postnatal life (from the 1st until the 7th days after birth of rats), but somewhat later (from the 10th until the 17th days). Early exposure to cold in the present experiments led to the opposite effect: a persistent delay in the formation of the digestive transport conveyor. It is important to note that the development of the intrinsic transport system responsible for transmembrane transport of "free" glucose under the present experimental conditions, underwent no appreciable change. This result suggests that the mechanisms of development of enzyme-transport systems are more sensitive to stress than the mechanisms of development of intrinsic transport systems. This is in agreement with the abundant data showing that in certain pathological states selective impairment of enzyme systems may be observed while the intestinal cells maintain normal transport functions [5, 6].

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ROLE OF β-ADRENORECEPTION IN REALIZATION OF GLYCOGENOLYTIC AND LIPOLYTIC EFFECTS OF AN EXCESS OF THYROID HORMONES

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Experiments on rats showed that chronic administration of the β-adrenoblocker propranolol in doses blocking glycogenolytic and lipolytic effects of exogenous adrenalin, does not prevent the fall in the glycogen level in the liver and myocardium and the rise in the serum free fatty acid level and in the lipolytic activity of adipose tissue in vitro arising under the influence of large doses of thyroxine.

KEY WORDS: thyrotoxicosis; adrenergic mechanisms; glycogenolysis; lipolysis.

Previous investigations [1] showed the catecholamine-independent action of thyroid hormones on function and metabolism of the myocardium. However, the role of adrenergic mechanisms in the genesis of the disturbances of lipid and carbohydrate metabolism arising during thyrotoxicosis has been inadequately studied. It has been shown that β-adrenoblockers prevent manifestation of the activating effect of thyroxine on heart

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TABLE 1. Glycogen Content (in g %) in Myocardium and Liver of Rats (M ± m)

Group of animals	Liver	Myocardium
Control (n = 10)	1,9±0,05 $P<0,01$	0,32±0,06 $P<0,01$
Receiving thyroxine (n = 10)	0,04±0,006	0,09±0,02
Receiving propranolol (n = 10)	2,03±0,04 $P<0,01$	0,38±0,04 $P<0,01$
Receiving thyroxine + propranolol (n = 10)	0,053±0,008	0,05±0,02

TABLE 2. Serum FFA Concentration (in μ eq/ml) and Lipolytic Activity of Adipose Tissue (in μeq FFA/ml medium) in Rats (M ± m)

Group of animals	Serum FFA	Lipolytic activity of adipose tissue
Control (n = 10)	0,64±0,005 $P<0,05$	2,09±0,3 $P<0,05$
Receiving thyroxine (n = 10)	0,89±0,006	4,56±0,06
Receiving propranolol (n = 10)	0,37±0,004 $P<0,5$	2,27±0,7 $P<0,05$
Receiving thyroxine + propranolol (n = 10)	0,54±0,003	4,36±0,4

muscle phosphorylase [8], but changes in the indices of carbohydrate metabolism still take place in patients with thyrotoxicosis even after administration of β-adrenoblockers [7]. The ineffectiveness of Inderal (propranolol) in relation to the metabolic effects of thyroid hormones has been noted by other workers [3, 11]. In the investigation described below the intensity of the glycogenolytic and lipolytic effects of large doses of thyroxine, administered for a long period to animals in the presence or absence of β-adrenoblockade, was compared.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats initially weighing 110-130 g. The animals were kept under ordinary animal house conditions. L-thyroxine (from Reanal, Hungary) was dissolved before use in alkalified physiological saline, which was then neutralized and injected subcutaneously into rats once a day in a dose of 400 μg/100 g body weight for 10-14 days. By producing experimental thyrotoxicosis in this way it was possible to cause emaciation of the animals (on average by 17%) and the appearance of marked tachycardia (a mean increase in heart rate by 150 beats/min). The animals were deprived of food on the evening before sacrifice. Water was not restricted. Thyroxine was injected (by the same scheme) into rats of the other group, superposed on chronic subcutaneous injection of propranolol (Obsidan, from East Germany) (three injections daily, 1.35 mg per injection, at 9 a.m., 5 p.m., and midnight). To obtain the necessary propranolol concentration, one tablet (40 mg) of Obsidan was crushed to a fine powder and suspended in 5 ml of an ampul solution of the same substance. The completeness of β-adrenoblockade was tested in special experiments by determining the lipolytic and glycogenolytic effects of a single subcutaneous injection of adrenalin (50 μg/kg) and also the effects of chronic administration of propranolol alone in the above-mentioned dose. The animals were decapitated. The free fatty acid (FFA) concentration in the blood serum was determined by Duncombe's method [6]. The liver was quickly removed and the glycogen content [13] determined in a weighed sample of the organ. Pieces of epididymal adipose tissue (100 mg) were incubated in Krebs–Ringer–bicarbonate buffer (pH 7.4) containing 3% fat-free bovine serum albumin (from the Research Institute of Experimental Medicine, Minsk). The buffer was aerated with a mixture of 96% O_2 and 4% CO_2 and the samples were incubated at 37°C for 1 h; the increase in the FFA concentration in the medium was determined. The significance of differences between the numerical data was assessed by the Fisher–Student criterion.

EXPERIMENTAL RESULTS

The results of determination of the glycogen level in the myocardium and liver of the experimental animals are given in Table 1.

