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Influence of Repeated Daily Exposure to Low Barometric Pressure on Urine Output.*

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Armstrong[1] has reported that humans subjected daily to a simulated altitude of 12,000 feet in a low-pressure chamber excreted on the average 100% more urine than at sea level. An even more marked polyuria has been invariably observed in white rats maintained at a level of 15,000 feet for periods of 3 hr;[2] though in the case of anesthetized dogs breathing low-oxygen gas mixtures, Van Liere *et al.*[3] and Toth[4] have observed oliguria to occur more frequently than polyuria. The present experiments were undertaken to determine whether, on repeated daily exposure to low barometric pressure, this polyuria would be maintained over a long period of time, or whether acclimitization and consequent normal urine output would result.

Healthy male white rats, weighing from 150 to 200 g, were maintained on a stock diet of Purina Dog Chow and liberal amounts of greens, with water allowed *ad libitum*. Food, but not water, was removed from the 12 animals comprising an experimental group 12 hr before the start of an experiment, and the following morning the rats were placed in wire-mesh metabolism cages set over graduated cylinders in a specially-designed low-pressure chamber (capacity 500 liters). The chamber was evacuated to a pressure of

* This investigation has been made with the assistance of a grant from the Committee on Therapeutic Research, Council of Pharmacy and Chemistry, American Medical Association.

1 Armstrong, H. G., *Principles and Practice of Aviation Medicine*, Baltimore, 1939, p. 284.

2 Silvette, H., unpublished observations.

3 Van Liere, E. J., Parker, H. S., Crisler, G. R., and Hall, J. E., PROC. SOC. EXP. BIOL. AND MED., 1935, **33**, 479.

4 Toth, L. A., *Am. J. Physiol.*, 1937, **119**, 127.

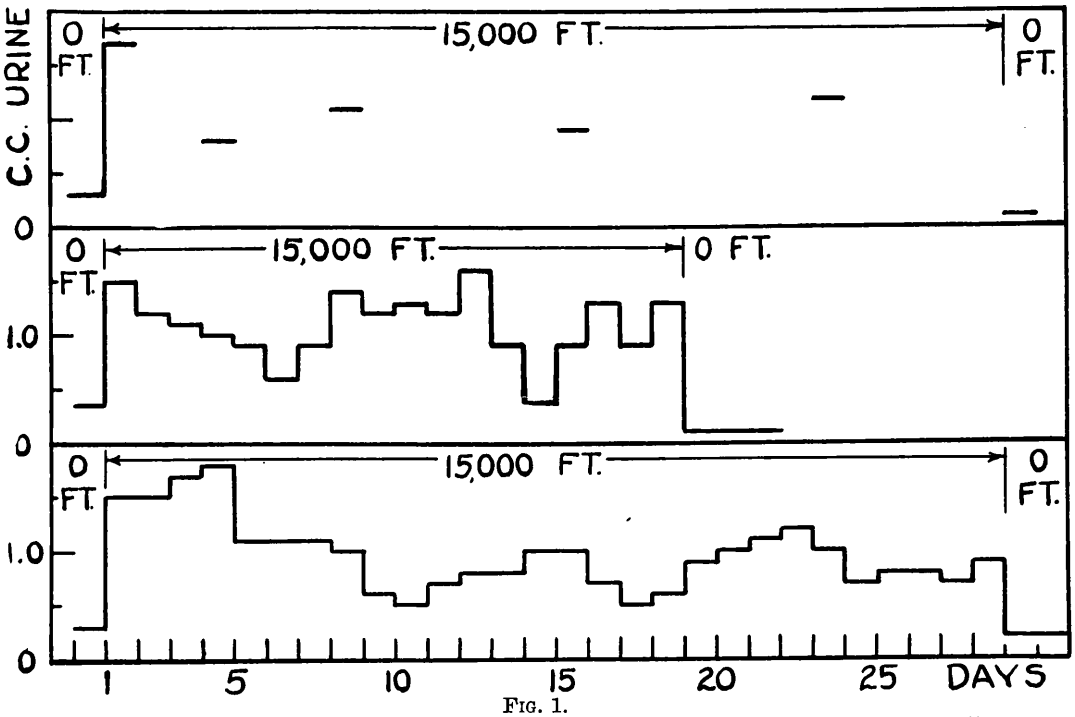

FIG. 1.

Effect of low barometric pressure on urine output of white rats exposed for 3 hours daily to an equivalent altitude of 15,000 feet (428.8 mm Hg).

Bottom curve, group I (12 animals); middle curve, group II (12 animals); top curve, group III (12 animals, *exposed daily* to 15,000 foot altitude, but daily urine collection not made); see text.

428.8 mm Hg (15,000 feet altitude equivalent) and maintained at this level for 3 hr, at the end of which time air was admitted; the animals removed; and the urine volume read and recorded. The temperature of the chamber was not precisely controlled; in each experiment, however, a thermometer inserted through the wall was observed to rise, in the course of the 3-hr period, from an initial 23° to a final 28°C.

