fusion of ammonia out of the bath fluid into the air however, may make erroneous an estimation of ammonia removal based on the amount of ammonia in the bath fluid. No fall in blood ammonia was noted on passage of blood through the artificial kidney if the cellophane loops were not immersed in the bath fluid. In fact a small but definite rise in blood ammonia was noted under these circumstances. Normal dogs without portacaval shunts when subjected to hemodialysis in the same manner as those with meat intoxication did not show any appreciable elevation of ammonia in the blood entering or leaving the kidney.

Comment. The invariable lowering of blood ammonia concentrations during passage through the artificial kidney and the appearance of ammonia in the bath water as dialysis proceeded indicated to us that hemodialysis removed blood ammonia in dogs with elevated blood ammonia levels.

We are presently using this method of removing blood ammonia to study certain aspects of liver disease. Whether hemodialysis may have any clinical value in the treatment of hepatic coma is also being investigated.

Summary. Blood ammonia, as measured by the microdiffusion technic of Conway, is removed efficiently from the blood of dogs with elevated blood ammonia levels by a Kolff type artificial kidney with a dialyzing surface of 12,000 cm^2. When flow through artificial kidney is 100 ml/minute the clearance of blood ammonia varies from about 50 ml/minute at lower arterial concentrations of blood ammonia to about 80 ml/minute at higher arterial concentrations.

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Hypothalamic Stimulation of ACTH Secretion. (22303)

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It has been shown that antidiuretic and oxytocic hormones of the hypothalamic-posthypophyseal system* may stimulate the anterior lobe of the pituitary gland to discharge ACTH. It has been demonstrated that these hormones produce, when injected into normal animals, significant fall of circulating eosinophils(2), adrenal ascorbic acid (3) and cholesterol(4); these actions which have not been observed in hypophysectomized animals(3,4), are apparently due to stimulation of the adenohypophysis. Release of ACTH occurs also in hypophysectomized rats bearing a hypophyseal graft in the anterior chamber of the eye after local injection of small amount of posterior pituitary hormones into the subconjunctival space(5). This observation rules out the possible participation of a "stress" reaction in the ACTH-releasing power of posterior pituitary hormones. These results are in agreement with the hypothesis(2-6) that hormones produced in the hypothalamic nuclei may act as neurohumoral agents in the hypothalamic control of the activity of the anterior lobe of the pituitary gland.

* There is much positive evidence to support the view that "posterior pituitary hormones" are produced by cells of the nuclei supraopticus and paraventricularis and pass along the axons of the tractus supraoptico-hypophyseus into the posterior lobe which serves as a storage-release center(1).

TABLE I. Effect of Continuous Injection of Antidiuretic (Pitressin, Parke-Davis) and Oxytocic Hormones (Pitocin, Parke-Davis) on Mean Weight of Body, Hypophysis and Adrenal Glands in Normal Rats; 10 Rats in Each Series, Treated 15 Days.

Treatment	Body wt (g) Initial	Final	Hypophysis wt (mg/100 g final body wt)	Adrenal wt (mg/100 g final body wt)
Pitressin (.5 U/rat)	148 ± 5	146 ± 8	4.41 ± .20	15.92 ± .8
Pitocin (.5 U/rat)	158 ± 7	154 ± 6	4.48 ± .21	15.02 ± .9
.9% NaCl	138 ± 5	145 ± 7	4.66 ± .30	11.76 ± .7
Inactivated Pitressin (.5 U/rat)	156 ± 8	162 ± 6	4.35 ± .20	10.85 ±1.1

The experiments here described confirm that both antidiuretic and oxytocic hormones may induce a conspicuous discharge of ACTH; these hormones produce, when chronically injected in normal rats, considerable modifications of adrenal weight and histology, which are prevented by hypophysectomy; injections of hormones previously inactivated with sodium thioglycollate are without any activity.

