to identical conditions never are afflicted. In a series of cases collected in South America there was a history of prior descent to sea level by previously acclimatized individuals followed by rapid reascent to his formerly well tolerated altitude with subsequent development of pulmonary edema." However, in his own series gathered in North America this relationship was not noted. Hultgren et al.(7) emphasized the importance of determining whether these people have underlying cardiac or pulmonary disease or an abnormal response to hypoxia. Their studies revealed no apparent abnormalities of the pulmonary circulation in patients who had experienced high altitude pulmonary edema and no difference in their response to short periods of acute hypoxia compared to acclimatized high altitude residents. They stated, "Previous clinical studies have not demonstrated any evidence of heart disease in a number of similar patients." Singh et al.(10) concluded that the clinical, radiological, and electrocardiographic findings are all against high altitude pulmonary edema being caused by myocardial

weakness. Fred et al.(9) reported the study of two episodes of acute pulmonary edema in a 48-year-old physician and noted that following a detailed physical examination and laboratory studies, no evidence of pulmonary infection or cardiac disease was noted. Cardiac catheterization studies during one of these episodes revealed an elevation of pulmonary artery pressure and a normal left atrial pressure. However, Menon (11) found a significant improvement in 66 of his patients who were treated with digitalis after oxygen inhalation had been used without success. He then suggested that the etiology of the condition might be myocardial dysfunction secondary to hypoxia.

Since the possibility of left ventricular failure contributing to the development of altitude pulmonary edema has not been definitely excluded, an attempt was made in our study to place a considerable stress on the cardiovascular system both at ground level and at altitude. While the ground-level step tests adequately stressed most subjects, it became evident that the altitude stress might have been increased. The significance of the ST depression seen in the ECG's of several subjects, either at ground level and/or altitude, remains open to question. It would appear to represent a change in the ventricular gradient not seen in other members of the study. While this could reflect myocardial ischemia, it might also reflect the atrial T wave or a change in ventricular conduction. The electrocardiographic findings among our subjects revealed considerable individual and intragroup variations.

The T wave inversion in $V_{2-4}$ on the Harvard step test at altitude in Subject 1 was similar to the T wave inversion reported by Milledge (20) during the 1960-61 Himalayan Scientific and Mountaineering Expeditions. Milledge's subjects, however, were partially acclimatized. He found inverted T waves in the right precordial leads of all tracings, which tended to spread across the chest with prolonged exposure of the subjects. In the present study one other subject had an ECG with inverted T waves at altitude, and these appeared in lead II. In Milledge's study, the frontal T vector tended to follow the QRS frontal vector to the right. Penaloza (21) has found that with exposure to hypoxia, the T wave tended to shift backward without variation in the frontal plane.

The changes in vital capacity and expiratory flow rates with altitude were similar to those described by other authors (22, 23). These changes occurred immediately upon ascent and persisted without significant change throughout the 36-hour exposure. The improvement in VC seen in Subject 7 on descent to ground level was undoubtedly due to improvement of his mild respiratory infection.

When considering the improvement in $FEV_{1\ sec}$ and $FEV_{3\ sec}$, it is important to note whether these values are expressed as volume or as a percentage of FVC. Thus, if the actual $FEV_{1\ sec}$ volumes were unaltered at altitude and the FVC reduced, when expressed as a percentage, the result would indicate a relative increase. For the purpose of this report the statistical analysis was carried out on the actual volumes, and, for convenience, these volumes have been expressed as a percentage of the ground level value (Table X). It can be seen from this table that there is an actual increase in the $FEV_{1\ sec}$ volumes

expired at altitude but that the $FEV_{3\ sec}$ volumes are slightly decreased. However, because of the reduction in FVC at altitude, the $FEV_{3\ sec}$ expressed as a percentage of the FVC is slightly greater than at ground level.

The blood gas values indicate that all subjects hyperventilated at altitude. Since the arterial $pO_2$ is a function of alveolar ventilation, hyperventilation, while increasing the $pO_2$, results in a secondary fall in alveolar and arterial $pCO_2$. Thus, adaptation involves a balance between acceptable degrees of hypoxemia and hypocapnea. The effect of further hyperventilation, more nearly approximating inspired and alveolar $pO_2$, is seen in Subject 12 who hyperventilated during the arterial puncture procedure.

The initial acclimative response has been described by Rahn and Otis (24) as a period of hyperventilation during which $CO_2$ elimination results in a lowering of alveolar and tissue $pCO_2$ and a rise in arterial pH. During this phase, described by Riley and Houston (25) as the period of $pCO_2$ equilibration, $CO_2$ elimination exceeds tissue production so that the respiratory exchange ratio is elevated and the body $CO_2$ stores depleted. When equilibrium is reached at the end of this first phase, the respiratory exchange ratio returns to normal, but there is a state of respiratory alkalosis with an elevated arterial pH. During the second phase, the period of bicarbonate equilibration, the rate of return of the pH is ultimately dependent upon the rate of electrolyte excretion by the kidneys. The present experiment therefore extends no further than the initial stages of bicarbonate equilibration and prior to any return of arterial pH towards normal.

