CONTENT AND DISTRIBUTION OF LIPIDS IN THE LIVER IN EXPERIMENTAL THYROID TOXICOSIS

M. E. Bronshtein and A. V. Negovskaya

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Feeding animals with thyroid is followed by profound changes in lipid metabolism in the liver, depending on the duration of thyroid administration or the severity of the thyrotoxicosis. These changes are reversible in character.

Previous investigations [1, 3] have shown that animals with experimental thyroid toxicosis develop a series of pathological changes in lipid metabolism. These changes are expressed primarily as an increase in the total lipid content in the liver. Lipids accumulate in the liver through disturbances of the formation of β-lipoproteins and phospholipids by the liver and their liberation from it and through a decrease in the glycogen content of the liver. This last factor is accompanied by increased mobilization of fat from the fat depots, i.e., by an increase in lipolytic activity of the adipose tissue and by an increase in the concentration of free nonesterified fatty acids in the blood serum [2]. A deficiency of lipid breakdown may also play a role of some importance in the accumulation of fat in the liver. The changes in lipid metabolism discovered in thyroid toxicosis are reversible in character.

The object of this investigation was to make a histochemical study of the content and character of distribution of lipids in the liver of animals with thyroid toxicosis at different stages of its development, and also in the repair period.

EXPERIMENTAL METHOD

Experiments were carried out on male rats weighing 200-240 g kept under the same conditions and receiving the same diet. The animals were divided into four groups: group 1 – the control, group 2 – animals fed with thyroid for 15 days, group 3 – animals receiving thyroid for 30 days, and group 4 – animals in the repair period, i.e., 1 month after the end of thyroid administration. Each group contained 10 animals. Thyroid was given daily by mouth, with an initial dose of 0.2 g and a final dose of 0.7 g. The development of of thyrotoxicosis was assessed by the characteristic appearance of the animals, the changes in their body weight, and their serum protein-bound iodine (PBI) concentration. To detect lipids, the liver of the control and experimental animals was fixed in 10-12% neutral formalin solution. The tissue was cut into sections 10-15 μ thick on a freezing microtome. The sections were stained with a solution of Sudan III + Sudan IV in alcohol and acetone and with an alcoholic solution of Sudan black B.

To confirm the lipid nature of the substances discovered, control sections were treated with cold acetone (in a refrigerator at 4°C) for 24 h. The sections were then rinsed in distilled water and stained in the same way.

Laboratory of Pathological Anatomy and Laboratory of Pathological Physiology, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Yudaev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 71, No. 2, pp. 25-27, February, 1971. Original article submitted June 26, 1970.

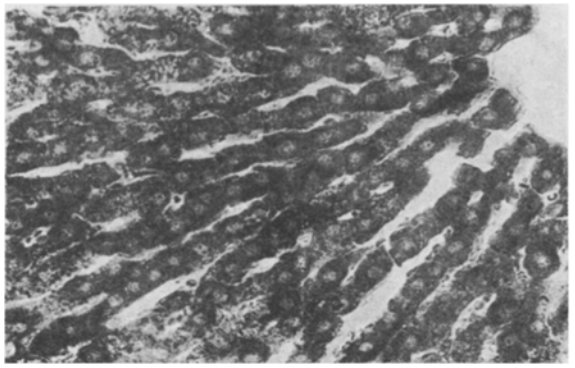

Fig. 1. Liver of animal from control group: most liver cells free from lipids; small lipid droplets diffusely scattered throughout cytoplasm of individual liver cells. Sudan III-IV, 200 ×.

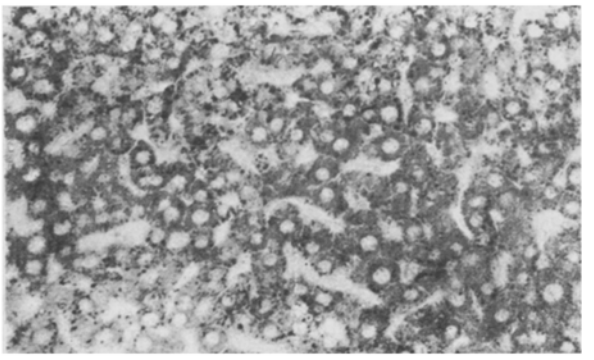

Fig. 2. Liver of animal with 15-day thyroid toxicosis: practically all liver cells contain lipid droplets of different sizes in their cytoplasm. Sudan black B, 200 ×.

