ADRENAL FUNCTION AND THYROTOXICOSIS

By

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Thyrotoxicosis provokes an increase in adrenal activity. In man, however, adrenal atrophy or necrosis is found in some cases of thyrotoxicosis, especially in thyrotoxic crisis (Järvinen, 1953). These observations are not necessarily contradictory. Thus during thyrotoxicosis the adrenals may develop different stages of function, ranging from an initial hyperactivity to terminal exhaustion after a thyrotoxic stress of long duration. Some authors suggest (Järvinen, 1953) that a temporary adrenal insufficiency may provoke thyrotoxicosis though this hypothesis is still not proved.

The purpose of the present work was to discover whether signs of adrenal insufficiency can be demonstrated by some functional tests performed in acute thyrotoxicosis.

METHOD AND MATERIAL

The adrenal function tests in use at present may indicate, whether there is a complete insufficiency, but quantitative changes in adrenal function cannot be determined. Furthermore, Kepler's water balance test is unsuitable in thyrotoxicosis as thyrotoxic disturbances of the water balance decrease the reliability of the test.

Thorn's i. v. ACTH-eosinophil test is fairly reliable. In the present work 20 mg. ACTH were given after an overnights fast by intravenous drip for 6 hours. The number of circulating eosinophils in the blood was determined several times during 24 to 48 hours. In connection with the test the 17-keto-
steroids in the urine were also determined during 3 days, starting 24 hours before the test.

The sensitivity to insulin, which is typical of adrenal insufficiency, was studied by an insulin tolerance test consisting of 0.1 units of insulin/kg. body weight given intravenously, and blood sugar determinations made before the administration of insulin and several times during the following 360 min.

Fifteen patients with marked thyrotoxicosis, 11 female and 4 male, were examined. The previous course of the disease was relatively short in each case, varying from one to six months. The diagnosis was based on the typical clinical symptoms and several laboratory findings, and was further confirmed by the fact that the patients became euthyroid after thyrostatic treatment or a subsequent thyroidectomy. In no case was there a thyrotoxic crisis. – Ten healthy subjects served as controls.

RESULTS

The results are shown in Figs. 1 to 4 and in Table 1.

1. ACTH test. The initial value for the eosinophils before administration of ACTH was indicated as 100 and the changes in the eosinophil count as percentages of the initial value. Fig. 1 shows the control cases. In no case was there a decrease of less than 69 per cent. All the cases with thyrotoxicosis
Fig. 2 showed a decrease of at least 84 per cent and the curves were also in other respects similar to those in the controls.

2. Insulin tolerance test. The curves for some controls are plotted in Fig. 3. The changes in blood sugar values are expressed as percentages of the initial value. In each case there was a marked decrease of 42 to 67 per cent within
15 to 39 min., followed by an increase to almost the initial value in 120 min. The corresponding curves for the cases of thyrotoxicosis are shown in Fig. 4. The curves are quite similar to those of the controls. In no case did the blood sugar values remain low, as is typical of adrenal insufficiency. The rise of the curve in one case was somewhat slower, which could perhaps be a sign of defective adrenal function, but the ACTH test in the same case yielded a very marked and persistent eosinopenia indicating good function.

The 17-KS values were within normal range. The values after administration of ACTH varied somewhat. Most of the controls and the patients responded with an increase, but both groups included a case in which the values decreased despite administration of ACTH. The determinations were unfortunately performed on a 24-hour urine and not on 12-hour specimens, as prescribed in the original method. As the increase in 17-KS after ACTH is very transient and followed by a decrease, it is possible that some of the increases are concealed in the 24-hour urine specimens in some of our cases. The case of thyrotoxicosis showing no increase in 17-KS after ACTH had a normal eosinopenic response and a normal insulin tolerance test.

The values for 11-oxysteroids were normal in all cases.

**DISCUSSION**

As adrenal insufficiency was not demonstrated in a single case, it cannot be regarded as an essential part of the clinical picture of thyrotoxicosis. When the
### Table 1.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age</th>
<th>17-ketosteroids in ACTH test before</th>
<th>during</th>
<th>after</th>
</tr>
</thead>
</table>
| Thyrotoxicosis Female cases
1 | 55 | 5.0 | | |
2 | 52 | 5.4 | | |
3 | 40 | 13.7 | 14.3 | 15.3 |
4 | 34 | 10.3 | 12.2 | 8.0 |
5 | 45 | 6.0 | 7.9 | 7.1 |
6 | 52 | 7.6 | 6.9 | 5.6 |
7 | 46 | 10.5 | 9.5 | 9.6 |
8 | 25 | 7.4 | 7.1 | 7.9 |
9 | 31 | 6.4 | 7.0 | 7.1 |
10 | 19 | 6.1 | 8.9 | 8.0 |
11 | 57 | 4.6 | 5.1 | 5.1 |

Thyrotoxicosis Male cases

12 | 54 | 9.4 | 12.5 | 13.6 |
13 | 51 | 7.0 | 9.8 | 10.2 |
14 | 57 | 10.5 | 12.1 | 11.5 |
15 | 31 | 9.3 | 10.9 | 9.5 |

Controls, female

1 | 43 | 8.3 | 7.8 | 5.0 |
2 | 39 | 5.0 | 7.6 | 6.0 |
3 | 52 | 6.8 | 8.2 | 6.6 |
4 | 52 | 5.7 | 7.4 | 6.7 |
5 | 55 | 4.0 | 5.5 | 5.4 |

Thyrotoxicosis is «compensated» it is more likely that the adrenals are overactive. This is supported by the results of some investigations on the chloride content of the thermal sweat in hyperthyroid patients (Koivusalo & Pekkarinen, 1953). In a «decompensation» or crisis, however, it may be otherwise. As is known, the sensitivity to thyroid hormones is markedly increased in adrenal insufficiency, and cortisone has turned out to be effective in thyrotoxic crisis (Szilagyi et al., 1952). It is possible that a thyrotoxic crisis develops when, during the course of thyrotoxicosis, the adrenals for some reason become insufficient. It is not, however, justified to consider adrenal insufficiency of primary importance in the development of thyrotoxicosis.

The increased demand for cortical hormones in thyrotoxicosis arouses interest in the question as to whether the adrenal cortical hormones counteract
the function of the thyroid and the formation of thyroid hormone. The publications in that field are numerous but contradictory (D’Angelo et al., 1953, Gabrilove & Soffer, 1950, Hill et al., 1950, Lederer, 1952, Means, 1948, and Money et al., 1951), and the question is not yet definitely answered. This, however, is beyond the scope of the present work.

SUMMARY

Fifteen cases of marked, relatively acute thyrotoxicosis were examined by the i. v. ACTH-eosinophil test and the insulin tolerance test; no signs of adrenal insufficiency were found.

REFERENCES