THE EFFECT OF THYROXINE ON THE COENZYME A CONTENT OF SOME TISSUES*

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While the rôle of thyroxine in the body's growth, development, and maintenance is important, as yet no definitive mechanism or locus of action for it has been delineated. In a recent review, Barker (1) has considered many of the enzymatic phenomena associated with different thyroidal states, and it is obvious from a consideration of the effects of this hormone that its action has wide-spread ramifications. Martius and Hess (2) and others (3, 4) have shown that thyroxine can act as an uncoupling agent. Drabkin (5) observed that tissue levels of cytochrome c were influenced by thyroxine. Much of this type of evidence implicates thyroxine with the energetics of the body. Recently coenzyme A (CoA) has been shown to be necessary in many biochemical processes (6), and it is known that a number of these CoA-dependent phenomena are influenced by thyroxine. Minz and Cohen (7) have suggested that there is a possible interrelationship between CoA and thyroxine in intestinal peristalsis. Because of the possible interrelationship between CoA and the tissue levels of thyroxine, it was considered to be worth while to investigate the influence of thyroxine on CoA levels in the tissues of the rat.

Procedure

General—Male albino rats (Wistar strain, Putney Farm) were used as experimental animals. In the first series of experiments the weight range was 90 to 150 gm., while in the second series it was 250 to 350 gm. The purpose of the first set of experiments was to determine the effect of thyroxine upon the CoA levels of liver, heart, brain, and intestine. In the second series, attention was directed to the changes in the liver CoA levels.

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The rats were divided into control and experimental groups. The experimental group was maintained for 1 month on a low iodine diet (8), and in the first study one of the control groups was also maintained on this diet. The remainder of the controls from the first study and all the controls in the second study were maintained on Purina laboratory chow.

Thyroidectomy—After 1 month on the low iodine diet, the rats to be thyroidectomized were each treated with a large subcutaneous dose of carrier-free $^{131}$I (750 μc.). Some 2 months later it was clear that these animals were thyroidectomized, and the experiments were then begun.

**Experimental Design**

When it was considered that the thyroidectomized animals were suitable for experimental purposes, they were separated into two groups, C and D, and to each member of the latter group were given 150 γ of sodium L-thyroxine pentahydrate per 100 gm. of body weight. (This dose of L-thyroxine has been shown to cause an increase in oxygen uptake within 48 hours.)

About 48 hours after the administration of the thyroxine, the rats in all the groups (Group A, normal controls; Group B, controls on a low iodine diet; and the two groups of thyroidectomized rats) were killed by a blow on the head. The tissues for examination were removed rapidly and prepared for CoA assay, which was carried out with the use of the method described by Kaplan and Lipmann (9).

In the second series of studies, an attempt was made to determine whether any effect *in vitro* could be produced by thyroxine. For this purpose 30 γ of sodium L-thyroxine pentahydrate were added to boiled aliquots of the tissue extracts obtained from Group C (the untreated thyroidectomized group) prior to incubation.

**Results**

The results of these experiments are presented in Tables I and II. The findings in the first study (Table I) are insufficient to carry out a statistical evaluation, but they do indicate that the liver is very rapidly affected by thyroxine with respect to its content of CoA. Table II presents the findings in the second series of studies, and here it is noted that the liver CoA levels in the three groups, normal controls, the thyroidectomized group, and thyroidectomized rats treated with thyroxine, are significantly different from one another, the thyroidectomized group being at the lowest level and the thyroidectomized group treated with thyroxine being at the highest level (some 78 per cent greater than the value found in the untreated thyroidectomized group). The addition of thyroxine (30 γ) to boiled aliquots of the liver extract (Group E, Table II) from the thyroidectomized group was found to increase the CoA content of these extracts by some 78 per cent.

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1 Private communication from Dr. D. Holtkamp.
tomized group did not result in a significant change in CoA concentration of the aliquot.

**Table I**

*Tissue CoA Concentrations in Various Thyroidal States*

The values are given as the average CoA units per gm. of fresh tissue.

