heterologous blood cells do not possess pyrogenic activity, probably because of the length of the period elapsing after phagocytosis of foreign cells (macrophages liberate pyrogen for 36 h [9]). Later removal of the exudate cannot be recommended because of the considerable contamination with granulocytes. The process of EP formation by macrophages can be triggered by phagocytosis of corpuscular particles: staphylococci or heterologous blood cells. EP formation by macrophages in the present experiments required additional stimulation *in vitro*. To determine the precise mechanism of EP formation by macrophages, and to elucidate the relationship between phases of activation and liberation of pyrogen, further investigations are required.

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EFFECT OF THYROID HYPOFUNCTION ON GROWTH OF THE MUSCULOSKELETAL SYSTEM AND BODY AS A WHOLE IN EARLY POSTNATAL RATS

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Depression of thyroid function by chronic administration of mercazolyl* to rats aged from 5-7 days to 4 months causes a reduction in motor activity of the animals, a decrease in the absolute and relative weights of the bones, muscles, and heart, reduced oxygen demand and cardiac activity, and also hypercholesteremia, combined with a fall in the cholesterol level in the skeletal muscle tissues. Delayed growth and development of the musculoskeletal system and the reduced oxygen consumption lead to a decrease in body weight of the experimental rats under the age of 1 month compared with that of control animals. In rats aged 1-4 months, these factors lead to an increase in the gain in weight because of disturbance of lipid metabolism, despite a decrease in weight of the muscles and bones.

KEY WORDS: thyroid gland; musculoskeletal system; autonomic systems.

Laboratory investigations have shown that in each period of postnatal development the intensity of growth, the level of energy metabolism, and activity of autonomic systems are determined mainly by the particular features of development of the skeletal muscles [1-3].

*1-methyl-2-mercaptoimidazole.

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In connection with existing data on delay of growth and development in thyroid hypofunction, it was decided to study to what extent this was connected with changes in the functions and development of skeletal muscles.

EXPERIMENTAL METHOD

Noninbred rats born in the animal house of the writers' institute were used. Eight rats were left in each litter. Starting from the 5th-7th day and until 4 months half the animals of the litter were given mercazolyl 5 times a week in a dose of 0.5 mg/kg, whereas the remaining rats received the same volume of physiological saline. The frequency of motor responses, on the basis of the number of movements ("jerks"), and the number of episodes of pulling and fibrillary activity [4] during sleep at 28°C were determined at the age of 10-14 days. At the age of 1 month, acetyl- and butyrylcholinesterase (AChE and BChE) activity in the blood was determined by Pokrovskii's method [5]. At the end of each month the body weight, oxygen consumption at rest [6], cardiac activity from the ECG in lead II, and the total blood cholesterol were determined. At the age of 4 months the animals were killed and the absolute and relative (as a percentage of body weight) weight of the bones, muscles, heart, lungs, and thyroid and adrenal glands were determined. The cholesterol concentration in the muscles also was studied by a slightly modified technique [7]; muscle tissue was extracted with an alcohol—ether mixture, and the subsequent course of the determination was the same as that in blood.

EXPERIMENTAL RESULTS

Blocking thyroid function was tested by the goitrogenic effect and the decrease in oxygen consumption. In the experimental rats at the age of 30 days the absolute and relative weights of the thyroid gland (10.25±1.1 mg and 0.039% respectively) were 41 and 60% higher than in the control (7.25±0.90 mg and 0.024%; $P<0.001$). At the age of 4 months the absolute weight of the gland (20.5±0.9 mg) was 8% higher than in the control (18.3±1.0). However, the relative weight of the thyroid gland did not differ (0.0079% respectively). By contrast with the action of methylthiouracil, the goitrogenic effect of mercazolyl was strong at an early age and almost undetectable in adult animals, as other workers have confirmed [8].

The results of determination of the oxygen consumption, body weight, heart rate (HR), and blood cholesterol concentration, month by month, are given in Table 1. They show that differences in body weight of the control and experimental rats depend on age. Under the age of 1 month, blocking thyroid activity with mercazolyl delayed the increase in body weight of the experimental rats (by 14%), but at the ages of 2, 3, and 4 months, on the other hand, a tendency was observed for the body weight to be higher (by 6, 14, and 13% respectively) than that of the control animals.

Delayed growth in the first month of life was combined with a lowered level of motor activity, oxygen consumption, and blood AChE and BChE activity. The number of motor responses of the experimental rats was 36.6% less than that of the controls (161±15 and 254±11 movements/h respectively). As a result of the less-marked motor activity of the experimental rats, natural stimulation of the hypothalamic-pituitary-adrenal system was evidently reduced. In rats aged 30 days receiving mercazolyl, a tendency was observed for the weight of the adrenals to be reduced (18.5±1.2 mg), for it was 4.5% less than in the control (19.5±1.3 mg). In rats aged 4 months the absolute and relative weights of the adrenals (31.5±4.9 and 0.012% respectively) were significantly lower (by 29 and 37%) than in the controls (44.2±3.5 mg and 0.019%; $P<0.05$). The oxygen consumption of the experimental rats aged 1 month was 12% less than in the control. This corresponds to strengthening of cholinergic control mechanisms. Blood AChE and BChE activity (0.45±0.005 and 0.63±0.007 i.u. respectively) were lower in these animals than in the controls (0.05±0.01 and 0.70±0.06 i.u.; $P<0.05$).

