THE EFFECTS OF ADMINISTERING LARGE AMOUNTS OF CORTIN ON THE ADRENAL CORTEXES OF NORMAL AND HYPOPHTHYECTOMIZED RATS

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It has been observed by Ingle, Higgins and Kendall that atrophy of the adrenal cortices of male rats occurs during treatment with massive doses of cortin. The simultaneous administration of the adrenotropic principle of the anterior lobe of the pituitary body was effective in preventing the regression of the adrenal cortex which follows treatment with cortin. This observation led Kendall and me to postulate that the effect of treatment with cortin is mediated through the anterior lobe of the pituitary body which may inhibit its adrenotropic activity in the presence of an excess of cortin. This hypothesis has further support in the established facts that a similar atrophy of the adrenal cortices occurs following removal of the anterior lobe of the pituitary body, that the adrenal cortices are repaired when the hypophysectomized animal is treated with the adrenotropic principle and that the adrenal cortex fails to show any degree of hyperplasia when the hypophysectomized animal is subjected to severe forms of stress.

The object of the present experiment was to determine whether or not treatment of the rat with massive doses of cortin would influence the adrenal cortices if the level of adrenotropic principle in the body were held constant. This was attained by removing the pituitary body and substituting for it a constant intake of adrenotropic principle in an amount which was known to be adequate to maintain the adrenal cortices of hypophysectomized rats at a normal size.

METHODS. Sixty male rats each having an initial body weight of 180 grams were used. Ten rats were hypophysectomized but did not receive treatment; ten normal rats had their food intake restricted to the level voluntarily adopted by the untreated hypophysectomized animals; ten normal animals had no dietary restriction; ten normal animals received 10 cc. of cortin daily in their drinking water (a slight voluntary reduction in the intake of food was noted); ten hypophysectomized rats received 0.5
cc. of adrenotropic hormone by intraperitoneal injection daily and 10 cc. of cortin daily in the drinking water, and ten additional hypophysectomized animals received 0.5 cc. of adrenotropic hormone daily but no cortin was administered. The food intake of the hypophysectomized rats which

### TABLE 1

<table>
<thead>
<tr>
<th>EXPERIMENTAL CONDITION</th>
<th>NUMBER</th>
<th>BODY WEIGHT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Average</td>
</tr>
<tr>
<td>Normal; restricted diet; no treatment</td>
<td>10</td>
<td>141</td>
</tr>
<tr>
<td>Hypophysectomy; no treatment; voluntary restriction of diet</td>
<td>10</td>
<td>142.9</td>
</tr>
<tr>
<td>Normal; no restriction of diet; no cortin administered</td>
<td>10</td>
<td>190.4</td>
</tr>
<tr>
<td>Normal; 10 cc. of cortin given daily; slight voluntary restriction of diet</td>
<td>10</td>
<td>151.7</td>
</tr>
<tr>
<td>Hypophysectomy; 0.5 cc. of adrenotropic principle administered daily; no cortin administered; restriction of diet</td>
<td>10</td>
<td>141.4</td>
</tr>
<tr>
<td>Hypophysectomy; 0.5 cc. of adrenotropic principle administered daily; 10 cc. of cortin given daily; voluntary restriction of diet</td>
<td>10</td>
<td>137.7</td>
</tr>
</tbody>
</table>

Fig. 1. Combined weights of pairs of adrenal glands

received the adrenotropic hormone was regulated in order to equate the loss of weight. To accomplish this it was necessary to restrict the food intake

1 The adrenotropic hormone was prepared by H. D. Moon, of the Institute of Experimental Biology of the University of California, and was supplied to me through his courtesy.
of the rats which did not receive cortin to a definitely smaller amount than was consumed by the rats which did receive cortin. At the end of seven days all of the animals were killed and necropsy was performed.

RESULTS. The data on body weights are presented in table 1 and the data on adrenal weights are shown in figure 1.

It is clear that the administration of large amounts of cortin to the male rat produces a marked atrophy of the adrenal glands. On the contrary, when the anterior lobe of the pituitary body is absent and the animal receives adrenotropic hormone in amounts adequate to prevent the atrophy occurring from hypophysectomy alone, there is no apparent effect of cortin on the adrenal cortex. There is a definite tendency for the cortin-treated animals to lose in general body weight. Extensive atrophy of the thymus of those animals which received cortin was noted, thus confirming our previous observations (1, 3).

COMMENT. It is evident from these experiments that the administration of massive amounts of cortin to the rat does not injure the adrenal cortices directly. The hypothesis that atrophy of the adrenal cortex may be due to restriction of the output of the adrenotropic principle of the anterior lobe of the pituitary body is supported by these observations.

The loss in adrenal weight is essentially cortical as we have shown. This loss in mass of cortex does not accompany a loss in total body weight which is induced by the restriction of food. It also has been observed by Dr. L. T. Samuels, Department of Physiology, University of Minnesota, that when the total body weight of the hypophysectomized rat is sustained at its preoperative level by forced feeding the adrenal cortices still undergo atrophy. The loss of volume of the adrenal cortex which occurs following the administration of cortin or following the removal of the anterior lobe of the pituitary body is probably causally independent of the concomitant loss in total body weight.

SUMMARY

When normal rats are treated with massive amounts of cortin an extensive atrophy of the adrenal cortices consistently occurs. When the pituitary body is absent and the animal receives adrenotropic hormone in constant amounts there is no apparent effect of cortin on the adrenal cortex.

REFERENCES

(4) SAMUELS, L. T. Personal communication to the author.