## OBJECTIVES OF THE STUDY

The purpose of this study was to record various cardiorespiratory values for each individual within the group at a baseline state and during a short exposure to moderate hypoxia in order to have such information available should any problems arise during his sojourn in the Antarctic. Of particular interest would be the development of acute pulmonary edema at altitude since, of the numerous incidences so far reported, none had been investigated fully before the edema developed. Several patients have been studied during an attack and followed into recovery and prior to reexposure but so far hypothesis concerning the condition preceding the attack has been purely speculative and might well be considerably biased by changes secondary to the attack itself. Acute pulmonary edema of altitude has been extensively discussed elsewhere; however, it is pertinent to mention certain aspects here.

The condition has never been reported as occurring in a decompression chamber where temperature and humidity are rarely controlled and daily total exercise levels are usually much less than in an unrestricted environment. While exercise is not invariably associated with the onset of acute pulmonary edema, it does appear to have been the precipitating factor in many reported cases. One of the problems to be faced in an investigation of the mechanism of acute pulmonary edema of altitude is the selection of the numerous possible factors worthy of closer scrutiny. A further complication is that it is likely that multiple factors, including considerable individual variation, are involved.

Until the causative factors can be consistently reproduced in a decompression chamber there is a need for a systematic epidemiological approach in the field using well-documented groups of subjects. The present group, and those who will succeed it, provide ideal material for such a survey. This group, therefore, has served as a pilot study to establish what can reasonably be accomplished in the laboratory and subsequently in the field without interfering with their primary (military) duties and without overly sophisticated experimental procedures or equipment.

Of the many factors in the causation of pulmonary edema, one, of which there is no doubt, is that all cases so far reported occurred after rapid ascent to altitude, usually above 10,000 feet, without adequate time for full acclimatization or reacclimatization. Secondly, clinical pulmonary edema was recognized only after a definite time lag, usually 24 to 96 hours following ascent to altitude, and it was felt that the edema had a progressive development rather than an instantaneous one. Thus it is likely that there is a significant incidence of subclinical pulmonary edema which never progresses to the overt condition, although a systematic search for this has yet to be reported. Examination of the chest x-rays reproduced in the literature reveals that the distribution of the edema throughout the lung fields appears most commonly in the mid-zones but uncommonly in the left apex. This might be explained on the basis of the asymmetric lymphatic drainage of the two lungs with the left upper lobe draining into the thoracic duct and the remaining lung segments draining via the right mediastinal trunk.

This pilot study, therefore, was directed toward detection of early acclimative changes of early edema by simple techniques such as complete daily documentation, physical examination, electrocardiography, and spirometry.

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Table I

Range of Baseline Biochemical Data

| Test | Minimum | Maximum | Mean | Average | Normal Range |
|---|---|---|---|---|---|
| PBI, mg% | 2.8 | 4.2 | 3.6 | 3.5 | 2.8 - 6.4 |
| Cholesterol, mgm% | 161 | 250 | 200 | 200 | 150 - 250 |
| A. I. | 43 | 106 | 52 | 61.5 | 59 - 65 |
| Fasting blood sugar, mgm% | 58 | 86 | 72 | 76.6 | 45 - 95 |
| 2-hr. post 100 gram carb. load, mgm% | 54 | 115 | 77 | 82.2 | >120 |
| K, meq/liter | 3.8 | 4.7 | 4.4 | 4.4 | 3.9 - 5.0 |
| Na, meq/liter | 131 | 139 | 138 | 136 | 133 - 143 |
| Cl, meq/liter | 103 | 111 | 105 | 106.2 | 95 - 105 |
| $CO_2$ content | 26.3 | 30.5 | 28.3 | 28.2 | 21 - 30 |
| HCT, % | 40 | 47 | 45 | 44.4 | 47 ± 7 |
| Retic.count, sea level % | 3 | 13 | 5 | 5.5 | 0.5 - 2.0 |
| Retic. count, during hypoxic exposure % | 4 | 14 | 9 | 8.4 | 0.5 - 2.0 |
| % Deviation lean body mass | -5.17 | +22.22 | +12.7 | 12.7 | - |
| Tilt table pulse pressure | 12 | 30 | 20 | 20.8 | * |
| Tilt table ▲pulse rate | 2 | 30 | 16 | 16.8 | * |

*For a detailed discussion of normal range, see: Graybiel, A., and McFarland, R.A., The use of the tilt table test in aviation medicine. J. Aviat. Med., 12:3-20, 1941.

