(an example of physical loading). With these steady-state values of $p_{\bar{v}}O_2$, $p_{\bar{v}}CO_2$, and $(\dot{V}_A/\dot{Q})_{mean}$, the dependences of ΔpO_2 and $\bar{p}_a$ are close (curves 2 and 3 in Fig. 1). Similar dependences of ΔpO_2 and $\bar{p}_a$ also were obtained for other examples of stationary gas exchange. When the gas exchange is not stationary, dependences of ΔpO_2 on $\bar{p}_a$ may differ considerably (curves 1 and 2, 3 in Fig. 1).

During stationary gas exchange, to determine $\bar{p}_a$ it is thus necessary to use ΔpO_2, whereas if the gas exchange is not stationary, ΔpCO_2 must be used. In conclusion, it will be noted that values of ΔpG depend not only on $\bar{p}_a$, but also on the blood pressure in the pulmonary veins. At high values of $\bar{p}_a$ the pressure in the pulmonary veins has a significant effect on ΔpG, but at low values of $\bar{p}_a$ this effect is negligible, as the experimental data in [6] confirm. If $\bar{p}_a$ exceeds 13 mm Hg (West's first zone is absent), ΔpG is determined by the size of the second zone, i.e., by the pressure in the pulmonary veins. In addition, at high values of $\bar{p}_a$ the slope of the curves in Fig. 1 relative to the pressure axis is shallow. These factors limit the application of the suggested method for determination of $\bar{p}_a$ to the range of normal (4 and 1 mm Hg) and high values of ΔpO_2 and ΔpCO_2. If other causes of nonuniformity of function of the lungs than gravitational are present, the blood pressure in the pulmonary arteries must be higher than that determined on the basis of the suggested dependence.

The results of this investigation thus enable the blood pressure in the pulmonary artery, an important parameter of the state of the respiratory and circulatory systems, to be determined, given certain conditions, from the values of ΔpO_2 or ΔpCO_2.

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MECHANISMS OF CARBOHYDRATE-INDUCED HYPERLIPEMIA

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KEY WORDS: hyperlipemia in rats; blood and liver lipoproteins; carbohydrate diet.

The term "carbohydrate-induced lipemia" was introduced by Ahrens in 1961 [2] to describe a hyperlipemic state caused in animals by feeding with a high carbohydrate diet. Data in the literature show correlation between the blood triglyceride level and its insulin and glucose levels [8, 9], and also with glucagon [5], which suggests that these hormones participate in the formation of the hyperlipemic state. Recent work has shown the unifying role of proteins in blood lipoprotein molecules and the importance of their composition for the normal formation, secretion, and catabolism of lipoproteins [15]. Meanwhile information on metabolism of apoproteins of the blood lipoproteins in hyperlipemic states is very scanty and the role of individual apoproteins in the mechanism of hyperlipemia is not clear.

Accordingly, the present investigation was undertaken with the aim of studying the rate of formation of the principal apoproteins of very low density lipoproteins in the liver and their ratio in the blood in carbohydrate-induced hyperlipemia and to compare these data with blood levels of insulin and glucagon.

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TABLE 1. Composition and Relative Proportions of Main Food Products (in % of total calorific value of diet; per 100 g body weight – 60 kcal)

Group of animals	Food products			
	casein	lard	starch	sucrose
Control	18	26	56	—
Experiment	18	11	30	41

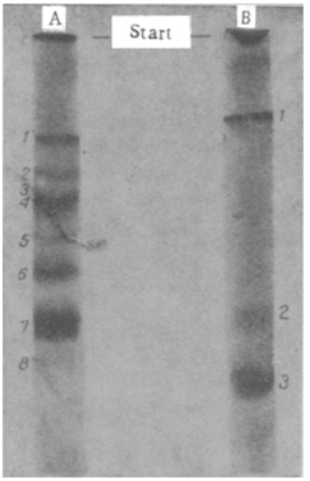

Fig. 1. Electrophoretic spectrum of VLDLP apoproteins in blood (A) and liver (B) of control rats in 10% PAG in the presence of sodium dodecylsulfate.

