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Course of Diabetes Insipidus Following Hypophysectomy in the Rat.

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In earlier studies on the hypophysectomized rat^{1, 2} we have been particularly concerned with the phase of acute diabetes which immediately follows pituitary ablation, and continues thereafter for several days. Earlier reports have affirmed the transitory nature of the diabetic condition in the rat.^{3, 4, 5} We have now extended our studies of fluid metabolism and urinary chloride excretion to include more protracted periods, up to 80 days after operation. Fluid exchanges were determined in individual metabolism cages fitted with graduated drinking tubes; the urine was collected under toluene in graduated cylinders, and the chloride concentrations determined by means of the Volhard titration.⁶ Over 70 individual tests were made, and the results compared with those obtained from 34 normal animals.

Study of the data obtained has led us to divide the post-operative diabetic state seen in the hypophysectomized rat into 3 arbitrarily determined stages: 1, a primary acute condition persisting for 3 to 5 days, in which polyuria predominates and the water-intake urine-

TABLE I.
Course of Diabetes Insipidus and Hypochloruria Following Hypophysectomy.*

Phase of diabetes insipidus	No. of cases	Post-operative period (days)	Avg water intake (100 g rat)	Avg urine output (100 g rat)	Avg urinary chloride (mg/cc)
Primary acute	30	0-5	6.3	7.1	0.34
Secondary acute	21	5-8	3.6	2.9	1.14
Tertiary chronic	26	8-72	2.3	1.9	2.12
Normals	34		1.7	1.5	2.78

*All metabolism tests were made over a 12-hour period. When repetitive tests were made on the same animals, 2 to 4 days were allowed for "rest" between runs.

¹ Silvette, H., and Britton, S. W., *Am. J. Physiol.*, 1938, **123**, 630.

² Corey, E. L., Silvette, H., and Britton, S. W., *Am. J. Physiol.*, 1939, **125**, 644.

³ Richter, C. P., *Am. J. Physiol.*, 1933, **106**, 80.

⁴ Richter, C. P., *Am. J. Physiol.*, 1934, **110**, 439.

⁵ Pencharz, R. I., Hopper, J., and Rynearson, E. H., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 14.

⁶ Peters, J. P., and VanSlyke, D. D., *Quant. Clin. Chem.*, Williams and Wilkins, 1932.

output ratio (W/U) is less than unity; 2, a secondary (but still acute) phase of about 3 days in which an emerging polydipsia becomes evident and during which water intake exceeds urine output, with an average W/U ratio for the period of more than 1; 3, a tertiary "chronic" condition of mild diabetes in which the hypophysectomized animal shows a slight but constant increased water intake and urine output, with a W/U ratio almost identical with that of normal controls.

These results confirm our own previously published findings and in part those of Richter concerning diabetes insipidus in the hypophysectomized rat. They further indicate that the condition is not "transitory" in nature, but that a mild, chronic diabetic state persists for at least 80 days. The recent observations of Schweizer, *et al.*,⁷ that a polyuric state persists in hypophysectomized rats until they become moribund are essentially in agreement with the above. That the alterations in the diabetic conditions described may be correlated with cortico-adrenal and gonadal atrophy may be considered. In this connection it has recently been shown in this laboratory⁸ that there is a specific antagonism between desoxycorticosterone and post-pituitary extracts in their effects on water balance. The former substance, in normal as well as adrenalectomized and hypophysectomized rats, produced increases in water intake and urine output and reductions in urinary chlorides, while the post-pituitary principle brought about reverse reactions in all cases.

Summary. The polydipsia, polyuria and hypochloruria which follow hypophysectomy in the rat have been described as primary acute, secondary acute, and tertiary or chronic. The mild, chronic diabetes persisted in these experiments for 80 days and terminated only shortly before death.

⁷ Schweizer, M., Gaunt, R., Zinken, N., and Nelson, W. O., *Am. J. Physiol.*, 1941, **132**, 141.

⁸ Britton, S. W., and Corey, E. L., *Science*, in press.