Table II

T Wave Changes

| Subj No | Harvard Step Test, Sea Level | | | Harvard Step Test ( 1' at 20 steps/min) At 14,000 feet (simulated altitude) | | |
|---|---|---|---|---|---|---|
| | 4' at 30 steps/min | 5' at 30 steps/min | 1' at 20 steps/min | 12 hrs | 24 hrs | 36 hrs |
| 1 | ↑ $V_{4-6}$ | ↓ I,AVF | (-)AVF | (-)II | (-)II | ↓ $V_{2-4}$ |
| 3 | (-)II,III,$V_{5-6}$ | ↑ II,AVF,III | (-)II | (-)II,AVF,$V_{5-6}$ | not done | not done |
| 4 | (-) | (-)AVF,III,$V_{5-6}$ | (-)$V_{5-6}$ | (-)III | (-)$V_{5-6}$ | (-)$V_{5-6}$ |
| 5 | 0 | 0 | 0 | 0 | (-)$V_{5-6}$ | 0 |
| 6 | 0 | 0 | 0 | (-)II | ↓ II | (-)AVF |
| 7 | 0 | (-)$V_{5-6}$ | (-)AVF,III | (-)I | (-)I | 0 |
| 8 | 0 | 0 | 0 | (-)III | 0 | (-)III |
| 9 | 0 | 0 | 0 | not done | not done | not done |
| 10 | (-)AVF,III,$V_{4-6}$ | (-)II,AVF,$V_{4-6}$ | 0 | (-)$V_{2-4}$ | not done | not done |
| 11 | 0 | 0 | 0 | (-)throughout | (-)II,AVF,III | (-)II,AVF,III,$V_{4-6}$ |
| 12 | (-)II,AVF,III,$V_{4-6}$ | (-) | 0 | 0 | (-)$V_{4-5}$ | 0 |

↑ = T inversion. (-) = T flattening. 0 = No significant change.

Table III

S-T Depression

| Subj No | Harvard Step Test, Sea Level | | | Harvard Step Test ( 1' at 20 steps/min) At 14,000 feet (simulated altitude) | | |
|---|---|---|---|---|---|---|
| | 4' at 30 steps/min | 5' at 30 steps/min | 1' at 20 steps/min | 12 hrs | 24 hrs | 36 hrs |
| 1 | 0 | (+) II, AVF, $V_{5-6}$ | 0 | 0 | 0 | 0 |
| 3 | (+) II, AVF, $V_5$ | (+) AVF, III, $V_{5-6}$ | 0 | (+) III, AVF | not done | not done |
| 4 | 0 | 0 | 0 | 0 | 0 | (+) $V_{4-5}$ |
| 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6 | 0 | (+) III, $V_6$ | 0 | 0 | 0 | (-) III, AVF |
| 7 | 0 | 0 | 0 | 0 | 0 | (-) II, AVF |
| 8 | 0 | 0 | 0 | 0 | 0 | 0 |
| 9 | 0 | 0 | 0 | not done | not done | not done |
| 10 | 0 | 0 | 0 | (+) $V_4$ | not done | not done |
| 11 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12 | 0 | 0 | 0 | 0 | 0 | 0 |

(+) = 1 mm or more ST depression. 0 = No significant change.

Table IV

Subjective Response During Hypoxic Period

| Subj No | Response |
|---|---|
| 1 | Headache developed within one hour and persisted throughout stay, Nauseated, vomited once. Profound anorexia. |
| 3 | Headache began 2 hrs after ascent and led to nausea and mild anorexia. |
| 4 | Headache for the first 24 hrs with moderate nausea for 2 hrs. Noted excessive fatigue on Harvard step test. |
| 5 | Headache developed following 12 hrs of exposure. "The Harvard step test for 1 min at 20 steps/min at altitude felt like 4 min at sea level." Had mild anorexia. |
| 6 | Headache developed after 3-4 hrs and lasted 24 hrs with moderate nausea and vomiting. Moderate anorexia. (Felt claustrophobic.) |
| 7 | Headache developed in 30 min and lasted 24 hrs. Nausea, vomited twice. Felt much better after 12 hrs. |
| 8 | Headache developed in 2 hrs and lasted 29 hrs. Little nausea. No anorexia. |
| 9 | Developed severe headache in 1 hr. Vomited four times; felt as if he "couldn't move." Severe malaise, dizziness. Removed from chamber after 6 hrs. |
| 10 | Developed headache, nausea, malaise after 2 hrs. Vomited ten times during 18 hrs in chamber. Removed after temperature noted to be 101°F (oral). |
| 11 | Headache developed within 1 hr with moderate nausea; vomited 3 times. He felt the step test for 1 min at 20 steps/min was easy. |
| 12 | No headache. "Never felt bad." Slight anorexia. No nausea or vomiting. |