A group of 36 animals, placed in metabolism cages for 3 hr at room pressure, excreted an average of 0.4 cc urine per 100 g body weight. The same animals, maintained for 3 hr at 15,000 feet, excreted on the average 1.7 cc, an increase of over 300%.

Three other groups of animals (12 in a group) were run in the low pressure chamber at 15,000 feet altitude equivalent for 3 hr a day for 29, 19 and 29 days respectively. The daily urinary output of the first group, expressed in cc urine per 100 g body weight per 3-hr metabolism period, is graphically shown in Fig. 1. It will be seen that the great initial diuretic response to high altitudes was not maintained. A degree of acclimitization seemed to occur; but at no time did the urine output for the 15,000 feet metabolic period fall to that observed at room pressure, and the average urinary output of the twelve rats throughout the 31 days of the experiment was 1.0 cc compared to 0.35 cc for the same animals at room pressure.

The cyclic character of the curve may perhaps be due to meteorological conditions prevailing during the course of the experiment, for a second group of animals, tested separately over the same period of time, showed a similar cyclic response of alternate profuse and less marked polyuria. In this second group, run for 17 days, no acclimitization to the high altitude was observed, so far as urine output was concerned. When both these groups were tested at room pressure at the end of the experimental period, the urine output was found to approximate that of normal animals never placed in the low-pressure chamber.

A third group of animals, similarly treated, was sacrificed at the end of 29 days, and the kidneys, adrenals, and other organs and tissues removed for weighing and histological examination. The average weight of the kidneys in the group run daily at 15,000 feet was 945 ± 14 mg (probable error of the average) per 100 g body weight; while the average weight of the kidneys in a series of normal animals, under precisely similar dietary and other conditions, save that these control rats were kept continually at room pressure, was 870 ± 14 mg. The kidneys of the experimental animals were 75 mg heavier than those of the controls, and this difference is statistically significant (probable error of the difference, ± 20).

The polyuric response of white rats to daily 3-hr exposure to an altitude of 15,000 feet is thus seen to be accompanied by renal hypertrophy. It should be emphasized that the conditions of the experiment were not critical. The animals emerged from each daily sojourn in the low-pressure chamber with no symptoms of strain or malaise, and during the course of the protracted experiment they gained weight normally and remained in excellent health. Nevertheless, these conditions (daily 3-hr exposure at 15,000 feet) were apparently severe enough to lead not only to hypertrophy of the kidneys, but also to hypertrophy of the adrenal glands and lymphoid tissue, findings which will be reported later by Dr. J. E. Kindred of the Department of Anatomy in another connection.

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The Search for a Physiologically Active Substance in Calf Thymus Tissue.

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During 1940, Bomskov and associates published a series of articles[1] in which they described a new hormone obtained by extracting fresh calf thymus tissue with lipoid solvents. Complete details of the method of preparation were not given. The hormone mentioned is described as the mediator of the pituitary diabetogenic effect, the effector of blood sugar elevation, and the initiator of intense growth. Involution of male gonads and adnexa and inhibition of the effect of the thyrotropic hormone follow its use. Sensitivity to chloroform is increased. The hormone is said to be transported by an increased number of circulating lymphocytes and to be detectable in small quantities of urine. In the tadpole growth is stimulated but metamorphosis is retarded. Greatest secretion and consequent urinary excretion is said to occur in those clinical states which exhibit most marked lymphocytosis, in carcinoma, and in Hodgkin's Disease.

Very recently Wells and associates[2] reported their inability to confirm Bomskov's results. Using the rat and Carneau pigeon as experimental animals they failed to observe any significant blood sugar or liver glycogen variations, ketonemia, or any constant leucocytosis following injection of their extracts. Neither tissue equivalents of extracts used nor nonspecific control tissue extracts were mentioned by these investigators.

The present study was begun two years ago in an attempt to establish the presence of a physiologically active, lipoid solvent soluble

[1] *a.* Bomskov, C., and Sladovic, L., *Deut. Med. Wchnschr.*, 1940, **66**, 589; *b.* Bomskov, C., and Holscher, B., *Z. Klin. Med.*, 1940, **137**, 745; *c.* Bomskov, C., and Sladovic, L., *Pflüger's Arch.*, 1940, **243**, 611; *d.* Bomskov, C., and Brachat, F., *Endok.*, 1940, **23**, 145; *e.* Bomskov, C., and Karl-Heinz, K., *Pflüger's Arch.*, 1940, **243**, 623; *f.* Bomskov, C., *Pflüger's Arch.*, 1940, **244**, 246; *g.* Bomskov, C., *Endok.*, 1941, **23**, 239; *h.* Bomskov, C., *Endok.*, 1941, **23**, 225.

[2] Wells, B. B., Riddle, O., Marvin, H. N., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 473.