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Urinary Output and Phosphorus Excretion in Human Subjects During Prolonged Exposures at Low Simulated Altitudes.*

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Among the many described effects of anoxia on the organism, those on the urinary secretion and the mineral metabolism are especially difficult of interpretation. Van Liere[1] has reviewed the evidence bearing on the problem and has indicated its controversial status. In neither the lower mammal nor in man are the results in good agreement. The anesthetized dog generally displays oliguria while breathing at reduced oxygen tensions equivalent to altitudes of 14,000 ft. and above, yet considerable variation and polyuria may occur.[2,3,4] In the unanesthetized animal at 18,000-20,000 ft. simulated altitudes polyuria appears to be the typical response.[5,6] Reports on the urinary output of the anoxic human being are also discordant. McFarland and Edwards[7] described increased urine elimination in certain of the crew, but not the passengers, at the beginning of prolonged trans-Pacific flights at altitudes of 8,000 to 12,000 ft. The diuresis was marked in the chronic anoxia experiments of Armstrong and Heim.[8] Urine output was increased from 100 to 300% of normal in subjects maintained for 4 or 7 hours daily at a 12,000 ft. simulated altitude. Bryan and Ricketts,[9] on the other hand, obtained essentially negative results at comparable as well as higher altitudes (11,500-18,000 ft.)

The scanty reports regarding the effect of altitude on the mineral metabolism are similarly conflicting. Acute anoxia in the dog produces a pronounced increase in the renal excretion of sodium, potassium, chloride, as well as lesser increases in the excretion of nitrogen and phosphorus.[5,6] These changes do not occur in the human subject. The species difference is particularly marked as regards phosphorus metabolism. Sundstroem,[10] Lewis *et al.*[6] and Bryan and Ricketts[9] have all demonstrated that phosphorus excretion in the human being is decreased rather than increased in anoxia. The physiological significance of this effect is still unclear. The present study represents one phase of a research project investigating the physiological responses of the human subject during prolonged exposures at moderately low simulated altitudes. The effects on the carbohydrate

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‡ Present address.

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6 Lewis, R. A., Thorn, G. W., Koepf, G. F., and Dorrance, S. S., *J. Clin. Invest.*, 1942, **21**, 33.

7 McFarland, R. A., and Edwards, H. T., *J. Av. Med.*, 1937, **8**, 156.

8 Armstrong, H. G., *Principles and Practices of Aviation Medicine*, Baltimore, Williams and Wilkins Co., 1939, 284.

9 Bryan, H. A., and Ricketts, H. T., *J. Clin. Endocrinol.*, 1944, **4**, 450.

10 Sundstroem, E. S., *Univ. California Publ. Physiol.*, 1919, **5**, 121.

and respiratory metabolism have already been reported.[11,12] This investigation presents data on the urinary output and the renal excretion of phosphorus in individuals maintained in the low pressure chamber at altitudes of 8,000 and 10,000 ft. for periods of 10 hours without supplementary oxygen.

Materials and Methods. The detailed procedure for the experiment has been previously described.[12] The data are based on a total of 72 man runs and represent additional measurements taken in the foregoing investigation. Each of the 5 subjects received at least 6 runs at ground level (800 ft.) and a minimum of 5 runs at the 8,000 or 10,000 ft. level. Flights were taken once weekly and alternated between altitude and ground level. Subjects reported to the laboratory in the post-absorptive state. No attempt was made to control the amount nor composition of the meal taken at the regular mess 12-15 hours the evening before. Various metabolic measurements were made in the initial fasting state and all urine was voided at this time. Each subject was then given a standard K-ration breakfast (884 cal.) with 250 cc of water. After consumption of this meal, the chamber was brought to the desired pressure altitude, and the subjects maintained there at rest for 10 hours breathing ambient air and without food. Although water was allowed *ad libitum* in the major experiment, the present data are based on runs during which no water was taken throughout exposure. The control runs were done in the pressure chamber under otherwise identical conditions. Urine collections were made at the end of the first, third, fifth, seventh, and tenth hours of exposure (the "first hour" collection period represents a 2-hour sample, that is, the time from which the initial fasting urine was voided to the end of the first hour of the experiment proper). Urinary phosphorus was determined by the method of Fiske and Subbarow.[13]

Results. Examination of the data in Table I reveals that the total output of urine at both altitudes studied was not appreciably altered from the ground-level condition. The mean hourly secretion of urine (all subjects combined), as averaged for the entire exposure period, was 55 cc at ground level as against 46 cc (2 subjects) and 59 cc at the 8,000 and 10,000 ft. altitudes respectively. In only one individual (G. B.) was the urine volume consistently and significantly increased at altitude (10,000 ft.) The mean hourly secretion in this instance was 57 cc at ground level and 76 cc at altitude, a mean increase of 25.9% at the 10,000 ft. level.