Table V

T Angles Frontal Plane

| Subj No | Fasting ECG | Harvard Step Test, Sea Level: 4' at 30 steps/min Pre | 4' at 30 steps/min Post | 5' at 30 steps/min Pre | 5' at 30 steps/min Post | 1' at 20 steps/min Pre | 1' at 20 steps/min Post | Harvard Step Test (1' at 20 steps/min) At 14,000 feet (simulated altitude): 12 hrs | 24 hrs | 36 hrs |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 7 | 16 | -5° | 0 | -19 | 45 | -16 | -30 -45 | -7 0 | -16 -30 |
| ▲ | | -21 | | -19 | | -29 | | -15 | +7 | -14 |
| 3 | 30 | 30 | 0 | 30 | 0 | 15 | 0 | 0 0 | ---- | ---- |
| ▲ | | -30 | | -30 | | -15 | | 0 | | |
| 4 | 60 | 60 | 60 | 50 | 60 | 49 | 60 | 53 71 | 53 5? | 53 57 |
| ▲ | | 0 | | +10 | | +11 | | +18 | 0 | +4 |
| 5 | 45 | 41 | 60 | 55 | 60 | 53 | 67 | 71 60 | 71 90 | 60 79 |
| ▲ | | +19 | | +5 | | +14 | | -9 | +19 | +19 |
| 6 | 30 | 30 | 20 | 30 | 20 | 30 | 30 | -16 -67 | -19 -49 | -30 50 |
| ▲ | | -10 | | -10 | | 0 | | -51 | -30 | -20 |
| 7 | 75 | 75 | 30 | 67 | 60 | 70 | 70 | 90 90 | 90 90 | 65 85 |
| ▲ | | -45 | | -7 | | 0 | | 0 | 0 | +20 |
| 8 | 35 | 35 | 45 | 40 | 75 | 55 | 70 | 35 50 | 60 60 | 50 45 |
| ▲ | | +10 | | +35 | | +15 | | +15 | 0 | -5 |
| 9 | 30 | 30 | ? | 53 | 68 | 60 | 60 | ---- | ---- | ---- |
| ▲ | | | | +15 | | 0 | | | | |
| 10 | 30 | 75 | 60 | 50 | 55 | 50 | 42 | 30 30 | ---- | ---- |
| ▲ | | -15 | | +5 | | -18 | | 0 | | |
| 11 | 65 | 65 | 68 | 71 | 56 | 62 | 70 | 75 63 | 50 60 | 71 64 |
| ▲ | | +3 | | -15 | | +8 | | -12 | +10 | -7 |
| 12 | 67 | 64 | 76 | 64 | 77 | 67 | 74 | 64 65 | 65 71 | 61 62 |
| ▲ | | +12 | | +13 | | +7 | | +1 | +6 | +1 |

- = shift to left in degrees. + = shift to right in degrees.

Table VI

QRS Angles Frontal Plane

| Subj No | Fasting ECG | Harvard Step Test, Sea Level: 4' at 30 steps/min Pre | Post | 5' at 30 steps/min Pre | Post | 1' at 20 steps/min Pre | Post | Harvard Step Test (1' at 20 steps/min) At 14,000 feet (simulated altitude): 12 hrs | 24 hrs | 36 hrs |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 ▲ | 49 | 60 | 73 (+13) | 60 | 68 (+8) | 60 | 64 (+4) | 62 | 71 (+9) | 47 | 60 (+13) | 60 | 67 (+7) |
| 3 ▲ | 75 | 80 | 80 (0) | 82 | 82 (0) | 72 | 78 (+6) | 81 | 87 (+7) | ---- | | ---- | |
| 4 ▲ | 50 | 50 | 50 (0) | 60 | 62 (+2) | 63 | 60 (-3) | 63 | 64 (+1) | 58 | 53 (-5) | 64 | 51 (-13) |
| 5 ▲ | 45 | 41 | 62 (+21) | 30 | 53 (+23) | 23 | 41 (+18) | 46 | 16 (-30) | 24 | 21 (-3) | 30 | 22 (-8) |
| 6 ▲ | 75 | 77 | 88 (+11) | 82 | 88 (+6) | 80 | 85 (+5) | 77 | 83 (+6) | 81 | 82 (+1) | 80 | 80 (0) |
| 7 ▲ | 69 | 72 | 74 (+2) | 74 | 75 (+1) | 75 | 75 (0) | 72 | 72 (0) | 68 | 71 (+3) | 75 | 70 (-5) |
| 8 ▲ | 87 | 85 | 95 (+10) | 90 | 100 (+10) | 85 | 90 (+5) | 90 | 90 (0) | 90 | 90 (0) | 85 | 90 (+5) |
| 9 ▲ | 60 | ---- | | 49 | 30 (-19) | 57 | 30 (-27) | ---- | | ---- | | ---- | |
| 10 ▲ | 84 | 84 | 90 (+6) | 80 | 90 (+10) | 80 | 80 (0) | 81 | 86 (+5) | ---- | | ---- | |
| 11 ▲ | 78 | 78 | 80 (+2) | 79 | 82 (+3) | 79 | 82 (+3) | 78 | 82 (+4) | 77 | 78 (+1) | 79 | 80 (-1) |
| 12 ▲ | 77 | 75 | 84 (+9) | 78 | 87 (+9) | 75 | 73 (-2) | 71 | 71 (0) | 76 | 71 (-5) | 78 | 84 (+6) |
| Calculated mean shift | | +8.4 | | +4.8 | | +1.7 | | +1.0 | | +0.5 | | -0.5 | |

- = shift to left in degrees. + = shift to right in degrees.