EXPERIMENTAL METHOD

Experiments were carried out on 60 male Wistar rats weighing initially 120-140 g and receiving a high-carbohydrate diet with sucrose (experimental group) and a balanced diet with the physiological amount of polysaccharides (control group) for 30 days. Both diets contained the essential quantities of salts and vitamins. The composition of the diets is given in Table 1. The development of hyperlipoproteinemia in the rats of the experimental group was determined by monitoring the total serum lipid level [7] and the concentration of triglycerides in the very low density lipoproteins (VLDLP) [3]. At the end of the period of feeding the animals on the above-mentioned diet, a solution of ^{14}C-lysine (50 μCi/100 g body weight) was injected intraperitoneally and the animals were decapitated 40 min later. VLDLP were isolated from blood serum by centrifugation at 100,000g [10], with a layer of NaCl solution with a density of 1.006 g/ml with 0.8 mM EDTA above the serum. The VLDLP were obtained from the liver of the rats also by preparative ultracentrifugation by the method described above. The blood serum and liver homogenate were first freed from chylomicrons, which were separated by centrifugation at 26,000g for 30 min. The isolated VLDLP were dialyzed against distilled water with 0.8 mM EDTA for 24 h, and delipidized with a mixture of butyl alcohol and diethyl ether (4:6). Apoproteins were dissolved in 0.2M Tris-HCl, pH 8.2, with 0.1M sodium dodecylsulfate and fractionated by electrophoresis (4 mA, 90 min) in 10% polyacrylamide gel (PAG). The quantity of protein taken for fractionation was 100 μg. Protein was determined by Lowry's method. The gels were stained with a 0.05% solution of Coomassie in 10% TCA. A Zeiss densitometer was used for densitometry of the gels. The stained regions of the gels were cut out (1-mm sections), placed in flasks, and disintegrated and decolorized with NCS solubilizer at 65°C for 1 h. Radioactivity in the samples thus obtained was measured on the "Isocap-300" counter (from Searle) in a system of toluene–dioxane–ethanol (5:3:2) with 0.4% diphenyloxazolyl and 0.15% diphenyloxazolylbenzene. The specific radioactivity of the apoproteins was calculated by using data obtained by measuring radioactivity of the corresponding zones of the gels and calculated values of the protein content in them. The serum insulin and glucagon concentrations were determined by radioimmunologic methods using kits of reagents from CEA-Sorin (France) from insulin and ASZ (USA) for glucagon.

TABLE 2. Specific Radioactivity (in cpm/mg protein) and Relative Content (in %) of Principal VLDLP Apoproteins in Liver and Blood (M ± m)

Fraction No.	Test object	Specific radioactivity		Relative content	
		control	experiment	control	experiment
1	Liver	661±100	1660±150*	340±24	520±71*
2		4600±680	6830±870	19±1,1	9,5±1*
3		1420±230	2250±320	48±6	39±5
1	Blood	4660±390	4 170±510	11,3±0,7	13,8±0,9*
3		3680±210	3 320±270	20,6±2,7	26±2,9
6		1910±290	10 150±900*	22,6±3	10,8±0,9*
7		1420±240	5470±430*	46,8±7,3	51,2±7,8

EXPERIMENTAL RESULTS

The blood lipid level in rats of the experimental group was considerably higher than the control (390 ± 24 and 213 ± 20 mg % respectively); the triglyceride content in VLDLP was increased by 76% (65 ± 7 mg % in the experiment, 37 ± 6 mg % in the control). As Fig. 1 shows, the protein component of VLDLP in the blood separated on electrophoresis in PAG into eight fractions. The experimental conditions (exposure for 40 min between administration of the labeled precursor and sacrifice of the animals) did not allow significant radioactivity to be detected in the minor components of the apoproteins of the blood VLDLP (fractions Nos. 2, 4, 5, and 8). According to data in the literature obtained during electrophoresis of apoproteins of rat blood VLDLP followed by identification of the proteins by immunologic methods and terminal amino acid analysis [6, 11], fractions Nos. 1, 3, 6, and 7 in the present experiments correspond to apoproteins B, E, C-II, and C-III. Apoproteins isolated from VLDLP of liver homogenate consisted of three fractions (Fig. 1) which are analogous in electrophoretic mobility to apoproteins B (fraction No. 1), C-II (fraction No. 2), and C-III (fraction No. 3) of blood VLDLP.

