WATER DIURESIS IN COLD ENVIRONMENT

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Our previous study indicated that the secretion of antidiuretic hormone from the posterior pituitary gland is reduced on exposure to cold (1). Enhanced water diuresis in cold environment might be attributed to a diminished antidiuretic potency of blood serum. However, cold exposure brings about increased discharge of adrenaline and adrenal cortical hormones which affect the rate of water elimination. These hormones may participate in the cold diuresis. The present study was undertaken to determine endocrine factors associated with the cold diuresis.

METHODS AND MATERIALS

Adult male rats of Wistar strain weighing about 150 g. were used. The rate of water excretion in hydrated animals (5 ml. per 100 g. body weight of water, by stomach tube) was measured by the method of Burn (2). Five milliunits of Pitressin (Parke-Davis) was injected intraperitoneally simultaneously with the water administration. Epinephrine and norepinephrine (Sankyo) and ACTH (Organon) were injected subcutaneously. DOCA (Schering), cortisone acetate and hydrocortisone acetate (Merck) were given subcutaneously two hours prior to the water and Pitressin administrations. In experiments of "cold" rats were exposed to an ambient temperature of 5° C. immediately after water gavage.

Adrenalectomy was performed through a mid-line incision in the skin of the back. Adrenalectomized rats were divided into the following two groups: (a) pellets of cortisone acetate were implanted, and (b) 0.9 per cent NaCl solution was given as drinking fluid. These rats were used for experiments 4 to 7 days after the operation. Demedullation of the adrenal gland was done as follows: The gland exposed through a mid-line incision was incised at the pole opposite to that at which the adrenal artery entered the gland substance. Medullary tissue was sucked out through a glass pipette and residual tissue cauterized electrically. These rats were used after 4 weeks. Pituitary gland was extirpated by the external auditory canal method and the rats were used after 7 to 10 days. Rats thyroidectomized surgically were used 2 to 3 weeks after the operation.

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RESULTS

The rate of urine excretion after water gavage was considerably higher in cold environment (5° C.) than at room temperature of about 20° C., as illustrated in fig. 1. In this figure it is also shown that the antidiuretic effect of Pitressin was distinctly reduced in the cold atmosphere.

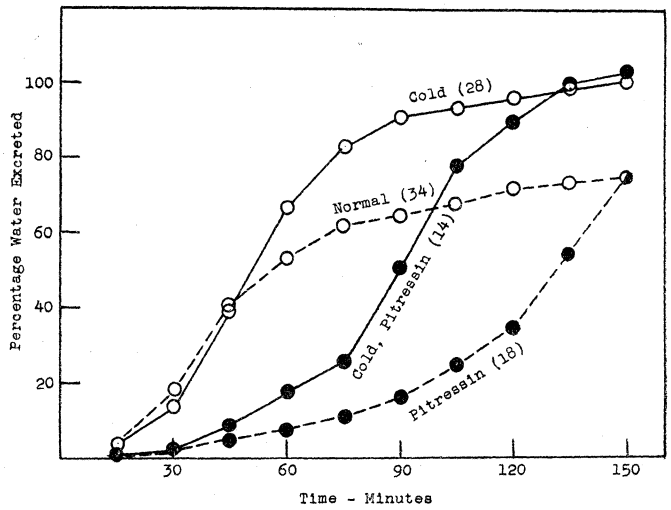

FIG. 1. Effect of cold exposure on the rate of water excretion. Numbers in parentheses represent numbers of rats.

Adrenal medullary hormones which are possibly discharged on exposure to cold may stimulate the water diuresis in the cold environment and antagonize the effect of endogenous antidiuretic hormone. When epinephrine or norepinephrine was subcutaneously injected in a dose of 0.01 mg. per 100 g. body weight into hydrated rats, the rate of water diuresis was not significantly altered. However, 0.04 mg. of these hormones caused a considerable increase in the water excretion rate. If injection of Pitressin was followed by these hormones (0.04 mg.), the antidiuretic effect of the former was markedly reduced (fig. 2). In these experiments the effect of norepinephrine was always greater than that of epinephrine. To clarify the participation of the adrenal medulla in the cold diuresis, demedullated rats were exposed to cold. As shown in fig. 3, the rate of water diuresis at room temperature was considerably low in these rats. However, when these rats were exposed to cold, water excretion was markedly accelerated. This result obviously indicates that the adrenal medulla is not associated with the cold diuresis.

