a 19-year-old white nullipara who died of myasthenia gravis. She had received 975 mg and 500 mg of ACTH 9 and 6 months respectively before death. The pituitary showed a focal increase of basophiles, resembling an adenoma. Differential counts done in a similar manner as described revealed 13.9% of basophiles, a few of which showed Crooke's changes. This focal adenomatoid accumulation of basophiles might represent a residual effect of ACTH therapy.

The therapeutic administration of ACTH may stimulate the adrenal cortex which then produces storage of endogenous ACTH in the anterior pituitary. The morphologic expression of this storage appears to be pituitary basophilism and Crooke's changes. Conversely a decrease in basophiles might be expected when the circulating adrenal cortical hormones are reduced and when the pituitary is released from their inhibiting effect. This occurs in Addison's disease where a decrease in the basophiles of the pituitary has been reported(8).

Our findings seem to indicate that morphologic changes are associated with alterations of the functional balance between the anterior pituitary and the adrenal cortex. Such morphologic changes might be useful in the experimental investigation of the relationship between these glands. The advent of ACTH and cortisone makes such an experiment quite feasible.

Summary. The administration of ACTH appears to have produced morphologic changes in the anterior pituitary of two patients. These changes consisted of an increase in the total number of basophiles, Crooke's hyaline cytoplasmic changes in these cells and basophilic stippling of many of the chromophobes. It is possible that these changes reflect the storage of endogenous ACTH following stimulation of the adrenal cortex by the therapeutic administration of this hormone.

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Experimental Nephrotoxic Nephritis in the Rat Treated with ACTH or Cortisone. (17939)

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Recent studies have demonstrated the marked effects of ACTH and cortisone on diseases involving hypersensitivity(1,2). The present work was carried out to determine whether experimental nephrotoxic nephritis, which is thought to involve a hypersensitivity reaction, could be prevented by the administration of these two agents.

Methods. Nephrotoxic serum was prepared according to the method used by Smadel (3). Nineteen black and white hooded rats of a specially inbred strain and averaging 250 g in weight, were studied. Weights, eosinophile counts, and white blood cell counts were determined. The urinary sediment was examined and the urinary albumin content was estimated, using both the heat and acetic acid and sulfosalicylic acid methods. Fourteen of these 19 rats received 1 cc of nephrotoxic serum per 100 g of body weight divided into 2 doses intravenously administered on successive days. Six rats

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TABLE I.
Outline of Results.

Material inj.	Rat No.	Alb'uria—days after 1st inj. 0	1	2	3	4	Hist.	Ed. and Asc.
Normal	C-1	0	0	0	0	0	0	0
rabbit	2	0	0	0	0	0	0	0
serum	3	0	0	0	0	0	0	0
NTS	N-1	0	0	2+	2+	4+	2+	0
alone	4	0	3+	3+	4+	4+	2+	0
	5	0	1+	2+	2+	2+	2+	0
	6	0	—	2+	2+	3+	2+	0
	8	0	2+	4+	4+	4+	2+	0
	9	0	2+	4+	4+	4+	2+	0
NTS +	A-1	0	2+	4+	4+	4+	2+	1+
ACTH	2	0	2+	4+	4+	4+	2+	1+
	3	0	2+	4+	4+	4+	2+	1+
	4	0	3+	4+	4+	4+	3+	4+
	5	0	2+	4+	4+	4+	3+	4+
ACTH	AC-1	0	0	0	0	—	0	0
alone	2	0	0	0	0	—	0	0
NTS +	CO-1	0	2+	4+	4+	4+	3+	4+
cortisone	2	0	2+	4+	4+	4+	2+	1+
	3	0	2+	4+	4+	4+	2+	1+

Alb'uria = Albumin in urine, graded from 0 to 4+.
Ed. and Asc. = Degree of edema and ascites found post-mortem, graded from 0 to 4+.
Hist. = Degree of renal damage estimated by histological examination, graded from 0 to 4+.
NTS = Nephrotoxic serum.