Data have been published on the electrophoretic spectrum of apoproteins of VLDLP isolated from the Golgi apparatus of rat liver [14]; most workers state that the main component is apo-B and that proteins of the C group are not present in the so-called nascent VLDLP [15]. However, other workers found the presence of other proteins besides apo-B in nascent VLDLP of the Golgi apparatus of rat liver [14], and found apo-C in perfusion fluid from the liver [13]. In the present experiments the presence of proteins of the C group in the electrophoretic spectrum of liver VLDLP was probably due to enrichment of the apoprotein composition of the VLDLP in the secretory vesicles by exchange with plasma lipoproteins through the plasma membranes.

Data on the specific radioactivity and relative content of VLDLP apoproteins of the liver of the control and experimental groups of rats are given in Table 2. A statistically significant increase in specific radioactivity was found in the animals of the experimental group in fraction No. 1 (by 2.7 times) and in other apoproteins (fractions Nos. 2 and 3). The relative content of fraction No. 1 in liver VLDLP of the rats of the experimental group was 18% higher than the control value on account of a decrease in the level of the other apoproteins. The percentage incorporation of labeled precursor into apoproteins of VLDLP from the liver of the experimental group of rats was 2.14 and of the control group 1.3. The specific radioactivity of fractions Nos. 1 and 3 of VLDLP of the experimental group of rats did not differ significantly from the control, whereas the specific radioactivity of fraction No. 6 was increased by more than 5 times, and the specific radioactivity of fraction No. 7 was 4 times higher than the control (Table 2). An increase in the relative content of fractions Nos. 1 and 3 also was observed (by 15 and 22% respectively). The blood insulin level in the animals of the experimental group increased by 25%, to 62 ± 3.6 microunits/ml in the experimental group from 47 ± 3.4 microunits/ml in the control. The glucagon level in the rats of the experimental group did not differ significantly from that in the control (60 ± 7 and 53 ± 6 pg/ml respectively), and the raio between the insulin and glucagon concentrations in the blood was 0.88 in the control and 1.1 in the experimental group.

Analysis of the blood levels of insulin and glucagon, on the other hand, and the rate of formation of the principal VLDLP apoproteins in the liver and their relative proportions in the blood, on the other hand, shows that in carbohydrate-induced hyperlipoproteinemia there is also a hyperinsulinemia, which is combined with activation of synthesis of protein B in the liver, by an increase in its relative content in the blood, and by high turnover of apoprotein C-III. The stimulating effect of insulin on protein biosynthesis in various animal tissues

including the liver has been discussed in the literature [1, 12]. Moreover, an increase in the rate of incorporation of ^{14}C-leucine into low density lipoproteins has been demonstrated on a model of alloxan diabetes [14]. Participation of insulin in the mechanisms of formation of hyperlipoproteinemia induced by a high carbohydrate diet will thus be evident.

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TRANSLOCATION OF DIFFERENT TYPES OF LIVER ESTROGEN RECEPTORS FROM CYTOPLASM TO NUCLEUS

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One of the most important properties of classical steroid hormone receptors is their ability to be translocated, in the form of a complex with the hormone after activation which is dependent on temperature and various other factors, from the cytoplasm of the cell into the nucleus – the main site of action of the hormone [10].

The aim of the present investigation was to determine whether different components of the heterogenous population of estrogen receptors (ER) found in the cytoplasm of the liver in male and female rats [1, 4, 5], possess this property, and also, should it be found that different forms of ER can be translocated, to study the basic principles of this process from the comparative point of view. The cytosol estradiol (E_2) receptor of the rat uterus, in which, as the writers showed previously [1], one form of liver ER is essentially similar in many of its physicochemical and hormone-binding parameters, was used for this comparative analysis. The tasks undertaken in the investigation are one approach to the solution of the problem of the functional role and significance of the existence of different forms of ER in the liver for the realization of the many different effects of estradiol both within the same tissue and also in different tissues.

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