Adrenocortical hormones are known to promote urinary excretion of administered water. The accelerated water elimination may countervail the effect of antidiuretic hormone. In this experiment adrenal cortical hormones were injected subcutaneously two hours prior to the administration of water. On averages, percentages of water excreted at 90 minutes after the water gavage

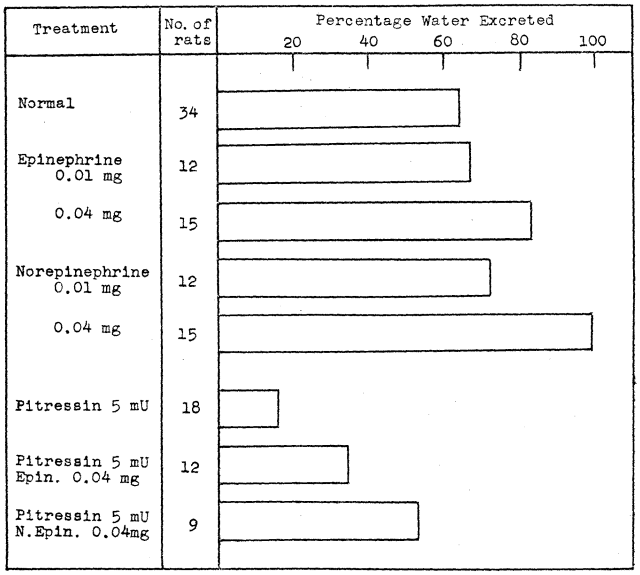

FIG. 2. Effects of epinephrine and norepinephrine on the rate of water excretion. Percentages of water load excreted at 90 minutes after water gavage are illustrated.

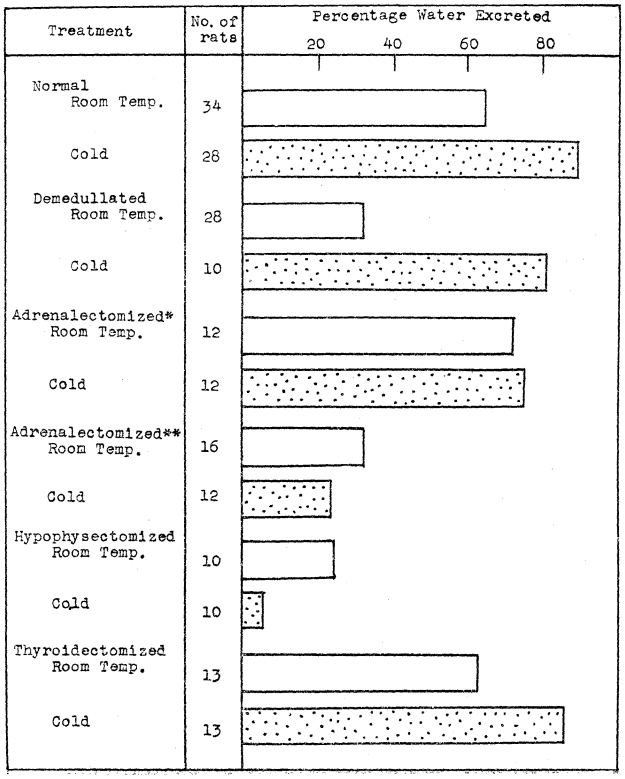

FIG. 3. Effects of adrenal demedullation, adrenalectomy, hypophysectomy and thyroidectomy on the cold diuresis. *This group of adrenalectomized rats was implanted cortisone pellets. **This group was maintained with 0.9 per cent NaCl. Percentages of water load excreted at 90 minutes after water gavage are illustrated.

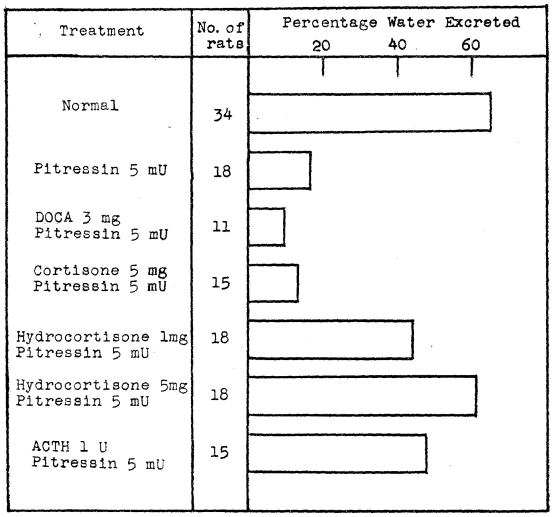

FIG. 4. Effects of adrenal cortical hormones and ACTH on the rate of water excretion. Percentages of water load excreted at 90 minutes after water gavage are illustrated.