The characteristic feature of urine elimination, as seen in this study, was the considerable degree of variation found in any individual at ground level or altitude. Urine volumes at corresponding time intervals varied widely in successive runs. As little as 200 cc or as much as 1200 cc of urine were voided over the entire 11-hour period on some occasions. The time in exposure at which maximal elimination occurred also differed among subjects. The highest rates of urine output were found within the first half of the exposure period at ground level or altitude, and very likely represented the elimination of the water ingested with the standard breakfast. There was no evidence to indicate that significant differences existed between ground level and altitude as regards urinary output in early as against late exposure. Total urine elimination for the entire experimental period was of the same order of magnitude in all subjects.

The renal excretion of inorganic phosphorus was significantly decreased in all subjects at altitude (Table II). The reduction bore no apparent relationship to urine volume (Table I). The mean total phosphorus output for the entire exposure period (all subjects combined) was 332 mg (range, 259-392 mg) at ground level, 244 mg (range, 227-261 mg) at 8,000 ft., and 233 mg (range, 195-298 mg) at the 10,000 ft. level. These values represent a mean decrease from the ground level excretion of 29.4% and 22.6% at the higher and lower altitude respectively. Figures for the 8,000 ft. level are based on determinations made in 2 subjects only, in one of

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13 Fiske, C. H., and Subbarow, Y., *J. Biol. Chem.*, 1925, **66**, 375.

TABLE I.
Urinary Output at Ground Level and Altitude with Exposure Time.

Subject	Time (hr)	Ground level (800 ft.)		8,000 ft.		10,000 ft.	
		Vol. (cc)	Rate‡ (cc/hr)	Vol. (cc)	Rate (cc/hr)	Vol. (cc)	Rate (cc/hr)
	*	†					
R.B.	IF-1	123±32		152±33		153±54	
	1-5	262±43		235±18		302±74	
	5-10	184±25	52	196±44	53	198±40	59
S.K.	IF-1	55±27				54±24	
	1-5	452±112				456±135	
	5-10	188±48	63			164±42	61
L.K.	IF-1	86±21		84±17		65±48	
	1-5	232±22		176±48		254±34	
	5-10	242±52	51	172±50	39	242±64	51
G.B.	IF-1	151±49				130±35	
	1-5	266±50				316±52	
	5-10	206±22	57			394±47	76
C.K.	IF-1	74±22				66±18	
	1-5	237±30				212±40	
	5-10	275±42	53			279±51	51
Combined avg			55		46		60

* Represents a 2-hour interval which includes an hour period at ground level when initial fasting determinations were made and breakfast consumed, and the first hour of the experimental period proper.
† Represents the mean urine volume ± the standard deviation.
‡ Refers to the mean hourly secretion of urine over the 11-hour period of observation.

TABLE II.
Phosphorus Excretion at Ground Level and Altitude with Exposure Time.

Subject	Time (hr)	Ground level		8,000 ft.		10,000 ft.		% decrease at alt.	
		P. excr. (mg/hr)	Total P.†	P. excr. (mg/hr)	Total P.	P. excr. (mg/hr)	Total P.	8,000	10,000
R.B.	IF-1	30.8(2.3)*		29.3(3.6)		25.4(4.3)			
	1-5	29.4(2.6)		20.0(3.9)		17.7(3.4)			
	5-10	38.4(2.0)	371	19.6(5.1)	227	20.8(2.3)	226	38.9	39.2
S.K.	IF-1	7.5(2.0)				10.0(0.8)			
	1-5	27.9(3.6)				20.1(2.1)			
	5-10	26.5(1.7)	259			20.6(2.3)	203		21.5
L.K.	IF-1	18.3(2.9)		28.4(2.6)		16.1(3.5)			
	1-5	20.3(2.3)		15.1(2.5)		15.5(2.0)			
	5-10	32.1(2.6)	278	28.7(5.6)	261	20.1(1.4)	195	6.3	30.0
G.B.	IF-1	25.6(4.1)				22.2(2.5)			
	1-5	32.3(5.0)				23.0(3.5)			
	5-10	42.3(3.2)	392			32.3(2.9)	298		23.9
C.K.	IF-1	15.0(2.1)				12.5(2.2)			
	1-5	23.6(4.1)				20.5(3.2)			
	5-10	47.4(3.2)	361			27.6(3.3)	245		32.2
Combined avg			332		244		233	22.6	29.4

* Represents the mean rate of phosphorus excretion, and in parentheses, the standard error of the mean.
† Refers to the total phosphorus excretion for the 11-hour period.

whom phosphorus excretion was just slightly diminished.

Excretion rates at ground level increased with exposure time so that the phosphorus content of urine was substantially greater during the last half of the experimental period. This increase with continuing exposure was either lessened or abolished at altitude, the diminution becoming apparent at either altitude level within the first half of the exposure period. Aside from relatively high values of phosphorus excretion during the first-hour interval in one subject, subsequent values at 8,000 ft. approximated those at the higher level and were significantly lower than those at ground level for corresponding time intervals.

