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Unilateral Adenectomy in the Cretin Rat.*† (24194)

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Compensatory enlargement of the remaining organ of a paired organ system generally occurs following unilateral removal of the adrenal(1), kidney(2,3), ovary(4), and testis(5). Factors which alter this response to sub-total removal of organ tissues include age, diet(6,7), sex, time between operation and autopsy, castration(8), hypophysectomy(9, 10,11) and thyroidectomy(9). Prior studies have principally involved the use of adult euthyroid rats. No data, however, have come to our attention in which compensatory enlargement of organs was compared in immature hypothyroid (cretin) rats and euthyroid controls of the same age.

Materials and methods. Inbred Vanderbilt rats, maintained, *ad libitum,* on Purina Fox Chow (meal) and tap water were used. Cretins were obtained by feeding 0.5% thiouracil§ in Purina Fox Chow to pregnant rats and subsequently to them and their litters from the 14th-16th day of gestation to end of experiment. Controls were maintained, with their mothers, on the same regimen without the thiouracil. Only male control and cretin rats whose body weights at 30 days ranged 100 to 109 g and 29 to 36 g, respectively, and female controls and cretins whose body weights were between 83-88 g and 28-35 g, respectively, were utilized. At 30 days of

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age either the left adrenal, thyroid lobe (including half of the isthmus and imbedded parathyroids), testis, ovary or kidney was removed from cretin and control rats under ether anesthesia. Unilateral removal of non-reproductive organs was performed in both sexes. The ablated organs were cleaned and weighed on a torsion balance to the nearest 0.5 mg and fixed in Orth's fluid. On the 15th post-operative day the animals were killed with ether and the following organs removed and weighed: testes, seminal vesicles, ventral prostate, ovaries, uterus (fluid expressed), liver, kidneys, thyroid, adrenals, heart (void of blood) and hypophysis. Unoperated male and female cretin and control rats were similarly studied at both 30 and 45 days of age. Testes, ovaries, adrenals and kidneys were fixed in Orth's fluid, embedded in paraffin, sectioned at 9 μ and stained with Harris' hematoxylin and eosin. Pituitary glands were fixed in Zenker-formol solution. Sections (4 μ thick) of each gland were stained with aldehyde fuchsin according to Halmi's technic(12). Other sections (6 μ thick) were stained by the periodic-acid Schiff technic. The response of a residual gland was evaluated, not by comparison with the previously excised contralateral gland, but rather, with the non-excised homolateral gland of an intact control or cretin of the same age(13).

Results. Pituitaries of intact male and female cretin rats contained rather small, very sparsely scattered gonadotrophs and thyrotrophs, virtually no acidophiles, and revealed no apparent sex difference. On the other hand, intact control rat pituitaries appeared to have attained the glandular appearance described for the adult with fewer gonadotrophs in the hypophyses of female rats. There was an apparent hypertrophy of gonadotrophs in only unilaterally castrated control rats of both sexes. These cells appeared large, pale staining, but not vacuolated. There was no change in number of gonadotrophs. Thyrotrophs, in pituitaries from all cretins of both sexes, appeared as only very early thyroidectomy cells and were not vacuolated.

Adrenal compensatory hypertrophy in cretins of both sexes was only 25% of that observed in control rats (Table I).

In male and female control rats, hemi-thyroidectomy resulted in 48.4% and 43.8% compensatory hypertrophy, respectively, of the remaining thyroid tissue. On the other hand, no significant hypertrophy of the already maximally stimulated residual thyroid lobe was detected in cretins of either sex.

There was no statistical difference in per cent compensatory hypertrophy of the remaining kidney, of either sex, of cretin or control rats as judged by weight (Table I).

Ovarian compensatory hypertrophy was significantly greater in cretin rats (34.4%) than in euthyroid controls (23.1%). Follicular hyperplasia was apparent in ovaries of both thiouracil-fed rats and controls following unilateral castration. No significant difference between uterine weights of hemi-ovariectomized rats (cretin or controls) and their respective intact counterparts was discerned.

Ability of cretins to compensate lost testicular tissue was 5 times greater than that of controls. Despite the dramatic increase in testis weight, no concomitant increase occurred in weights of accessory sex organs of either group.

Although there was pronounced testis hypertrophy in unilaterally orchidectomized cretins, no germinal elements more mature than primary spermatocytes were found. On the other hand, mature spermatozoa were present in both intact and hemi-orchidectomized euthyroid control rats. Hypertrophy of the seminiferous tubules was obvious in residual testes of both control and cretin rats following unilateral castration.

Discussion. Cretinism did not appear to produce differential or selective effects upon splanchnic and somatic growth, inasmuch as renal and body weights remained parallel, but impaired. This is in agreement with the constant relation maintained between renal and whole body growth rates of intact rats(6,14). Neither did cretinism affect degree of renal compensatory hypertrophy. On the other hand, responses of certain endocrine glands to unilateral removal, in the cretin, differed markedly from that of the kidney for there was decreased response of adrenals, apparent

TABLE I. Comparison of Extent of Compensatory Hypertrophy of Various Glands 15 Days after Unilateral Adenectomy in 30-Day-Old Cretin Rats with That in Control Rats.