(N) received no further treatment. Five rats (A) were given ACTH before the first injection of nephrotoxic serum. Three of these (A-1, A-2 and A-3) received an effective dose of .4 mg of ACTH (Armour, Lot 77-S) per 100 g of body weight every 6 hours starting 9 hours before the first injection of NTS and continuing throughout the experiment. This dose of ACTH did not produce a drop in eosinophile count. Two additional rats (A-4 and A-5) received increasing doses of ACTH (Armour, Lot 44A, 2 & 3) starting at 0.8 mg per 100 g every 6 hours subcutaneously and increasing daily to reach 3 mg per 100 g every 6 hours on the fourth day. Only after this large dose was given did the eosinophiles decrease to 0 and remain there for the duration of the experiment. The first injection of nephrotoxic serum was given to these two rats following the eosinophile decline on the fourth day. The remaining 3 rats (CO) of the 14 that were given nephrotoxic serum, were treated with cortisone acetate (Merck) 5 mg per 100 g twice a day subcutaneously for 24 hours prior to administration of the nephrotoxic serum and for the remainder of the experiment. This dose was sufficient to cause the eosinophile count to drop from the normal range of 2-400 to 0-40 cells per cmm. All of these animals were sacrificed 4 days after the first injection of nephrotoxic serum. Their organs were fixed in formalin and examined by routine histological technics.

An additional control group of 3 rats (C) was given normal rabbit serum in a manner similar to the previous groups. A further control group (AC) was treated with ACTH alone, 0.4 mg per 100 g subcutaneously every 6 hours for 4 days before sacrifice.

Results. The results, summarized in Table I, show that the animals treated with ACTH and cortisone developed the same or an even slightly greater degree of nephritis than those given nephrotoxic serum alone. All of the animals given nephrotoxic serum showed im-

mediate marked albuminuria. There were no erythrocytes, but a few hyaline casts were found occasionally in the urinary sediment. The histological picture of the kidneys was uniformly that of a moderate degree of acute glomerulonephritis, with increased cellularity, avascularity and swelling of the basement membrane of the glomerular tufts. The kidneys of rats A-4 and A-5 showed slightly more severe glomerular involvement, and the tubules in these two rats were moderately dilated. All the rats given ACTH and cortisone showed some edema and ascites, which was very marked in rats A-4, A-5 and CO-1. In these 3 rats the spleen was greatly decreased in size.

Discussion. The present findings are similar to those recently reported by Knowlton, *et al.*(4), who found that cortisone did not prevent the development of cytotoxic serum nephritis in the rat. Our data further indicates that ACTH, in the large dosage necessary to give a continued depression in the eosinophile count, also did not prevent the lesions from developing. ACTH has been shown to affect the experimental cardiovascular lesions in rabbits produced by anaphylactic hypersensitivity to horse serum(2). The failure to prevent the renal lesions produced by the injection of nephrotoxic serum suggests that, in this condition, a different mechanism may be involved.

Conclusion. Both ACTH and cortisone failed to inhibit the development of renal lesions in the rat produced by the injection of rabbit anti-rat kidney serum.

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Distribution of Radioiodine in Erythrocytes and Plasma of Man.* (17940)

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Abundant data concerning the distribution of chloride and bromide between the erythrocytes and plasma are available. However, there is a lack of similar data on the distribution of iodide, owing to the difficulties in the chemical determination of iodine. Because of the ease with which I^{131} may be determined we have reinvestigated with the aid of radioiodine, the distribution of iodide in the cells and plasma of man.

Experimental. Venous blood was drawn from normal individuals and immediately heparinized. Various amounts of labeled sodium iodide in a volume of 0.1 to 0.3 cc were added to 25 cc of blood. This volume ratio was chosen so as to disturb the osmotic relationship to a minimal degree. The tubes containing the blood were then rotated for 20 minutes to obtain complete mixing. An aliquot was transferred to a Wintrobe tube for the determination of the corpuscular volume percentage (hematocrit) by means of centrifugation in the cold for 2 hours at 3,000 revolutions per minute. Another aliquot of the blood was taken for analysis of radioactivity by the method previously described (1) and for determination of chloride according to a modification of the method of Keys (2). The remainder of the blood was centrifuged to obtain plasma, in which the I^{131} and chloride concentrations were also determined.

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