The sharper decrease in oxygen consumption and HR in the rats aged 2, 3, and 4 months receiving mercazolyl than in the control series, beginning at the age of 1 month, reflecting deepening thyroid hypofunction, caused an increase in the gain in weight, not retardation as previously. HR in animals aged 1, 2, 3, and 4 months was 15.7, 16.0, 20.6, and 10.0% respectively below the corresponding control values (Table 1). The increase in body weight of the rats aged 2, 3, and 4 months receiving mercazolyl cannot be interpreted as true acceleration of growth, for it was accompanied by a decrease in weight of the skeletal muscles (93.5±8.2 g) compared with that in the control animals (98.0±5.2 g; $P<0.05$). The relative weight

TABLE 1. Body Weight, Oxygen Consumption, Heart Rate (HR), and Serum Cholesterol Concentration in Rats Aged 1, 2, 3, and 4 Months (control and experimental; M±m)

Factor	1 Month		2 Months		3 Months		4 Months	
	control	expt.	control	expt.	control	expt.	control	expt.
Body weight, g	54,4±1,6	46,8±2,8	128,7±13,1	136,3±8,0	200,4±11,8	232,4±6,4	230,0±15,2	260,0±17,0
P		<0,05		>0,05		<0,05		>0,05
Oxygen consumption, ml/kg/min	67,0±1,4	59,0±2,0	46,8±0,5	42,0±0,6	42,3±1,0	34,9±1,6	37,9±1,5	29,2±2,0
P		<0,01		<0,01		<0,01		<0,01
HR, beats/min	496±10,0	438±10,0	450±7,0	398±9,0	390±11,0	310±11,0	350±12,0	315±9,0
P		<0,01		<0,01		<0,01		<0,05
Blood cholesterol concentration, mg %	106,0±6,3	127,3±6,2	83,6±1,1	100,2±4,1	72,5±4,0	98,0±5,3	72,6±6,2	98,5±4,5
P		<0,05		<0,01		<0,01		<0,01

of the muscles in the former was 35.8±1.6%; it was 15.8% less than in the control (42.5±1.1%; $P<0.05$). The weight of the bones in the experimental rats (8.6±0.7 g) was 16.5% less than in the control (10.3±0.3 g; $P<0.05$), and their relative weight was 27% less (3.3 and 4.5% respectively; $P<0.01$).

Delay of development of the musculoskeletal system causes retarded development of active organs functionally connected with it in the experimental animals, namely the heart and lungs, the weights of which (802±26 and 1270±40 mg respectively) were 9 and 12% less than in the control rats (882±24 and 1440±50 mg; $P<0.01$-0.05).

The relative weight of these organs also was less in the experimental rats (0.31 and 0.48%) than the corresponding control values (0.38 and 0.60%).

The serum cholesterol concentration in the rats receiving mercazolyl was on average 16% higher at all times of investigation than in the control rats. Disturbances of lipid metabolism also were expressed as increased deposition of fat in the subcutaneous areolar tissue, discovered at autopsy on the experimental rats.

Other workers also have observed excessive deposition of fat and disturbance of skeletal muscle functions in hypothyroidism [9, 10]. By contrast with changes in the blood, chronic administration of mercazolyl caused a decrease, not an increase, in the cholesterol concentration (51.6±1.5 mg %) in the skeletal muscles by the age of 4 months by 24.4% compared with its level in the control animals (68.1±5.5 mg; $P<0.01$). Protein synthesis also is depressed in the skeletal muscles in hypothyroidism [11, 12]. The decrease in the cholesterol and protein concentration in the muscle tissue of the experimental rats was combined with a decrease in the total weight of the muscles. To assess the level of cholesterol, as a structural material in muscle tissue, its content in the muscles was determined in control rats in the first month of life, when the growth constant is particularly high [1, 3]. The cholesterol content in the muscles at the age of 7-28 days was shown to vary from 138 to 191 mg %; it was much higher than in the control rats aged 4 months (68.1±5.5 mg %), when the growth constant was sharply reduced [1, 3]. It can be concluded from the results showing a reduction in motor activity, in the absolute and relative weights of the muscles, and a fall in their cholesterol concentration, that the disturbances of body growth in hypothyroid rats were largely associated with delayed growth and development of the musculoskeletal system, and not simply with disturbance of lipid and protein metabolism.

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