THE EFFECT OF EXPERIMENTAL OBSTRUCTIVE JAUNDICE ON THE RAT THYROID

By

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The early observations of Hürthle (1894) and Wiener (1901) suggested that ligation of the common bile duct and derivation of the bile outside the body affects the thyroid. The experimental studies of these effects performed up to date show conflicting results. Hürthle (1928) states that ligation of the common bile duct increases the staining of the colloid, and that there are drops of colloid in the epithelium, which suggests activity of the gland. On the other hand, Rosselli del Turco & Matteini (1949) could observe no distinct changes in the thyroids of rabbits after ligation of the common bile duct.

The derivation of the bile outside the body calls forth an increased activity of the thyroid according to Latteri (1933) and Uffreduzzi (1933), whereas Wiener (1901), Altenburger (1926), Leriche & Jung (1935) and Verne & Verne (1940) observed a low epithelium and increased amount of colloid, i.e. a thyroid inactive as far as the histological picture is concerned. Recently, Allara & Le Brun (1952) found that the histological picture of the thyroid of dogs was inactive during the first few months after bile derivation outside, after which it showed signs of increased activity.

The object of the present study was to find out whether ligation of the common bile duct affects the thyroid gland in rats. Observations were also made on the other endocrine organs.

MATERIAL AND METHODS

Thirty-five male albino rats of the Wistar strain weighing 200–225 gm. were used. Ligature of the common bile duct was performed in 20 of them by means of a silk suture under evipan-sodium (Evipan-Natrium »Bayer«) anaesthesia. In addition, the

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common bile duct was cut below the suture. Fifteen animals served as controls. An intra-abdominal sham operation was performed in 10 of them under evipan-sodium anaesthesia. After one to four weeks the experimental and the respective control animals were killed by decapitation and bled. The thyroid, pituitary, adrenal and thymus glands and the testes were removed and weighed. After fixation in Bouin’s fluid they were embedded in paraffin and stained with Mallory’s azan method. For the determination of the relative proportion of the thyroid epithelium, colloid and stroma, the method of Uotila & Kannas (1952) was used. Specimens of the liver were taken from some of the experimental animals.

RESULTS

Three of the experimental animals died 2–4 days after the operation with symptoms of peritonitis. Two animals developed a fistula between the gall-bladder and the duodenum through omentum, and no jaundice appeared. These five animals were excluded from the experimental series.

A severe obstructive jaundice developed in all the remaining experimental animals within a few days. They lost appetite and weight, and the formation of ascites was observed. After killing the animal a yellow pigmentation of several internal organs was seen. The surface of the liver was very finely granular. Histological examination of the liver revealed somewhat increased connective tissue and infiltrations by inflammatory cells.

Histological examination of the thyroid of the experimental animals showed an increased amount of colloid and a low epithelium as compared with controls.

Fig. 1.
The thyroid of a control rat. 275 X.
The proportion of the epithelium, colloid, and stroma as measured according to the method of Uotila and Kannas was as follows:

<table>
<thead>
<tr>
<th></th>
<th>Epithelium</th>
<th>Colloid</th>
<th>Stroma</th>
</tr>
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<tbody>
<tr>
<td>Control animals</td>
<td>79.2 ± 1.4</td>
<td>13.6 ± 1.2</td>
<td>7.2 ± 0.2</td>
</tr>
<tr>
<td>Experimental animals</td>
<td>65.4 ± 1.4</td>
<td>25.7 ± 1.4</td>
<td>8.9 ± 0.3</td>
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</tbody>
</table>

*Fig. 2.*
The same thyroid of a control rat. 600 ×.

*Fig. 3.*
The thyroid of an experimental rat. 275 ×.
The same thyroid of an experimental rat. 600 X.

The sum of the epithelium, colloid, and stroma was denoted by 100. The differences between the values of both the epithelium and the colloid were statistically significant. The values of the epithelium of the experimental group varied from 56 to 75 per cent and those of the control group from 72 to 89 per cent, the values of the colloid in the experimental group from 17 to 34 per cent and those of the control group from 8 to 23 per cent. The highest values of the epithelium in the experimental group were in general noted in animals killed three or four weeks after the ligature. No differences were seen between the values of the control animals either submitted or not submitted to operation.