TABLE 3. Effect of Adrenalin (3 μg/ml) on Lipolytic Activity of Adipose Tissue in Rats (M ± m)

Experimental conditions	Without adrenalin	With adrenalin	P
Thyrotoxicosis (n=10)	4,56±0,6	7,12±0,5	<0,05
Thyrotoxicosis + propranolol (n - 10)	4,36±0,4	3,33±0,8	>0,05

Clearly experimental thyrotoxicosis was accompanied by a sharp fall in the tissue glycogen concentration. This fall was evidently unconnected with activation of adrenergic mechanisms, for it was completely unaffected by administration of the β-adrenoblocker propranolol. The effects of α-adrenoblockers were not tested, for experiments in which Inderal and phentolamine were given showed conclusively that the glycogenolytic action of catecholamines is mediated through a β-adrenoreceptor mechanism [3].

To verify the completeness of the adrenoreceptor blockade in the present experiments, special tests were carried out in which adrenalin was injected into rats which had been given propranolol by the scheme described above. The animals were decapitated 15 min after injection of adrenalin. Corresponding tests showed that adrenalin reduced by half the liver glycogen level in the control rats but did not change this index in animals receiving propranolol beforehand. Adrenalin lowered the glycogen content in the myocardium of control rats to 0.15 ± 0.01 g %, but its content in the heart of animals receiving propranolol was virtually unchanged compared with intact rats (0.38 ± 0.03 g %).

The glycogenolytic action of an excess of thyroid hormone, it can thus be concluded, is not realized by adrenergic mechanisms.

The results of determination of the serum FFA level and lipolytic activity of adipose tissue of the experimental animals are given in Table 2. Under the influence of large doses of thyroxine, as would be expected [5], the serum FFA level was distinctly increased. At first glance, this increase was blocked by propranolol. However, this conclusion is incorrect, for the serum FFA concentration in animals receiving propranolol alone was considerably lower than in the control rats, and the increase in this index produced by thyroxine was fully preserved. The changes found are very reminiscent of the effect of adrenoblockade on the heart rate in thyrotoxicosis [4, 12]. Propranolol evidently blocks only the "sympathetic component" of regulation of the blood FFA level, and the relative contribution of this component in thyrotoxicosis cannot be increased, for the degree of lowering of the FFA level as a result of the action of propranolol was virtually identical in the control rats and rats with thyrotoxicosis.

No inhibitory action of propranolol on the lipolytic activity of adipose tissue was found in vitro. The role of the "adrenergic component" in the regulation of spontaneous lipolysis in vitro is evidently relatively unimportant. Just as in the case of the serum FFA level, propranolol did not abolish the increase in this index in rats receiving thyroxine. These observations confirm and extend the results of investigations by Bray [3], who found that propranolol does not block the increase in lipolytic activity of the adipose tissue in rats receiving one injection of tri-iodothyronine. Similar results were obtained by other workers using somewhat different experimental conditions [14].

Special tests showed that the doses of propranolol used were adequate to block β-adrenoreceptors in adipose tissue. For instance, whereas in control animals the serum FFA level increased by almost 50% after injection of adrenalin, in rats receiving propranolol for a long period adrenalin caused no increase in this index. Moreover, adrenalin (3 μg/ml) constantly increased FFA liberation from incubated adipose tissue of rats receiving thyroxine alone, whereas the tissues of animals receiving thyroxine+propranolol did not respond to the addition of adrenalin to the incubation medium (Table 3).

It can thus be concluded that propranolol, in doses blocking the lipolytic effect of adrenalin, does not prevent the increase in the serum FFA concentration or activation of lipolysis in adipose tissue which take place in thyrotoxicosis.

In recent years it has been shown on myocardial tissue that the number of β-adrenoreceptors is increased in hyperthyroidism [15], and this could be responsible for the increased tissue sensitivity to catecholamines. First, however, this increase was observed in by no means every case of clinical or experimental thyrotoxicosis [2, 9, 10] and, second, an increase in sensitivity to exogenous substances in a particular disease cannot in

principle be regarded as proof of the their role in the origin of the symptoms of that disease, for as a rule sensitivity rises in the case of a deficiency of endogenous effects of the corresponding factors.

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RELATIONS BETWEEN PLATELET AND PLASMA-COAGULATIVE COMPONENTS OF HEMOSTASIS IN HEALTH AND DISEASE

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The adhesive-aggregative activity of the platelets and the rate of blood clotting were compared in 125 healthy subjects during an emergency adaptation reaction (emotional stress, ACTH loading) and in 157 patients with heart and circulatory diseases during the period of crisis, and also during acute drug therapy. Changes in the platelets and plasma-coagulative components of hemostasis were found to be opposite in direction, and on this basis new ideas were put forward to explain the hemostatic function of the platelets.

KEY WORDS: blood clotting; adaptation; platelets.

The problem of the relationship between adhesive-aggregative properties of platelets and the clotting power of the blood have been studied chiefly in vitro and in model experiments. The results are contradictory and largely depend on the concentration of procoagulants and the number of platelets.

The aim of the present investigation was to determine relations between the platelet and plasma-coagulative components of hemostasis in an emergency adaptation reaction in healthy subjects and in patients with diseases of the heart and blood vessels.

EXPERIMENTAL METHOD

The following parameters were determined in one blood sample before and after external intervention: the aggregating power of the platelets by Born's method [7], recorded graphically by O'Brien's method [10], adhesion of platelets to glass by the method of Moolten and Vroman [9], the number of platelets (in a humid

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