Appearance of an Antidiuretic Substance in the Urine of Man after Various Procedures. (17628)

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Although there are many reports on the liberation of an antidiuretic substance in the body after dehydration, emotional stress, electrical stimulation and fainting, there are few studies on man of the excretion in the urine of antidiuretic substances. Under most conditions where an antidiuretic effect is noted in the body, the evidence supports the theory that stimulation of the posterior lobe of the pituitary takes place with a resulting release of antidiuretic substance. This preliminary report describes the extraction of an antidiuretic substance from the urine in various conditions and suggests that this substance is due to posterior lobe activity.

Methods. Antidiuretic assay has been conducted by the method of Burn(1) using the 50% urine excretion of the hydrated rat as the standard. Extracts were administered by both subcutaneous and intraperitoneal injection. Some extracts may be toxic and cause an apparent antidiuretic action only on intraperitoneal injection. The results from extracts which show such an effect are therefore discarded and are considered non-specific. The zinc ferrocyanide method for adsorbing posterior lobe hormones from urine described in 1939(2) has continued to yield excellent results.

Results. 1. *Recovery of posterior pituitary extract added to urine.* Extracts of urine from normal individuals do not exhibit any antidiuretic activity even though concentrates equivalent to 24 hour samples are prepared. The extraction process is effective in recovering from 85-100% of the activity when from 1 to 10 units of posterior lobe extract is added to 1 litre of normal urine. For quantitative estimations it is necessary to inject the extracts intraperitoneally. Subcutaneous injections show an apparent increased potency due to the effects of augmentation by substances in the urine extract(2).

2. *Excretion of intravenous posterior pituitary extract.* The urine from 9 subjects who had received doses of 2 to 5 units of pitressin intravenously† has been extracted and assayed. In all cases an antidiuretic substance appeared in the urine and was completely excreted within 3 hours. Quantitative studies on 7 subjects showed a recovery of from 4.8 to 23%, average 11.2%, of the injected pitressin.

3. *Dehydration.* Partial dehydration of 3 subjects has been accomplished by reducing all free fluid intake and restricting the diet to solid foods. All urine samples obtained after 16 to 23 hours of dehydration exhibited antidiuretic activity. In 1 case it was estimated that after 33 hours of dehydration the secretion of posterior lobe hormone by the pituitary was 6.5 mU/kg/min and this increased to 8 mU after 48 hours of dehydration.

4. *Venesection and Fainting.* Seven subjects† were subjected to experimental venesection and transfusion. None of these fainted. Urine samples obtained throughout the experiment did not contain antidiuretic activity. Seven other subjects subjected to the same procedure fainted at some time during the experiment. Urine samples obtained after the faint in all cases contained an antidiuretic substance. Three persons (not associated with the above experiments) who fainted spontaneously also exhibited antidiuretic activity in urine samples collected immediately after the faint.

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1. Burn, J. H., *Biological Standardization,* Oxford Press, 1939.

2. Noble, R. L., Kinderknecht, H., and Williams, P. C., *J. Physiol.,* 1939, v96, 293.

† These experiments and those on subjects subjected to hemorrhage were made possible through the cooperation of Dr. O. G. Edholm, Department of Physiology, and his collaborators.

5. *Blackout.* The urines from 9 subjects‡ who lost consciousness due to experimental acceleration (blackout rating of from 4.0 to 6.5 G) were examined. In no case was antidiuretic activity demonstrated in the urine.

6. *Electro-Convulsive Therapy.* Pooled urine samples were obtained from 3 separate groups of psychotic patients before and after E.C.T. The control specimens were devoid of activity, but following therapy marked antidiuretic activity was found.

7. *Eclampsia.* The urine of 7 cases of pre-eclampsia and of one eclamptic was examined and did not contain antidiuretic activity. The negative findings were not related to the associated albuminuria.

Discussion. The results which have been described show that an antidiuretic substance appears and may be extracted from the urine following certain procedures in man. The evidence, although indirect, indicates that this may be the posterior pituitary antidiuretic hormone. A more detailed discussion of these findings and the possible physiological mechanisms involved will be presented in a later paper(3).

Summary. An antidiuretic substance may be extracted from human urine following the intravenous injection of posterior lobe hormone, dehydration, fainting and electro-convulsive therapy.

The urine of normal persons, and subjects following loss of consciousness associated with "blackout" does not contain antidiuretic activity under the experimental conditions described. The urine of eclamptic women was also inactive.

‡ These experiments were conducted through collaboration with Dr. W. R. Franks, R.C.A.F. Institute of Aviation Medicine, Toronto.

3. Noble, R. L., Plunkett, E. R., and Taylor, N. B. G., *Rec. Advances Hormone Res.*, Vol. IV, Academic Press, N.Y., 1949.

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Production of a Hemorrhagic State by the Infusion of Hemolyzed Blood.* (17629)

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While conducting experiments relative to the development of a mechanical pump-oxygenator for the temporary deviation of blood from the heart and lungs of dogs, hemolysis was frequently encountered. At this time, dogs died of a previously undescribed hemorrhagic state which closely simulated a condition seen on occasion in man. It was therefore deemed advisable to devise a more simple method of reproducing this condition. Since that time, changes in pump-oxygenator have been effective in eliminating hemolysis, and the incidence of this syndrome has been diminished.

This entity is characterized by prolonged or infinite blood coagulation time, and poor clot retraction. This blood will clot *in vitro* by the addition of small amounts of thromboplastin or fresh blood from another dog. This reversal is only temporary *in vivo*, however. Hemorrhage occurs from the entire gut which is contracted, pitted, granular and is studded throughout with petechiae. Bloody effusions invade the serous cavities. Petechiae also appear in the lungs, serosal surfaces and along blood vessels. Microscopically the liver and spleen show parenchymal congestion with erythrocytes and pigment and the kidney tubules and glomeruli also contain pigment. Portions of this syndrome

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