Methods. Normal and hypophysectomized male Sprague-Dawley rats, average weight 150 g, were used. All animals were given a commercial diet and drinking water *ad libitum*. Ten normal rats were given 0.5 U/rat of antidiuretic hormone (Pitressin, Parke-Davis) in daily subcutaneous injections, through 15 days; 10 rats were given 0.5 U/rat of oxytocic hormone (Pitocin, Parke-Davis) in same manner and time: 10 rats were daily treated with 0.5 U/rat of Pitressin previously inactivated in accordance with Van Dyke's thioglycollate method(7); 10 control rats were daily injected with 1 ml of 0.9% NaCl solution. An analogous experiment was carried out in rats hypophysectomized by the usual parapharyngeal approach. The rats were killed 24 hours after last injection. Pituitaries and adrenals were carefully dissected out and weighed. The pituitaries were then stained by Rasmussen-Ignesti's technic; the adrenals were stained with hematoxylin and eosin, with Sudan III and with Smith-Dietrich's method. The lipase content of adrenals was studied by Gomori's method.

Results. Body and organ weights of normal rats treated with posterior pituitary preparations are shown in Table I.

Neither antidiuretic nor oxytocic hormones cause significant changes in weights of body and anterior pituitary. After treatment with either antidiuretic or oxytocic hormones a conspicuous and significant enlargement of the adrenal glands was observed: the inactivated hormone was completely ineffective.

The histological picture of the anterior pituitary gland after treatment with active Pitressin or Pitocin showed a higher incidence of basophilic cells. Adrenal glands of animals treated with active hormones showed a characteristic enlargement of the "zona fasciculata" and a conspicuous increase of sudanophilic material (Fig. 1 and 2); lipasic activity was also enhanced. These effects were not obtained with the inactivated preparation.

In hypophysectomized rats the posthypophyseal extracts did not produce any modification of weight and of the histology of the suprarenal glands (Table II).

Discussion. The results of these experiments completely agree with Moehlig's(8) and Hantschmann's(9) observations; these authors have described adrenal hypertrophy in rabbits after treatment with whole posterior pituitary extract; Heinbecker's(10) observation that posterior pituitary hormones

TABLE II. Effect of Continuous Injection of Antidiuretic (Pitressin, Parke-Davis) and Oxytocic Hormones (Pitocin, Parke-Davis) on Mean Weight of Body and Adrenal Glands in Hypophysectomized Rats; 10 Rats in Each Series, Treated 15 Days.

Treatment	Body wt (g) Initial	Final	Adrenal wt (mg/100 g final body wt)
Pitressin (.5 U/rat)	165 ± 7	155 ± 8	9.11 ± .9
Pitocin (.5 U/rat)	170 ± 9	158 ± 7	8.20 ± .7
.9% NaCl	168 ± 7	157 ± 8	9.02 ± .9

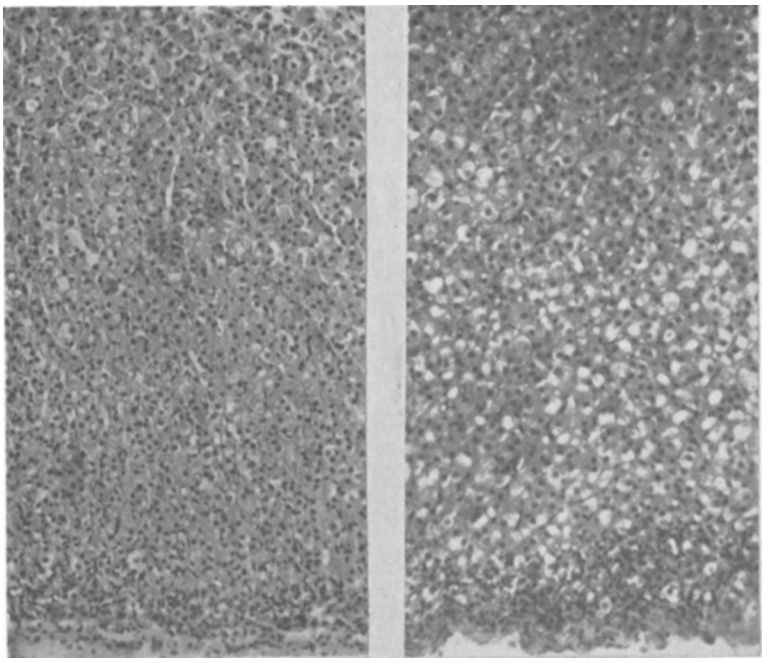

Fig. 1 Fig. 2

Adrenal cortices fixed in 10% formalin and stained with hematoxylin and eosin.