Discussion. The results of these experiments indicate that urinary water secretion is not appreciably affected in the resting subject during prolonged exposures at moderately low altitudes. These findings are in accord with those of Bryan and Ricketts[9] at higher altitudes but fail to confirm the results of Armstrong and Heim[8] at the 12,000 ft. level. The former group exposed subjects to altitude pressures of 11,500, 16,600 and 18,000 ft., for 4 to 6 hours, 6 days a week, from 4 to 6 weeks under controlled metabolic conditions. In only one individual was there a significant increase in the volume of urine passed at altitude (16,600 ft.) McFarland and Edwards[7] did describe increased urine elimination in actual flight at altitudes comparable to those in this study. The polyuria, however, was best associated with the nervous tension of piloting the ship. Diet and fluid intake, moreover, were not controlled.

The considerable variation found in the output of urine, despite controlled conditions of food and water intake, indicates the importance in studies such as these of making sufficient measurements over reasonably long periods of observation. In this regard, it must be stated that the 24-hour urine volume was not determined, nor was the fluid intake for each subject known prior to the experimental period. It is believed, however, that determination of the urine volume over an 11-hour period should reveal any existing effect of moderately low altitude on urinary output. There was no indication that at altitude an initial polyuria occurred which was subsequently compensated for by oliguria, as may occur in the rat. Silvette[14] described a marked and sustained polyuria in rats given daily 3-hour exposures at 15,000 and 25,000 ft., whereas, Swann and colleagues[15,16] found no appreciable change in urine output, despite negative water balances, in longer exposures (6-24 hours) at an 18,000 ft. level.

It becomes evident as studies on anoxia continue that physiological changes begin to occur in the body at altitudes lower than previously thought. The present study indicates that the renal excretion of phosphorus may be affected at altitudes as low as 8,000 ft. We can advance no explanation for this effect at present. Since it is elicited at ground level breathing appropriate nitrogen-oxygen mixtures, it is more clearly attributable to the reduced oxygen tension than the reduced barometric pressure *per se*.[6] In the experiments of Bryan and Ricketts[9] the excretion of phosphorus was definitely decreased in the urine passed at altitude, but the 24-hour output was unchanged. Urinary calcium decreased also, but in a manner unrelated to phosphorus.

Whether or not the diminished excretion of phosphorus is primarily a reflection of an acid-base shift in the anoxic organism, or whether it fundamentally reflects some change in the intermediary metabolism is not clear. Alteration in phosphate concentration of the body fluids in acidotic and alkalotic states is well established. The intimate relationship between phosphorus and carbohydrate metabolism is also well known, and needs no elaboration here. In this study, the phosphorus excretion could not be correlated directly with changes in the respiratory metabolism.[12] Although phosphorus output was decreased to a greater extent in sub-

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16 Collings, W. D., Swann, H. G., Dernehl, C. U., and Cline, J. K., *Fed. Proc.*, 1943, **2**, 7.

jects showing respiratory alkalosis, it appears significant that in the one subject (S. K.) displaying no change in respiration urine phosphorus was appreciably diminished. The changes in the renal excretion of inorganic phosphorus may well reflect some change in the carbohydrate metabolism. Leipert and Kellersman[17] found in human subjects at 5500-6200 meters that a decrease in the phosphorus of blood and urine was compensated for by an increase of phosphate ester in the blood, an effect further augmented by glucose. Similar changes in rats could be correlated with greatly increased liver glycogen. Whether this relationship existed in the present experiments at moderately low altitudes cannot be stated. In this connection, it was found that the blood sugar level remained unaffected at the 8,000 and 10,000 ft. levels.[11]

Conclusions. 1. No appreciable change in total urine output from ground level values was found to occur in human subjects during prolonged exposures to simulated altitudes of 8,000 and 10,000 ft. under conditions of restricted food and water intake.

2. The renal excretion of phosphorus was significantly decreased at altitude.

3. These experiments indicate that alteration in the mineral metabolism may occur in the unacclimatized human being at altitudes as low as 8,000 ft.

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Blood Agglutinins in Filariasis.

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In a recent study of filariasis on Okinawa,[1] data on the frequency distribution of the A, B blood groups were collected. Certain differences in the frequencies of the blood groups, in comparison to the systematic variation in the general population, were noted to occur in filarial patients who had circulating microfilariae; these differences warrant a brief note at this time.

The blood-group percentages of 1,000 persons from the villages of Fukeyama, Jinusza and Soke[2] (approximately 5% of the population) were compared with the frequency distribution of the A, B blood groups in 180 persons, from the same villages, who had circulating microfilariae. The degree of microfilaremia was determined by dilution counting[1] and its relationship to the blood group percentages was also studied. As noted in Table I, the incidence of filaremia is greater in persons whose sera contain no natural antibody to group A red blood cells. When the data were examined without reference to the variables that influence the degree of filaremia, it was found that persons whose blood did not contain α-agglutinins had, as a rule, higher microfilarial counts. High α- and β-isoagglutinin titers (800-1600) were observed in the sera of many filarial patients, even in those who did not have microfilaremia. In several instances, the sera contained ag-

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2 Fink, Harold, report to be submitted.