Table VII

Frontal QRS-T Angle Before and After Exercise in Degrees

| Subj No. | Harvard Step Test, Sea Level | | | | | | Harvard Step Test (1' at 20 steps/min) At 14,000 feet (simulated altitude) | | | | | | Average ▲ QRS-T | Base QRS-T |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 4' at 30 steps/min | | 5' at 30 steps/min | | 1' at 20 steps/min | | 12 hrs | | 24 hrs | | 36 hrs | | | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | |
| 1 | 44 | 78 | 60 | 87 | 15 | 43 | 92 | 116 | 54 | 60 | 76 | 97 | 24.0 | 42 |
| ▲ | 34 | | 27 | | 33 | | 24 | | 6 | | 31 | | | |
| 3 | 50 | 80 | 52 | 82 | 57 | 78 | 81 | 87 | ---- | | ---- | | 24.0 | 45 |
| ▲ | 30 | | 30 | | 31 | | 6 | | | | | | | |
| 4 | 10 | 10 | 10 | 2 | 14 | 0 | 10 | 7 | 5 | 0 | 11 | 6 | -6.0 | 10 |
| ▲ | 0 | | 8 | | 14 | | 3 | | 5 | | 5 | | | |
| 5 | 0 | 2 | 25 | 7 | 30 | 26 | 25 | 44 | 47 | 69 | 30 | 57 | 5.8 | 0 |
| ▲ | 2 | | 18 | | 4 | | 19 | | 22 | | 27 | | | |
| 6 | 47 | 68 | 52 | 68 | 50 | 55 | 93 | 150 | 100 | 131 | 110 | 130 | 25.0 | 45 |
| ▲ | 21 | | 16 | | 5 | | 57 | | 31 | | 20 | | | |
| 7 | 3 | 44 | 7 | 15 | 5 | 5 | 18 | 18 | 22 | 19 | 10 | 15 | 8.5 | 6 |
| ▲ | 41 | | 8 | | 0 | | 0 | | 3 | | 5 | | | |
| 8 | 50 | 50 | 50 | 25 | 30 | 20 | 55 | 40 | 30 | 30 | 35 | 45 | 6.7 | 50 |
| ▲ | 0 | | 25 | | 10 | | 15 | | 0 | | 10 | | | |
| 9 | 40 | ? | 4 | 38 | 3 | 30 | ---- | | ---- | | ---- | | 30.0 | 30 |
| ▲ | | | 34 | | 27 | | | | | | | | | |
| 10 | 9 | 30 | 30 | 35 | 20 | 38 | 51 | 56 | ---- | | ---- | | 9.8 | 54 |
| ▲ | 21 | | 5 | | 18 | | 5 | | | | | | | |
| 11 | 13 | 12 | 8 | 26 | 17 | 12 | 3 | 19 | 27 | 18 | 8 | 16 | 4.5 | 13 |
| ▲ | 1 | | 18 | | 5 | | 16 | | 9 | | 8 | | | |
| 12 | 11 | 8 | 14 | 10 | 8 | 1 | 7 | 6 | 11 | 0 | 17 | 22 | 3.3 | 10 |
| ▲ | 3 | | 4 | | 7 | | 1 | | 11 | | 5 | | | |

Table VIII

Average Delta QRS-T Angles Before and After Exercise at Simulated Altitude

| Subject Number | | Delta Degree QRS-T |
|---|---|---|
| 9 | | 30.0 |
| 6 | | 25.0 |
| 1 | | 24.0 |
| 3 | | 24.0 |
| 10 | | 9.8 |
| 7 | Mean | 8.5 |
| 8 | | 6.7 |
| 5 | | 5.8 |
| 11 | | 4.5 |
| 12 | | 3.3 |
| 4 | | -6.0 |

Table IX

Effect of 36-Hour Exposure to a Simulated Altitude of 14,000 Feet Upon Vital Capacity and Forced Vital Capacity*

| Subj No | Vital Capacity (VC), 14,000 Feet | | | | Forced Vital Capacity (FVC), 14,000 Feet | | | |
|---|---|---|---|---|---|---|---|---|
| | 12 hrs | 24 hrs | 36 hrs | Post-Alt GL | 12 hrs | 24 hrs | 36 hrs | Post-Alt GL |
| 1 | 93.7 | 93.9 | 91.3 | 103.9 | 98.7 | 97.0 | 95.5 | 102.0 |
| 3 | 100.0 | 101.9 | 96.8 | 103.4 | 103.1 | 103.3 | 98.3 | 103.8 |
| 4 | 95.2 | 93.9 | 98.9 | 100.4 | 99.2 | 98.2 | 97.8 | 99.4 |
| 5 | 96.9 | 99.6 | 99.4 | 108.0 | 95.8 | 98.4 | 95.6 | 99.6 |
| 6 | 92.6 | 91.7 | 92.4 | 97.6 | 93.3 | 92.6 | 93.7 | ---- |
| 7 | 97.8 | 95.7 | 100.2 | 111.6 | 93.9 | 95.2 | 94.8 | 100.0 |
| 8 | 96.9 | 95.3 | 96.3 | 99.3 | 94.8 | 95.0 | 94.4 | 96.9 |
| 9 | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- |
| 10 | 87.6 | ---- | ---- | ---- | 92.1 | ---- | ---- | ---- |
| 11 | 94.3 | 94.4 | 95.1 | 98.2 | 92.9 | 96.4 | 96.6 | 97.8 |
| 12 | 95.3 | 94.7 | 94.4 | 96.3 | 98.2 | 94.3 | 94.3 | ---- |
| Mean N = 9 | 95.9 | 95.7 | 96.1 | 102.1 | Mean N = 7 | 96.9 | 97.6 | 96.1 | 99.3 |
| | -4.1 | -4.3 | -3.9 | +2.1 | | -3.1 | -2.4 | -3.9 | -0.7 |

*GL = Ground Level. All volumes expressed as the percentage of pre-altitude ground level value for each individual.