Unilateral	No. rats ♀	No. rats ♂	Body wt (g) at start and end ♀		Body wt (g) at start and end ♂		RGW‡ (mg/100 g) at autopsy ♀	RGW‡ (mg/100 g) at autopsy ♂	% hypertrophy§ ♀	% hypertrophy§ ♂
Adrenalectomy										
*Intact controls	8	8	85	135	105	163	8.9 ± .1 (12.0)	6.3 ± .2 (10.4)		
Operated "	9	8	87	139	103	183	12.9 ± .4 (17.9)	8.9 ± .1 (16.1)	44.9	41.2
†Intact cretins	8	8	30	51	32	51	7.8 ± .2 (4.0)	6.9 ± .3 (3.4)		
Operated "	7	8	31	52	34	60	8.8 ± .2 (4.6)	7.6 ± .2 (4.5)	12.8	10.7
Thyroidectomy										
*Intact controls							4.1 ± .1 (5.5)	3.3 ± .1 (5.5)		
Operated "	8	9	83	131	107	163	5.9 ± .3 (7.2)	4.9 ± .2 (8.2)	43.8	48.4
†Intact cretins							34.9 ±1.8 (17.8)	37.4 ±1.6 (19.1)		
Operated "	7	7	33	54	36	54	35.4 ±2.2 (19.1)	38.6 ±2.5 (20.7)	1.4	3.2
Nephrectomy										
*Intact controls							446 ± 6 (602)	462 ± 21 (753)		
Operated "	8	8	85	131	104	161	615 ± 12 (809)	656 ± 16 (1057)	37.9	42.0
†Intact cretins							516 ± 15 (263)	494 ± 9 (252)		
Operated "	7	6	35	53	34	52	733 ± 22 (393)	691 ± 18 (359)	42.0	39.9
Ovariectomy										
*Intact controls							20.4 ± .6 (27.1)			
Operated "	9		87	133			25.1 ±1.2 (33.3)		23.1	
†Intact cretins							16.6 ± .9 (8.5)			
Operated "	8		35	57			22.3 ±1.1 (12.7)		34.4	
Orchidectomy										
*Intact controls								546 ± 15 (885)		
Operated "		8			102	161		639 ± 9 (1030)		17.0
†Intact cretins								264 ± 8 (136)		
Operated "		12			33	50		488 ± 12 (244)		84.8

* Indicates same group of intact controls. † Indicates same group of intact cretins.

‡ RGW = Right glandular wt in mg/100 g body wt. Actual organ wt appears in parentheses.

§ $\%\ \text{hypertrophy} = \frac{\text{RGW (operated)} - \text{RGW (intact)}}{\text{RGW (intact)}} \times 100.$

absence of compensatory response in the thyroids, and an increased degree of compensatory hypertrophy of ovaries and testes. Maintenance and growth of these latter glands depend largely upon specific trophic hormone stimulation. but no such specific dependence of the kidneys has been demonstrated. On the other hand, the parallelism between renal and body weights might well reflect decreased growth hormone secretion. The well-known paucity of pituitary acidophiles in hypothyroid rats was apparent in the cretins. The catholic influences of growth hormone, however, could scarcely be expected to affect splanchnic and somatic growth selectively.

Thyroid hormone deficiency may(15-18) or may not(9,19) result in adrenal atrophy. Winter and Emery(9) reported that thyroidectomy affected neither size of adrenal nor degree of compensatory hypertrophy in the adult rat. Our data indicate roughly only 12% adrenal compensatory hypertrophy in the cretin, compared with 44% in the normal rat. The virtual absence of pituitary acidophiles in cretin rats might possibly account for the decreased adrenal response.

Absence of thyroid gland compensation in cretin rats may probably be explained as inability of an already maximumly stimulated thyroid to respond to the additional stimulus of hemi-thyroidectomy.

An increase in the number of gonadotrophs in pituitaries of cretin rats following unilateral castration might readily account for the observed increased response of testes and ovaries. However, the essentially chromphobic nature of the pituitary glands of intact cretins mirrored the appearance of pituitaries

from hemi-castrated cretins. It would seem, therefore, that either rapid depletion of gonadotrophin from these cells had occurred or that a slight, but sustained, secretion of hormone stimulated a very sensitive residual gonad. The increased sensitivity of testes and secondary sex organs of thyroidectomized animals(19,20) and of ovaries of thiouracil-fed rats(21,22) to gonadotrophins seems to support the latter possibility.

The various peripheral effects of hypothyroidism upon target-organ responses to pituitary hormones(19-22) must be considered in interpreting our data. On the other hand, the effect may be central, so that the imbalance of the pituitary-thyroid axis in the cretin, induced by thiouracil administration, affects other pituitary-target-organ axes and thereby mechanisms through which compensation normally occurs are either hampered or facilitated.

Summary. Degree of compensatory hypertrophy of various glands in the cretin rat was compared with that in euthyroid controls. Per cent renal compensatory hypertrophy in the cretin of either sex was equal to that of the normal animal. Compensatory responses of certain endocrine viscera, however, are dramatically affected. Such responses appear to be greatly lessened in adrenals, virtually abolished in thyroids, and markedly increased in testes and ovaries of cretin rats. Correlations of various glandular responses with pituitary cytology are considered.

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Latex Agglutination Test for Disseminated Lupus Erythematosus.* (24195)

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Evidence has been presented which suggests that the LE cell factor reacts specifically with materials of nuclear origin. Holman and Kunkel(1) and Friou(2), using immunofluorescent technics, have demonstrated localization of γ globulin from sera of patients with disseminated lupus erythematosus (DLE) onto whole nuclei and nucleoprotein. Robbins *et*

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