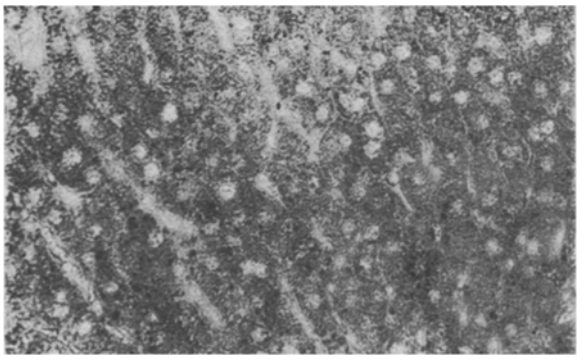

Fig. 3. Liver of rat in repair period: many liver cells contain various numbers of relatively large lipid droplets. Sudan black B, 200 ×.

EXPERIMENTAL RESULTS

Control Animals (Group 1). Most of the liver cells of the intact rats as a rule contained no histochemically-detectable lipids. Sometimes individual cells contained small single drops, stained with Sudan III-IV and Sudan black B, in their cytoplasm. Very rarely, small lipid droplets diffusely filled the whole cytoplasm of groups of two or three cells (Fig. 1). A very small quantity of fat was found also in the interlobular connective tissue.

Animals Receiving Thyroid for 15 Days (Group 2). Practically all the liver cells of these animals, unlike the controls, contained a certain quantity (usually average) of fat which was uniformly distributed throughout the cytoplasm. The fat droplets were mostly circular in shape and of different sizes (Fig. 2). Occasionally individual cells appeared overloaded with fat. Large lipid droplets also appeared in the liver stroma, mainly beneath the capsule.

Animals Receiving Thyroid for 30 Days (Group 3). In the animals of this group, far fewer cells contained fat than in the animals of group 2, although the total number of cells with lipid inclusions was still much higher in the liver of these animals than in those of the control group. Usually single or small groups of cells in a lobule contained a variable number of lipid droplets. As a rule these droplets were smaller than in the animals with a 15-day toxicosis, but there could be many more of them in the cell.

Animals in the Repair Period (Group 4). Many of the liver cells in the animals of this group contained lipid droplets (Fig. 3). The cytoplasm of these cells contained either solitary, relatively large lipid droplets or a few tiny lipid granules scattered throughout its area. In some lobules, small groups of cells were so loaded with fat that the cell borders could not be distinguished. The lipid droplets were considerably increased in size and altered in shape: instead of circular, they were shapeless.

The results of these histochemical investigations show that nearly all the fat detected in the liver of intact rats and of rats with thyrotoxicosis is bound with the cytoplasm of the liver cells. They also demonstrate a definite correlation between the lipid content in the liver and the severity of the thyrotoxicosis. On the 15th day of development of thyrotoxicosis, for example, the total lipid content in the liver of the experimental animals was sharply increased. Whereas the total lipid content in the liver of the intact rats, as previous experiments showed [1], is 14.07 ± 0.717 g%, in the animals of group 2 it was 20.82 ± 1.48 g%. This increase in content occurred both through an increase in the number of cells containing lipids and an increase in the number of lipid droplets in the individual liver cells, as well as through an increase in the

size of the lipid droplets themselves. However, on the 30th day of thyroid administration, when the thyrotoxicosis reached its greatest severity, the quantity of histochemically detectable fat was considerably reduced. Similar results were obtained previously in a biochemical investigation of the liver [1]. The total content of lipids in the liver of the animals of group 3 fell to 16.95 ± 0.695 g% compared with the lipid content in the liver of the animals of group 2. The number of cells in which lipids were detected and the size of the cytoplasmic lipid droplets were reduced. Despite the decrease in the lipid content in the liver of these animals, it was still higher than in the liver of the intact rats. In thyrotoxicosis, the change in the lipid content in the liver is thus fluctuating in character. Stopping thyroid administration (the repair period) was accompanied by further accumulation of fat, but in the period investigated it did not reach the level characteristic of the animals of group 2. The lipid droplets also were increased in size, and some cells appeared to be overloaded with lipids, which was never observed in the animals of the other groups. Biochemical tests showed that the lipid content in the liver during the repair period is 15.4 ± 0.49 g%.

It is clear from these results that feeding animals with thyroid produces profound changes in lipid metabolism in the liver. These changes depend on the duration of thyroid administration and, consequently, on the severity of the experimental thyrotoxicosis. They can be clearly demonstrated both by biochemical and by histochemical studies of the liver of these animals. However, as the results of the present investigations showed, changes in the lipid content observed at different times of experimental thyroid toxicosis are reversible in character.

LITERATURE CITED

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