Table X

Effect of 36-Hour Exposure to a Simulated Altitude of 14,000 Feet upon $FEV_{1\ sec}$, $FEV_{3\ sec}$, and Maximum Mid-Expiratory Flow Rate*

| Subj No | $FEV_{1\ sec}$, 14,000' | | | | $FEV_{3\ sec}$, 14,000' | | | | MMFR liters/second B.T.P.S. | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 12 hrs | 24 hrs | 36 hrs | Post-Alt GL | 12 hrs | 24 hrs | 36 hrs | Post-Alt GL | Pre-Alt GL | 12 hrs | 24 hrs | 36 hrs | Post-Alt GL |
| 1 | 103.2 | 103.5 | 103.2 | 106.8 | 103.2 | 100.5 | 100.8 | 104.5 | 5.2 | 6.7 | 7.4 | 7.0 | 6.0 |
| 3 | 103.4 | 108.7 | 100.3 | 102.5 | 101.8 | 104.1 | 100.8 | 102.8 | 3.0 | 3.0 | 4.1 | 3.1 | 2.9 |
| 4 | 119.0 | 114.5 | 113.8 | 109.1 | 100.2 | 97.5 | 99.2 | 99.0 | 4.0 | 4.8 | 4.7 | 4.8 | 4.6 |
| 5 | 102.6 | 106.8 | 109.1 | 103.7 | 99.6 | 101.3 | 101.6 | 101.1 | 2.7 | 3.0 | 3.2 | 3.5 | 2.9 |
| 6 | 103.2 | 101.4 | 101.6 | ---- | 96.6 | 95.7 | 97.0 | ---- | 7.7 | 11.1 | 10.0 | 10.0 | ---- |
| 7 | 104.0 | 102.4 | 103.7 | ---- | 99.8 | 98.0 | 101.6 | ---- | 2.6 | 3.1 | 3.0 | 2.9 | ---- |
| 8 | 99.7 | 104.5 | 101.9 | 98.2 | 94.4 | 94.7 | 94.1 | 96.9 | 6.4 | 6.8 | 8.3 | 7.9 | 6.3 |
| 9 | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | 4.5 | ---- | ---- | ---- | ---- |
| 10 | 99.2 | ---- | ---- | ---- | 93.5 | ---- | ---- | ---- | 7.2 | 8.2 | ---- | ---- | ---- |
| 11 | 122.3 | 113.1 | 114.1 | 107.6 | 94.5 | 97.8 | 98.1 | 99.2 | 4.3 | 6.2 | 6.2 | 6.2 | 5.2 |
| 12 | 107.2 | 100.0 | 104.5 | ---- | 101.1 | 97.5 | 97.2 | ---- | 5.2 | 6.6 | 6.5 | 6.88 | ---- |
| Mean N = 6 100% | 108.4% | 108.5% | 107.1% | 104.6% | 99.0% | 99.3% | 99.0% | 100.6% | 4.3 | 5.1 | 5.7 | 5.4 | 4.7 |
| | +8.4% | +8.5% | +7.1% | +4.6% | -1.0% | -0.7% | -1.0% | +0.6% | | +18% | +32% | +25% | +9% |

*$FEV_{1\ sec}$ and $FEV_{3\ sec}$ volumes are expressed as the percentage of the pre-altitude ground level value for each individual.

Table XI

Pulmonary Data

Analysis of Variance

| Test | Significant Interactions | Degree of Significance | Number of Subjects |
|---|---|---|---|
| Vital capacity | Altitude | 0.1 | 9 |
| | Subject altitude | 0.1 | |
| | Subject order | 2.5 | |
| Forced vital capacity | Altitude | 0.5 | 6 |
| | Subject altitude | 0.1 | |
| Forced expired volume 1 sec. | Altitude | 0.1 | 6 |
| | Subject altitude | 0.1 | |
| Forced expired volume 3 sec. | Subject altitude | 0.1 | 6 |
| MMFR | Altitude | 2.5 | 6 |
| | Subject altitude | 0.1 | |

Table XII

Newman-Keuls

Simultaneous Significance Test

| Test | At 5% Level of Significance at | Not Significant |
|---|---|---|
| VC | Pre-alt - 12 hr Alt<br>Pre-alt - 24 hr Alt<br>Pre-alt - 36 hr Alt<br>Post-alt- 12 hr Alt<br>Post-alt- 24 hr Alt<br>Post-alt- 36 hr Alt | (pre-alt - post-alt)<br>Any "at altitude" score to any other "At Alt" score |
| FVC | Pre-alt - 12 hr Alt<br>Pre-alt - 36 hr Alt<br>Post-alt - 12 hr Alt<br>Post-alt - 36 hr Alt<br>Pre-alt - 24 hr Alt<br>Post-alt - 24 hr Alt | Any "at altitude" score to any other "At Alt" score<br><br>Pre-alt - Post-alt |
| $FEV_{1\ sec}$ | Pre-alt - 12 hr Alt<br>Pre-alt - 24 hr Alt<br>Pre-alt - 36 hr Alt<br>Post-alt - 24 hr Alt<br>Post-alt - 36 hr Alt<br>Pre-alt - Post-Alt<br>Post-alt - 12 hr Alt | Any "At Alt" score with any other "At Alt" score |