The mean weights of the animals and their endocrine glands were as follows:

<table>
<thead>
<tr>
<th></th>
<th>Control animals</th>
<th>Experimental animals</th>
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<tbody>
<tr>
<td>Initial body weight (gm.)</td>
<td>221.3 ± 11</td>
<td>217.4 ± 10</td>
</tr>
<tr>
<td>Final body weight (gm.)</td>
<td>228.3 ± 11</td>
<td>187.6 ± 9</td>
</tr>
<tr>
<td>Weight of the thyroid (mg.)</td>
<td>23.8 ± 1.7</td>
<td>20.3 ± 2.1</td>
</tr>
<tr>
<td>Weight of the adrenals (mg.)</td>
<td>32.4 ± 1.7</td>
<td>55.0 ± 4.9</td>
</tr>
<tr>
<td>Weight of the hypophysis (mg.)</td>
<td>7.1 ± 0.6</td>
<td>6.7 ± 0.7</td>
</tr>
<tr>
<td>Weight of the thymus (mg.)</td>
<td>180.5 ± 8.5</td>
<td>87.3 ± 7.2</td>
</tr>
<tr>
<td>Weight of the testes (mg.)</td>
<td>2432.0 ±103</td>
<td>1979.0 ± 95</td>
</tr>
</tbody>
</table>

The differences in the final body weights, the weights of the adrenals, thymus, and testes between the two groups were statistically significant.

Histological examination of the adrenals of the experimental group revealed marked hypertrophy of the adrenal cortex in most of the cases (Fig. 5). In the pituitary glands of the experimental animals the number of basophil cells was somewhat increased. The thymus glands showed a clear involution. In the
testes, a slight involution of the germinal tissue was noticeable. All these changes were not present in all of the experimental animals.

**DISCUSSION**

According to our results, the obstructive jaundice obtained by ligature of the common bile duct seems to have a uniform depressing effect on the thyroid of the rat. This depressing effect can be attributable to the fact that at an early stage of the bile stasis the blood shows a remarkable concentration of bile acids, the principal constituents of the bile. The bile acids are cholesterol derivatives. Many of them have been observed to have a depressing effect on the thyroid or a protective effect against thyroxin, like cholesterol itself (Winebrenner & Marx, 1949), oestrogens (Chamorro, 1949), and cardiac glycosides (Kuusisto, 1952). After prolonged obstruction the concentration of bile salts in the blood diminishes, due presumably to the diminished synthesis of these substances as a result of progressive hepatocellular damage. Our results indicate that the depressing effect of obstructive jaundice on the thyroid is less pronounced after prolonged obstruction.

Some of our test animals showed changes in other endocrine glands similar to those of the general adaptation syndrome (Selye, 1950). Hypertrophy of the adrenal cortex, involution of the thymus and the testes, and increased basophilia in the hypophysis are characteristic of this syndrome. Hence, experimental obstructive jaundice can also be considered as a stress. There is rela-
tively little evidence of the reaction of the thyroid during stress, and perhaps, as Uotila & Pekkarinen (1951) stated, the significance of the thyroid in the adaptation syndrome has hitherto been underestimated. According to Selye (1951) the response of the thyroid to stress is usually bi-phasic and depends largely on conditioning factors. Uotila & Pekkarinen (1951) observed that in man there is, during the stress, at first an activation of the thyroid which diminishes afterwards when the reaction time is prolonged. Using rats as experimental animals l'sotalo (1954) observed that both acute and continuous stress seem to diminish the activity of the thyroid. If obstructive jaundice is considered as a prolonged stress, the thyroids of our test animals seem to react to this stress with decreased activity.

SUMMARY

The effect of experimental obstructive jaundice, obtained by ligature of the common bile duct, on the rat thyroid was investigated. Simultaneously, observations were also made on the other endocrine glands. The results indicate that experimental obstructive jaundice has a depressing effect on the thyroid of the rat. The causes of this effect are discussed.

REFERENCES

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Uffredduzzi, O.: Arch. ital. di chir. 40, 5, 1933.