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>No. of rats</th>
<th>Liver</th>
<th>Heart</th>
<th>Brain</th>
<th>Intestine</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Normal; normal diet</td>
<td>4</td>
<td>91 ± 18.7</td>
<td>32 ± 4.3</td>
<td>13 ± 0.9</td>
<td>13 ± 0.7</td>
</tr>
<tr>
<td>B</td>
<td>&quot; low iodine diet</td>
<td>5</td>
<td>84 ± 7.3</td>
<td>29 ± 1.7</td>
<td>8 ± 1.2</td>
<td>11 ± 3.4</td>
</tr>
<tr>
<td>C</td>
<td>Thyroidectomized; low iodine diet</td>
<td>5</td>
<td>49 ± 7.8</td>
<td>18 ± 2.1</td>
<td>9 ± 0.3</td>
<td>7 ± 1.3</td>
</tr>
<tr>
<td>D</td>
<td>Thyroidectomized; low iodine diet + 150 γ Na L-thyroxine</td>
<td>4</td>
<td>121 ± 13.2</td>
<td>25 ± 1.7</td>
<td>12 ± 1.4</td>
<td>10 ± 1.3</td>
</tr>
</tbody>
</table>

**Table II**

*Effect of Thyroxine upon CoA Level of Liver*

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>No. of rats</th>
<th>Mean CoA units, per gm. fresh tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Normal; normal diet</td>
<td>8</td>
<td>129.5 ± 3.6*</td>
</tr>
<tr>
<td>C</td>
<td>Thyroidectomized</td>
<td>10</td>
<td>93.2 ± 8.5*</td>
</tr>
<tr>
<td>D</td>
<td>&quot; + 150 γ Na L-thyroxine pentahydrate</td>
<td>11</td>
<td>166 ± 8.9*</td>
</tr>
<tr>
<td>E†</td>
<td>Group C + 30 γ thyroxine</td>
<td>10</td>
<td>80.5 ± 8.1</td>
</tr>
</tbody>
</table>

* All the values differ significantly statistically.
† In each instance an aliquot of boiled extract from Group C had 30 γ of Na L-thyroxine added prior to incubation. The CoA levels recorded did not differ significantly from those found in Group C.

**DISCUSSION**

The control levels of coenzyme A (Group A, Table I) do not agree with those previously reported (9). On the other hand, the control values in Table II (Group A) are in close agreement with the figures reported by Kaplan and Lipmann. It is probable that the differences in these data can be attributed to the differences in weight of the animals of the two groups (90 to 150 gm. in Table I; 250 to 350 gm. in Table II). Kaplan and Lipmann do not report the weights of the animals used.

It appears quite clear from Table I that thyroxine exerts an influence upon the level of CoA in various tissues. In the second series, in the case of the liver this influence is shown to be significant, although there was not as great a change (78 per cent increase compared with 147 per
cent). In collateral studies it was demonstrated that triiodothyronine had a similar influence upon the CoA levels of tissues, but, as in most other tests comparing the effects of thyroxine with those of triiodothyronine, the latter was found to be more active (3 to 5 times).  

The addition in vitro of thyroxine to aliquots of liver from the thyroidec-tomized animals, carried out in the second series of investigations, showed that, while in vivo effects could be demonstrated following the administration of thyroxine, no such changes were observed following the addition in vitro of thyroxine in relatively high amounts (30 γ).

It seems reasonable to expect that thyroxine would raise the concentration of CoA in various tissues, but not necessarily at the same rates. A possible explanation for the marked effects observed upon the liver in contrast to other tissues is found in the experiments of Albert and Keating (10), who observed that the liver seems to collect thyroxine so that, by 36 hours after administration of labeled thyroxine, the liver contains much more thyroxine than the rest of the body.

If thyroxine influences the energetics of the organism, it may be assumed that increased amounts of adenosinetriphosphate will be formed. Since Novelli (11) has demonstrated that adenosinetriphosphate is involved in the formation of CoA from pantetheine, the influence of thyroxine on CoA concentration may be secondary to a general enhancement of metabolic processes.

SUMMARY

The coenzyme A levels of liver, heart, brain, and small intestine have been determined in rats which were either normal, thyroidectomized, or thyroidectomized and treated with 150 γ of sodium L-thyroxine pentahydrate.

It was determined that the level of coenzyme A in the tissues was influenced markedly by thyroxine.

BIBLIOGRAPHY


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