# APPENDIX A

# TABLES

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Table A 1

R/S Ratio $V_4$

| Subj No | Fasting ECG | Harvard Step Test, Sea Level: 4' at 30 steps/min Pre | 4' at 30 steps/min Post | 5' at 30 steps/min Pre | 5' at 30 steps/min Post | 1' at 20 steps/min Pre | 1' at 20 steps/min Post | Harvard Step Test (1' at 20 steps/min) At 14,000 feet (simulated altitude): 12 hrs | 24 hrs | 36 hrs |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2.17 | 3.25 | 1.85 | 4.35 | 1.62 | 3.00 | 2.00 | 2.00 - 1.57 | 2.00 - 1.50 | 1.00 - 1.00 |
| 2 | 1.88 | 2.55 | 1.32 | ---- | ---- | ---- | ---- | ---- ---- | ---- ---- | ---- ---- |
| 3 | 0.25 | 2.50 | 1.56 | 3.60 | 1.50 | 1.00 | 0.64 | 1.08 - 0.72 | ---- ---- | ---- ---- |
| 4 | 3.00 | 19.50 | 8.75 | 14.30 | 5.00 | 15.00 | 15.00 | 12.00 - ? | 2.12 - 5.30 | 6.82 - 5.00 |
| 5 | 2.60 | 2.50 | 1.86 | 2.00 | 1.33 | 5.33 | 4.00 | 3.40 - 3.20 | 2.30 - 1.63 | 6.00 - 3.20 |
| 6 | 2.05 | 7.68 | 1.45 | 6.25 | 1.89 | 8.35 | 5.00 | 5.40 - 3.12 | 14.50 -10.30 | 8.65 - 4.00 |
| 7 | 12.00+ | 15.00+ | 6.50 | 17.00+ | 6.50 | 16.00+ | 30.00 | 21.00+- 9.00 | 18.00+-16.00 | 16.00 -19.00 |
| 8 | 1.80 | 1.80 | 0.86 | 1.84 | 0.78 | 1.12 | 1.25 | 2.40 - 1.67 | 1.57 - 1.25 | 1.57 - 1.25 |
| 9 | 0.91 | 1.22 | 0.69 | 0.88 | 0.69 | 1.00 | 0.88 | ---- ---- | ---- ---- | ---- ---- |
| 10 | 1.00 | 9.00 | 3.17 | 9.35 | 2.94 | 10.03 | 5.75 | 6.40 - 4.42 | ---- ---- | ---- ---- |
| 11 | 4.00 | 23.00 | 2.80 | 6.34 | 2.20 | 22.00 | 5.67 | 6.66 - 4.25 | 7.67 - 4.50 | 16.00+-14.00 |
| 12 | 5.50 | 4.67 | 1.67 | 6.20 | 1.50 | 4.35 | 3.50 | 4.50 - 3.29 | 4.35 - 3.50 | 4.17 - 2.85 |

Table A II

Pulse Rates

| Subj No | Resting | Harvard Step Test, Sea Level: 4' at 30 steps/min Pre | 4' at 30 steps/min Post | 5' at 30 steps/min Pre | 5' at 30 steps/min Post | 1' at 20 steps/min Pre | 1' at 20 steps/min Post | Harvard Step Test (1' at 20 steps/min) At 14,000 feet (simulated altitude): 12 hrs | 24 hrs | 36 hrs |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 70 | 72 | 125 | 85 | 135 | 65 | 100 | 85 - 105 | 88 - 120 | 88 - 120 |
| 3 | 75 | 85 | 170 | 105 | 175 | 75 | 120 | 100 - 130 | ---- ---- | ---- ---- |
| 4 | 68 | 60 | 125 | 75 | 130 | 60 | 80 | 70 - 82 | 70 - 100 | 80 - 85 |
| 5 | 60 | 60 | 130 | 60 | 115 | 60 | 90 | 60 - 80 | 60 - 115 | 65 - 100 |
| 6 | 75 | 68 | 120 | 80 | 130 | 85 | 97 | 105 - 125 | 130 - 120 | 105 - 110 |
| 7 | 55 | 55 | 125 | 60 | 125 | 72 | 89 | 80 - 120 | 80 - 85 | 75 - 90 |
| 8 | 65 | 60 | 115 | 60 | 115 | 55 | 75 | 85 - 97 | 85 - 105 | 75 - 82 |
| 9 | 65 | 65 | 100 | 75 | 125 | 67 | 70 | ---- ---- | ---- ---- | ---- ---- |
| 10 | 60 | 67 | 135 | 75 | 150 | 58 | 82 | 105 - 120 | ---- ---- | ---- ---- |
| 11 | 75 | 65 | 120 | 80 | 140 | 65 | 85 | 100 - 125 | 90 - 125 | 98 - 123 |
| 12 | 68 | 60 | 145 | 84 | 155 | 68 | 90 | 62 - 68 | 72 - 90 | 108 - 118 |
| Average Increase | | | | | | ▲22.50 | | 17.77 | 27.85 | 16.75 |
| Average Pre-exercise | 70.0 | 65.1 | | 75.8 | | 66.3 | | 85.0 | 81.0 | 86.7 |

