

especially since the pyrrol test is not a specific test for this group. Gelatin is known to be difficultly hydrolysable. While the present experiments do not wholly deny the existence of the amino acid described by Van Slyke and his associates, they nevertheless indicate that more decisive proof must be advanced before the substance can be considered as an accepted amino acid.

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Necessary Concurrence of Thyroid in the Marked Adrenal Cortical Hypertrophy Following Beef Anterior Pituitary Implants.

MORVYTH MC QUEEN-WILLIAMS. (Introduced by Herbert McLean Evans).

From the Anatomical Laboratory, University of California.

Emery and Atwell¹ showed that the administration to normal animals of extracts of whole sheep pituitaries provoked a marked increase in adrenal weight due predominantly if not exclusively to the hypertrophy of the cortex. Independently, we had obtained the same effect in rats from implants of beef anterior pituitary tissue. The present communication reports a striking diminution in this effect when a preceding ablation of the thyroids has been performed.

Fresh beef hypophyses were washed in alcohol before dissection, and to eliminate all chance of infection, both merthiolate (1:10,000) and hexylresorcinol (1:13,000) were added to many of the batches immediately after grinding. Of 214 adult male and female rats, some of which were unilaterally adrenalectomized, 41 had been previously hypophysectomized, 69 including many first thyroidectomized received pituitary implants, 67 including thyroidectomized were left untreated, and a group of 37 normals was sacrificed and right and left adrenals weighed separately.

Results. 1. Implants of adequate amounts of finely ground beef hypophyses, whether freshly prepared or stored at 0°C. for several months, induced marked adrenal hypertrophy in every case in which the animal possessed intact thyroids, but had little or no effect on thyroidectomized rats (Tables I and II).* 2. Two grams of an-

¹ Emery, F. E., and Atwell, W. J., *Anat. Rec.*, 1933, **58**, 17.

* In 37 normal male rats (64 to 82 days) the left adrenals averaged 18.3 mg., the right 16.0 mg.; only once did the right exceed the left. Consequently, in all the experiments only left unilateral adrenalectomies were performed.

Autopsies of unilaterally adrenalectomized rats revealed that the right adrenal always exceeded the left, extirpated 5 days to 4 months previously. More extended study on this compensatory hypertrophy is contemplated.

TABLE I.
Showing That Adrenal Weight Increase Following Beef Hypophyseal Implants in Rats Is Greatly Diminished in Absence of Thyroid.

Exp.	No. Rats (Male, except Group 1)	Approx. Age at Autopsy (Days)	Total days since Thyroid- ectomy	Total Mg. Beef Ant. Pituitary Implanted	Aver. Wt. of 2 Adrenals (Mg.)			Aver. Wt. of 2 Thyroids (Mg.)	
					No. Implants	Untreated	Thyroid- ectomized Implanted	Untreated	Implanted
1	2	190	—	2000	5	20*	53*	—	—
2	20	65	40	2000	4	34	73	31	35
3	4	60	35	1850	5	36	62	28	34
4	4	45	—	1300	1	19	29	—	—

*Weight of one adrenal.

TABLE II.
Showing That Adrenal Weight Increase Following Beef Hypophyseal Implants Is Also Diminished in Unilaterally Adrenalectomized Rats in Absence of Thyroid.

Exp.	No. Rats (Male)	Approx. Age at Autopsy	Total Days		Total Mg. Beef Ant. Pituitary Implanted	Av. % Increase in Adrenal Wt.		Thyroid- ectomized Implanted	Aver. Wt. of 2 Thyroids (Mg.)		
			Elapsed after Left Unilat. Ad- renalectomy	Elapsed after Thyroid- ectomy		Untreated	Implanted		Normal	Untreated	Implanted
1	11	154	12	125	2050	42	170	56	—	47	31
2	3	140	25	108	1975	40	100	85*	—	43	34
3	10	80	30	50	1850†	97	281	105	31	32	26
4a	10	80	17	60	2600	38	137	57	29	27	21
4b	3	80	17	60	1450	—	73	20	—	28	21
5a	3	63	13	33	1900	—	91	43	24	—	20
5b	2	63	13	33	2000	—	105	54	—	—	21
5c	1	63	5	—	1500	—	74	—	—	—	16
5d	3	63	5	—	550	14	53	—	—	24	20
5e	3	63	5	—	100-250	—	44	—	—	—	20
6	3	60	10	30	570	24	56	27	—	22	—
7	6	45	5	—	—	20	—	—	—	22	—

*One mg. fragment of thyroid remaining.

†Administered 5 implants; in the other groups 2 implants were made.

terior pituitary implants increased the adrenal weight of rats with intact thyroids to at least double that of the controls, larger or smaller amounts producing proportionate effects. 3. In one case where 60 days had elapsed between the last treatment and autopsy, the adrenal had maintained its increased size, being palpable during the whole period, and weighing at autopsy 80 mg., that of a sibling control being 26.5 mg. 4. The adrenal cortex was chiefly affected by the preparations employed. The hypertrophied adrenals, stained with Mallory-Azan, exhibited the zona reticularis and fasciculata cells greatly increased in size and, especially in the former zone, highly vacuolated, indicating lipid increase.

The extremely slight response of *thyroidectomized* animals to beef pituitary implants is excellent evidence that the adrenal hypertrophy in rats with intact thyroids is attributable to the action of a pituitary hormone acting by way of the thyroid and is not due to bacterial or to foreign protein influence. Possibly the anterior hypophysis possesses 2 hormones, one acting directly on the adrenal and the other acting on the adrenal via the thyroid. Evidence for the direct hypophyseal action is offered by (1) the maintenance of adrenal weight in thyroidectomized rats; heavy adrenals (av. 73.5 mg.) were found in 14 female rats thyroidectomized for 12 to 20 months; all had large hypophyses (av. 17.0 mg.). (2) Compensatory adrenal hypertrophy occurred in unilaterally adrenalectomized thyroidectomized animals, but not in hypophysectomized rats that had been unilaterally adrenalectomized 8 to 21 days before autopsy; in 41 rats (av. 274 gm.) hypophysectomized by the writer, each adrenal degenerated to 4.6 mg. (av.). It would appear that the pituitary hormone which acts through the thyroid exists in considerable amount in the normal beef hypophyses implanted, but that the directly acting hormone is not present to any great extent.