FIG. 1. Adrenal cortex of control rat.
FIG. 2. " " " rat treated with antidiuretic hormone through 15 days.

may induce a marked basophilism in the pituitary gland is also confirmed.

The evidence herein presented supports earlier observations(2-6) that both oxytocic and antidiuretic hormones can activate the adrenal cortex by causing the release of adrenocorticotrophic hormone; experiments in hypophysectomized rats eliminate the possibility that the effects observed may be due to contamination with ACTH of the injected hormones. Complete inefficacy of the inactivated posterior pituitary preparation seems to indicate that the ACTH-releasing power is strictly linked to the posterior pituitary hormonal molecule and not to an impurity contained in posterior pituitary extracts as suggested by Saffran(11).

These experiments strongly suggest that the "posterior pituitary hormones" or some related compounds may be considered as a neurohumoral agent linking the hypothalamus to the anterior pituitary through the portal blood flow(12). Considerable additional evidence is now available in favour of this hypothesis.

Green(13), Palay(14) and Scharrer(1) have found considerable Gomori-positive neurosecretory material, (containing posterior lobe hormones) in the proximity of the hypophyseal portal vessels, in the median eminence and in the infundibular stem. Rothballer(15) and Barrnett(16) have shown that after exposure of rats to pain stimuli the neurosecretory material of the hypothalamo-hypophyseal system is depleted from the median eminence and from the infundibular process into the portal vessels. Mirsky(17) has reported an acute elevation in blood antidiuretic hormone levels after various stimuli, such as pain and adrenalectomy, all associated with augmented ACTH discharge. McCann(18) observed in rats that hypothalamic lesions, which produce diabetes insipidus, uniformly block ACTH secretion; ACTH secretion appears to be produced in operated rats by Pitressin administration. Sobel(19) demonstrated that Pitressin causes an increased excretion of urinary corticoids by guinea pigs.

Summary. 1) Both antidiuretic and oxytocic hormones of the hypothalamic-posthypo-

physeal system produce, when chronically injected in normal rats, a significant enlargement of the adrenal glands and a conspicuous increase of the adrenal sudanophilic material. 2) The hormones do not produce modification in hypophysectomized animals. 3) An inactivated preparation of antidiuretic hormone is completely ineffective. 4) These results are consistent with the hypothesis that antidiuretic and oxytocic hormones of the hypothalamo-posthypophyseal system may act as neurohumoral agents linking the hypothalamus to the anterior pituitary through the portal blood flow.

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Actions of Reserpine and Chlorpromazine Hydrochloride on Rat Brain Oxidative Phosphorylation and Adenosinetriphosphatase.* (22304)

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The use of chlorpromazine and reserpine in treating psychiatric disorders has been discussed by several investigators(1-8). Chlorpromazine is widely used as a tranquilizing agent for mentally disturbed patients and is regarded as a general central nervous system depressant capable of potentiating certain other depressant drugs(9-11). The sedative and hypotensive actions of reserpine have been attributed to a central inhibition of the sympathetic nervous system(12-14). Although chlorpromazine and reserpine are similar in their clinical actions, a number of opposing pharmacological characteristics have been reported. In contrast to chlorpromazine, reserpine facilitates production of convulsions by caffeine or metrazol and antagonizes actions of barbiturates and anti-convulsive drugs(15-17). Chlorpromazine-HCl, at concentrations of 10 mg% (2.8×10^{-4} M) or greater, has been reported to depress oxygen uptake by brain slices(18).

In the present investigation, effects of chlorpromazine and reserpine upon two important high energy phosphate enzymatic reactions were studied. These compounds were tested separately and in combinations in order to detect possible synergistic or antagonistic actions. For comparison chlorpromazine was tested in combinations with sodium pentobarbital, the latter drug also being known to uncouple oxidative phosphorylation(19).

Materials and methods. Adult Sprague-Dawley albino rats were used. Fifteen percent brain homogenates were prepared in isotonic sucrose with a Potter-Elvehjem type

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