were 64.5 per cent in 34 normal control rats and 87.0 per cent after 1 mg. of hydrocortisone in 12 rats. Though the effect of Pitressin was not influenced by prior treatment with 2.5 mg. of DOCA or 5 mg. of cortisone, hydrocortisone in a dose of 1 mg. resulted in a significant subsidence of the antidiuresis due to Pitressin and in a dose of 5 mg. this compound vanished the effect of Pitressin completely. Subcutaneous injection of 1 unit of ACTH caused similar influence as hydrocortisone (fig. 4). To determine whether hydrocortisone is involved in the augmented water elimination due to cold exposure, adrenalectomized and hypophysectomized rats were exposed to cold and the rate of their water excretion was measured. As shown in fig. 3, the water excretion was significantly reduced even at room temperature in rats adrenalectomized and maintained with saline and in rats hypophysectomized, while rats adrenalectomized and implanted cortisone pellets showed normal rate of the water excretion. When these rats were exposed to cold, the rate was not increased. In hypophysectomized rats the rate was rather reduced at low temperature. These results indicate that the adrenal cortical hormone, particularly hydrocortisone, plays a part in bringing about the cold diuresis.

Since thyroid hormone is also known to stimulate water elimination, similar experiment was done in thyroidectomized rats. In this group of rats cold exposure caused a definite increase in the rate of water excretion (fig. 3). It is, therefore, inferred that the thyroid hormone does not participate in the cold diuresis.

DISCUSSION

Discharge of adrenaline under conditions of acute exposure to cold is a well-known fact. However, as to effect of epinephrine and norepinephrine on the urine formation conflicting results have been reported. According to Handley and Moyer (3), epinephrine and norepinephrine cause diuresis at low rates of infusion, but usually reduce urine output when infused at a rate that will increase the mean blood pressure above approximately 170 mmHg. Langston and Guyton (4) claimed that these hormones seem to affect urine formation in two ways: First, by increasing the arterial pressure which indirectly increases urinary output, and, second, by acting directly on the kidney to decrease the output. In hydrated and non-hydrated rats Giere (5) has found that subcutaneous administrations of the adrenal medullary hormones cause increased water excretion. In the present experiments it was shown that relatively small amount of epinephrine and norepinephrine augmented water excretion in hydrated rats and that the effect of these hormones counteracted against the antidiuretic effect of Pitressin. Notwithstanding the above findings, adrenal medullary hormones may not be involved in bringing about the cold diuresis. This is inferred from the fact that demedullated rats did show stimulated water diuresis by cold exposure.

As mentioned already, adrenal cortical hormone, particularly hydrocortisone, was effective to augment water excretion in hydrated rats. Gaunt *et al.* (6) reported that hydrocortisone and predonisolone antagonized the antidiuretic effect of Pitressin, while DOCA in the presence of Pitressin had no effect on water excretion. This finding was confirmed in this study. There is no doubt that the secretion of hydrocortisone increases under condition of cold stress. Accordingly the cold diuresis may be, at least in part, caused by the increased discharge of this cortical hormone. The presumption that the adrenal cortex plays a part in causing the cold diuresis is strongly supported by the fact that adrenalectomy and also hypophysectomy vanish the cold diuresis. On the other hand, thyroid gland seems to be not associated with this diuretic response, since thyroidectomy did not affect the water diuresis due to cold exposure at all.

The present investigation is not intended to dispute the possibility of the participation of the antidiuretic hormone in the cold diuresis. However, it should be noted that the sensitivity of the kidney to the antidiuretic hormone appears to be altered according to the internal circumstances, as indicated in the experiments of cold exposure and those of epinephrine, norepinephrine and hydrocortisone.

SUMMARY

1. In hydrated rats the rate of water excretion increased on exposure to cold. Antidiuretic effect of Pitressin was significantly diminished in a cold atmosphere.

2. In hydrated rats administrations of epinephrine, norepinephrine and hydrocortisone resulted in an increase of urinary excretion of water and

countervailed antidiuretic effect of Pitressin. ACTH showed similar effect. DOCA and cortisone were without effect.

3. In adrenalectomized and hypophysectomized rats cold exposure did not cause any increase in water excretion, while adrenal demedullated rats and thyroidectomized rats showed an increased water excretion on exposure to cold.

4. It was concluded that the secretion of the adrenal cortex participates in bringing about the increased water elimination on exposure to cold.

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REFERENCES

1. ITOH, S. *Jap. J. Physiol.* 4 : 185, 1954.
2. BURN, J. H. *Quart. J. Pharmacol.* 4 : 517, 1931.
3. HANDLEY, C. A. AND J. H. MOYER. *Amer. J. Physiol.* 178 : 309, 1954.
4. LANGSTON, J. B. AND A. C. GUYTON. *Amer. J. Physiol.* 192 : 131, 1958.
5. GIERE, F. A. *Endocrinology* 55 : 448, 1954.
6. GAUNT, R., C. W. LLOYD AND J. J. CHART. *The Neurohypophysis,* p. 233. London : ed. by Heller, H., Butterworths Sci. Publ., 1957.