The results demonstrate that the combination of theophylline with these mercurial diuretics modifies their action after absorption as well as before.

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Recovery in the Rat from the Diabetes Insipidus Caused by Posthypophysectomy.

H. G. SWANN.

From the Department of Physiology, University of Chicago.

Richter[1] and Pencharz, Hopper and Rynearson[2] have shown that after removal of the posterior lobe of the hypophysis ("posthypophysectomy") of the rat, with minimal damage to the anterior lobe, there ensues a profuse diabetes insipidus. Both were of the opinion that the condition was permanent; Richter followed the water intake of his rats for about 60 days and Pencharz, *et al.*, for 100 days. White,[3] using rats posthypophysectomized by Pencharz, reported 3 animals to be clearly diuretic a year after operation. In our experience, however, recovery from the diabetes insipidus produced by the same operation customarily occurs in time. Fig. 1 shows the

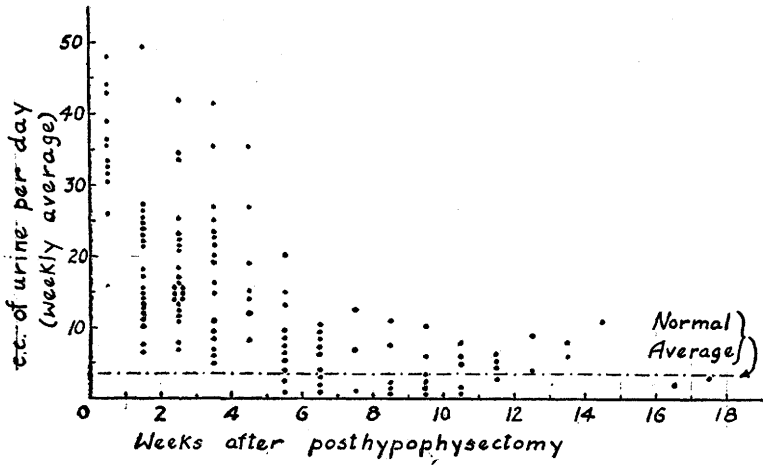

FIG. 1.
Urinary excretory rates after posthypophysectomy in the rat.

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

2 Pencharz, R. I., Hopper, J., and Rynearson, E. H., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 14.

3 White, H. L., *Am. J. Physiol.*, 1937, **119**, 5.

excretory records of a group of 50 rats whose urine output was measured in each case at various times postoperatively. It will be noted that in the rat there is no "latent phase" of low fluid exchange such as is seen in the cat and the dog after denervation of the pars nervosa. By approximately 8 weeks after operation most of the rats were excreting urine within the range of the normal animals. Some rats were excreting at normal rates 6 weeks after operation; but others were still excreting above the normal rate for as long as 15 weeks postoperatively. This same slow recovery has also been observed by Dodds, Noble and Williams.[4] Three rats have been observed for 16 months postoperatively. At the end of this period, they were excreting at a rate of 4-6 cc per day—well within the normal range.

Histologic examination of the contents of the sella turcica of these recovered animals showed normal anterior lobe tissue (also, the females had normal estrual cycles). But invariably there was no remnant of pars intermedia. In the rat this structure surrounds the pars nervosa on all sides except the dorsal; the two structures are so closely applied to each other that it is impossible to pull them apart by traction with aspirators such as are employed in the operation. Therefore, since the surgical technic evidently removes entirely the pars intermedia and since the pars nervosa follows the intermedia in this operation, we feel certain that in the original operation all of the pars nervosa was removed except the few cells left around the attachment of the stalk. However, the histologic examination of the tissues left in the sella turcica of these recovered animals revealed the presence of large quantities of pars nervosa tissue. In some cases it was normal in both appearance and in gross quantity. It had, presumably, regenerated.

Fisher, Ingram and Ranson[5] (*cf.* also Gersh[6]) have emphasized that tissue resembling pars nervosa can be found in the infundibulum and hypothalamus and that all of this tissue must be removed to produce diabetes insipidus in cats. Fig. 1 shows that in the rat diabetes insipidus can be produced by removal of the tissue in the sella turcica only. Its transience, however, we feel to be due to incomplete removal with regeneration from the fragments of infundibular tissue left in the sella at operation.

The "transience" of our diabetes insipidus was far different from

[4] Dodds, E. C., Noble, R. L., and Williams, P. C., *J. Physiol.*, 1937, **91**, 202.

[5] Fisher, C., Ingram, W. R., and Ranson, S. W., "Diabetes Insipidus, etc.," Ann Arbor, Mich. 1938.

[6] Gersh, I., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 395.

that reported in dogs and monkeys by Keller, Noble and Hamilton[7] and by Mahoney and Sheehan.[8] Whereas their transient diureses are light and relatively short in duration (approximately 3 weeks), the diuresis in the rat was great (averaging 200 cc per kilo) and long in duration (8 weeks).

Although recovery can be shown in rats, no such phenomenon has been observed in cats after lesions to the supraoptico-hypophyseal tracts which causes a functional insufficiency of the pars nervosa.[5] The Ranson group have observed no recovery in one cat for 9 months after operation and in other animals for 5 months. Several explanations of this difference between their experiments and ours are possible. The most plausible is that mentioned above, *viz.,* incomplete removal of the tissues secreting antidiuretic hormone. That a permanent diabetes insipidus can be produced in the rat has been shown by Richter[9] with a technic entailing the transection of the pituitary stalk.

As has been previously reported,[10] giving these diuretic rats NaCl in their drinking solutions prevented the spontaneous recovery from posthypophysectomy that we have observed in the rat and, in fact, aggravated the diabetes insipidus considerably. It was also found that this aggravation could be prevented by giving $CaCl_2$ along with the saline solutions. Parathormone, however, was found to have no effect.

Studies of the basal metabolic rate in both operative diabetes insipidus and in salt-aggravated diabetes insipidus showed that this constant was not elevated, no matter how great the fluid exchange. It was also found that the presence of the thyroid was not necessary for the continuation of a salt-aggravated diabetes insipidus.

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7 Keller, A. D., Noble, W., and Hamilton, J. W., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 794.

8 Mahoney, W., and Sheehan, D., *Am. J. Physiol.*, 1935, **112**, 250.

9 Richter, C. P., The Pituitary Gland. Baltimore, Md., 1938.

10 Swann, H. G., and Penner, B. J., *Am. J. Physiol.*, 1938, **123**, 199.