Table A III

Hematologic Changes Following Return to Sea Level

| Subj No | Date | HCRIT | RET | WBC | SEG | LYM | Mono | EOS | Baso | Bands |
|---|---|---|---|---|---|---|---|---|---|---|
| 5 | 1/22 | 51 | 0.5 | 10,000 | 44 | 52 | 4 | 0 | 0 | 0 |
| | 1/24 | 52 | 0.7 MB<br>0.9 CB | 15,000 | 75 | 24 | 1 | 1 | 0 | 0 |
| | 1/27 | 53 | 0 | 14,000 | 70 | 21 | 3 | 2 | 0 | 3 |
| | 2/2 | 54 | 0 | 7,300 | 54 | 40 | 4 | 2 | 0 | 0 |
| | 2/15 | 49 | 0 | 6,500 | 44 | 53 | 3 | 0 | 0 | 0 |
| 6 | 1/22 | 55 | 0.4 | 8,250 | 45 | 52 | 3 | 0 | 0 | 0 |
| | 1/24 | 54 | 0.4 MB<br>1.1 CB | 7,100 | 42 | 53 | 2 | 3 | 0 | 0 |
| | 1/27 | 56 | 0 | 9,500 | 43 | 53 | 2 | 2 | 0 | 0 |
| | 2/2 | 50 | 0 | 7,900 | 72 | 25 | 2 | 1 | 0 | 0 |
| | 2/15 | 47 | 0 | 8,100 | 70 | 25 | 4 | 1 | 0 | 0 |
| 7 | 1/22 | 50 | 0.6 | 12,850 | 37 | 57 | 5 | 0 | 1 | 0 |
| | 1/24 | 50 | 0.7 MB<br>0.8 CB | 12,150 | 39 | 52 | 7 | 2 | 0 | 0 |
| | 1/27 | 51 | 0 | 10,000 | 65 | 32 | 2 | 1 | 0 | 0 |
| | 2/2 | 49 | 0 | 11,200 | 52 | 42 | 5 | 1 | 0 | 0 |
| | 2/15 | 48 | 0 | 7,250 | 56 | 39 | 5 | 0 | 0 | 0 |
| 8 | 1/22 | 53 | 1.5 | 8,150 | 51 | 45 | 3 | 1 | 0 | 0 |
| | 1/24 | 49 | 1.0 MB<br>1.0 CB | 7,300 | 43 | 45 | 7 | 5 | 0 | 0 |
| | 1/27 | 58 | 0 | 8,100 | 58 | 33 | 3 | 5 | 0 | 0 |
| | 2/2 | 50 | 0 | 7,250 | 69 | 24 | 3 | 4 | 0 | 0 |
| | 2/15 | 46 | 0 | 6,500 | 69 | 38 | 2 | 0 | 0 | 0 |
| 9 | 1/22 | 46 | 0.2 | 11,200 | 54 | 40 | 6 | 0 | 0 | 0 |
| | 1/24 | 47 | 0.2 MB*<br>0.4 CB‡ | 9,300 | 60 | 30 | 8 | 2 | 0 | 0 |
| | 1/27 | 47 | 0 | 8,500 | 61 | 36 | 2 | 1 | 0 | 0 |
| | 2/2 | 46 | 0 | 7,100 | 62 | 31 | 6 | 0 | 1 | 0 |
| | 2/20 | 44 | 0 | 7,000 | 55 | 41 | 4 | 0 | 0 | 0 |
| 10 | 1/22 | 49 | 1.1 | 9,200 | 36 | 60 | 4 | 0 | 0 | 0 |
| | 1/24 | 47 | 1.2 MB<br>1.6 CB | 9,000 | 43 | 46 | 5 | 3 | 2 | 1 |
| | 1/27 | 49 | 0 | 7,000 | 46 | 48 | 2 | 4 | 0 | 0 |
| | 2/2 | 45 | 0 | 13,250 | 54 | 43 | 2 | 1 | 0 | 0 |
| | 2/15 | 44 | 0 | 7,100 | 45 | 49 | 4 | 1 | 1 | 0 |

* Methyl Blue ‡Cresyl Blue

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13 ABSTRACT

The pathogenesis of acute pulmonary edema of high altitude remains unknown. The present study was designed to evaluate the baseline and acute cardiorespiratory acclimation data of a group of young males selected to construct and maintain a scientific station on the Antarctic Plateau (pressure altitude 13,500 feet). Should serious altitude sickness or pulmonary edema develop in any of these subjects, it might be possible to determine which investigations, if any, could be used to screen potentially susceptible subjects and to identify avenues for more extensive studies.

The baseline studies revealed the subjects to be in good health. The acute cardiorespiratory changes, both in the altitude chamber at 14,000 feet after 36 hours and following return to sea level, were similar to those described by other authors. No evidence of overt or insipient pulmonary edema was detected. However, there was an unexpectedly high incidence of protracted nausea and vomiting, necessitating the removal of two of the subjects from the chamber.

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| 14. KEY WORDS | LINK A | | LINK B | | LINK C | |
|---|---|---|---|---|---|---|
| | ROLE | WT | ROLE | WT | ROLE | WT |
| Pulmonary edema | | | | | | |
| Hypoxia | | | | | | |
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