STIMULATION OF ADRENOCORTICOIDIOGENESIS BY PRECORTICOTROPHIN AFTER ACTIVATION

By

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ABSTRACT

Precorticotrophin (precursor of corticotrophin) after acid treatment, enhanced the rate of steroid biosynthesis in the adrenal cortex of hypophysectomized rats. The corticosterone content of both adrenal tissue and the adrenal vein blood were unchanged when the rats were treated with a pig pituitary precorticotrophin preparation. However, after the precorticotrophin preparation was activated by acid treatment, a significantly higher content of corticosterone was found both in the adrenal tissue and in the adrenal venous plasma.

Mammalian adenohypophyses appear to contain a material (precorticotrophin) which exhibits corticotrophic activity after treatment with acid or urea (Dasgupta & Young 1958; Dixon et al. 1959). The existence of this material was demonstrated by the measurement of the ascorbic acid depletion in adrenals of hypophysectomized rats (Sayers et al. 1948). However, a more specific method should be the one based on the measurement of the increase of the rate of biosynthesis of adrenocorticoids (Nakao & Hirai 1961). The present report confirms the existence of precorticotrophin using this more rigorous assay procedure.

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**MATERIALS AND METHODS**

An extract of pig anterior pituitary glands prepared according to Dasgupta & Young (1958) in 0.9 per cent sodium chloride solution (1 ml of extract was equivalent to 10 mg wet hypophyseal tissue) was divided into two equal portions. One portion was adjusted to pH 3 with 2 N HCl and 0.9 per cent NaCl was added to the other to adjust its volume only. Both the portions were then incubated at 37°C for 1 hour. The pH of the acid treated sample was next brought back to 6.5 (the pH of the original untreated preparation) by the addition of 2 N NaOH. The female hypophysectomized (2 days previously) Wistar rats were treated, at the rate of 0.5 ml per 100 g body weight, by the subcutaneous route in the interscapular region. The control group received saline injections (0.9 per cent NaCl) only at the same rate. Two hours after treatment, blood was collected from the left adrenal vein for a 15 minute period. Estimations of corticosterone of the collected blood plasma and of the adrenal tissue were performed as described by Nakao & Hirai (1961).

**RESULTS AND DISCUSSION**

Table 1 represents the results obtained with the untreated original anterior pituitary extract (OAPE), treated anterior pituitary extract (TAPE) and the saline. The importance of the estimations of corticosterone of the adrenal

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Corticosterone (Mean value ± Standard error)</th>
<th>Secretion μg per kg body weight per adrenal per h (Range)</th>
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<tbody>
<tr>
<td></td>
<td>Production μg per g adrenal</td>
<td></td>
</tr>
<tr>
<td>Saline only</td>
<td>3.94 ± 0.21 (5)†</td>
<td>0.74 ± 0.077 (5)</td>
</tr>
<tr>
<td></td>
<td>(3.39 – 4.50)</td>
<td>(0.46 – 0.82)</td>
</tr>
<tr>
<td>OAPE</td>
<td>5.10 ± 0.19 (6)*</td>
<td>1.69 ± 0.20 (6)*</td>
</tr>
<tr>
<td></td>
<td>(4.40 – 5.56)</td>
<td>(0.97 – 2.39)</td>
</tr>
<tr>
<td>TAPE</td>
<td>7.37 ± 0.50 (6)**</td>
<td>5.11 ± 0.76 (6)**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(3.13 – 7.78)</td>
</tr>
</tbody>
</table>

OAPE = Untreated original anterior pituitary extract.
TAPE = Treated anterior pituitary extract.
† Figures within parentheses indicate the number of animals whose corticosterone values were individually determined.
* are not statistically different from their respective control values.
** are significantly higher than their respective control values \(P < 0.05\).
tissue and the adrenal vein blood source individually has been discussed (Nakao & Hirai 1961). Pincus & Hirai (1964) found some difference in the secretory rate of corticosterone from the adrenal gland during different phases of the oestrous cycle of rats.

The response measured in terms of corticosterone, due to OAPE (Table 1) was not statistically different from that due to the administration of saline only (control group). On the other hand, the administration of TAPE to the test animals induced a corticosterone production rate in the adrenal (7.37 ± 0.50 μg per g adrenal) as well as a corticosterone secretory rate from the

![Graph]

**Fig. 1.** Amounts of corticosterone after treatment with OAPE or TAPE as compared with control groups in hypophysectomized female rats.

Test animals were used 24 h after hypophysectomy.

OAPE = Original anterior pituitary extract.

TAPE = Treated anterior pituitary extract.

1 = intact (dioestrus + oestrus)*

2 = hypophysectomized only.

3 = hypox. + ACTH (maximal response).

4 = hypox. + OAPE.

5 = hypox. + TAPE.

2 and 4 not significantly different in both adrenal gland and its vein blood.

2 and 5 significantly different in both adrenal gland and its vein blood (P < 0.05).

* Pincus & Hirai (1964).
adrenal \((5.11 \pm 0.76 \text{ } \mu g \text{ per kg body weight per adrenal per h})\) – both significantly higher than that of the control group \((3.94 \pm 0.21 \text{ } \mu g \text{ per g adrenal and } 0.74 \pm 0.077 \text{ } \mu g \text{ per kg body weight per adrenal per h})\) \((P < 0.05)\). The results are shown diagramatically in Fig. 1.

Clearly the present experimental results provide additional evidence for the existence in the mammalian adenohypophysis of an inactive material (pre-corticotrophin) which is activable to corticotrophin by an acid treatment.

The principal object of the present study was to demonstrate simply in a qualitative way that the adenohypophyseal preparation made by us, after acid treatment would indeed stimulate the rate of biogenesis of steroids in the adrenal as it could cause depletion of adrenal ascorbic acid content of hypophysectomized rats \((\text{Dasgupta et al. 1967})\).

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REFERENCES

\textit{Dasgupta P. R. \\& Young F. G.}: Nature (Lond.) \textbf{82} (1958) 32.

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