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## AGE DIFFERENCES IN THE ATHEROGENIC EFFECT OF DIFFERENT FORMS OF HYPERLIPOPROTEINEMIA ON THE AVIAN VASCULAR WALL

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**KEY WORDS:** age; hyperlipoproteinemia; atherosclerosis.

The development of atherosclerosis and of its clinical manifestations is linked with the existence of risk factors, among the most important of which are disturbances in lipid and lipoprotein metabolism [2, 8]. It is generally considered that those types of hyperlipoproteinemia (HLP) that are characterized by an increased blood level of low-density lipoproteins (LDLP) and very low-density lipoproteins (VLDLP), namely types II, III, and IV, are the most atherogenic. HLP due to the accumulation of chylomicrons (CM) in the blood do not give rise to any significant atherosclerotic lesions in blood vessels [9, 11]. The character of the atherogenic effect of different types of HLP has not been studied from the age aspect, although we know that the number of persons with disturbances of lipid and lipoprotein metabolism increases with age [6, 13], as also does mortality from cardiovascular diseases of atherosclerotic origin [3]. HLP obtained in individuals following administration of cholesterol and intramuscular injection of estrogenic preparations provide convenient experimental models for the study of differences in the effects of HLP of different origin [12].

The object of this investigation was an experimental study of the atherogenicity of different types of HLP in young and old cocks.

### EXPERIMENTAL METHOD

Cocks of the Russian White breed, aged 5-6 months and 3.5-4 years, were used. HLP and atherosclerosis were induced in the birds by peroral administration of cholesterol (CS) in a dose of 2 g/kg body weight (50% solution in sunflower oil) for 4 months or by intramuscular injection of the estrogen diethylstilbestrol propionate (DESP) as a 0.5% oily solution in a dose of 5 mg/kg body weight 3 times a week for 4-5 months. In order to identify the character of the disturbances in the lipid and lipoprotein composition of the blood, total CS, triacylglycerols (TG), the total TG-rich fraction of lipoproteins (CM), VLDLP and LDLP (total lipoprotein fraction - TLPF), and the lipoprotein spectrum were determined on the basis of the technical recommendations of Klimov and Ganelina [4]. To measure the content of total CS and TG in the aortic tissue, a total lipid extract was first obtained [10]. The results were subjected to statistical analysis by Student's t test.

### EXPERIMENTAL RESULTS

Administration of CS or DESP caused unequal changes in the blood lipid and lipoprotein levels in young and old cocks (Table 1). The absolute content of TLPF, total CS, and TG increased more in the birds receiving DESP, irrespective of age. Analysis of the lipid and lipoprotein spectrum shows that hyperlipidemia and HLP in birds of this group were due to a predominant increase in the content of TG and CM, respectively. The total CS/TG ratio was much lower in the birds after injection of DESP than in normal birds, thus confirming that they had indeed developed hypertriacylglycerolemia.

Peroral administration of CS caused hypercholesteremia, an increase in the total CS/TG ratio, and accumulation of LDLP and VLDLP in the blood. In this case a higher level of HLP was found in birds aged 3.5-4 years than in those aged

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TABLE 1. Blood Serum Levels of Lipids and Lipoproteins in Birds of Different Ages, under Normal Conditions and after Administration of CS and DESP ( $M \pm m$ )

Age of birds	Parameter	Time of investigation, days				
		initial value	60		120	
			CS	DESP	CS	DES
5—6 months	TLPF, g/liter	4,27±0,28	8,60±0,48 <sup>b</sup>	115,62±9,16 <sup>b,d</sup>	17,70±0,7 <sup>b,c</sup>	125,62±4,92 <sup>b,d</sup>
3 1/2—4 years		3,99±0,28	12,43±0,63 <sup>a,b</sup>	120,74±8,44 <sup>b,d</sup>	16,80±0,81 <sup>a,b,c</sup>	119,07±5,11 <sup>b,d</sup>
5—6 months	Total CS, g/liter	1,22±0,08	4,24±0,29 <sup>b</sup>	10,58±0,58 <sup>b,d</sup>	5,45±0,40 <sup>b,c</sup>	11,33±0,49 <sup>b,d</sup>
3 1/2—4 years		1,30±0,10	5,70±0,35 <sup>a,b</sup>	11,05±0,84 <sup>b,d</sup>	7,01±0,54 <sup>a,b</sup>	10,86±0,63 <sup>b,d</sup>
5—6 months	TG, g/liter	0,41±0,04	0,99±0,07 <sup>b</sup>	19,07±1,34 <sup>b,d</sup>	1,20±0,08 <sup>b</sup>	19,17±1,63 <sup>b,d</sup>
3 1/2—4 years		0,55±0,03 <sup>a</sup>	1,12±0,08 <sup>b</sup>	18,97±1,56 <sup>b,d</sup>	1,35±0,09 <sup>b</sup>	19,06±1,59 <sup>b,d</sup>
5—6 months	Total CS/TG	2,96±0,19 <sup>a</sup>	4,28±0,27 <sup>b</sup>	0,55±0,02 <sup>b,d</sup>	4,54±0,30 <sup>b</sup>	0,59±0,03 <sup>b,d</sup>
3 1/2—4 years		2,36±0,14	5,08±0,39	0,58±0,03 <sup>b,d</sup>	5,19±0,36 <sup>b</sup>	0,57±0,03 <sup>b,d</sup>

**Legend.** Differences statistically significant ( $P < 0.05$ ): a) between young and old birds, b) compared with initial values, c) between values on 60th and 120th days of experiment, d) between birds receiving CS or DESP (at least 11 birds in each group).

TABLE 2. Lipid Content in Aorta of Birds of Different Ages under Normal Conditions and after Administration of CS and DESP ( $M \pm m$ )

Experimental conditions	Parameter studied, g/100 g tissue	Age of birds	
		5-6 months	3.5-4 years
Normal	Total CS	0,29±0,01	0,36±0,01 <sup>a</sup>
	TG	0,54±0,02	0,62±0,02 <sup>a</sup>
	Total CS/TG	0,54±0,02	0,58±0,03
Administration of CS	Total CS	0,73±0,03 <sup>b</sup>	0,94±0,04 <sup>a,b</sup>
	TG	0,86±0,04 <sup>b</sup>	1,05±0,06 <sup>a,b</sup>
	Total CS/TG	0,85±0,04 <sup>b</sup>	0,90±0,04 <sup>b</sup>
Injection of DESP	Total CS	0,53±0,02 <sup>b,c</sup>	0,60±0,02 <sup>a,b,c</sup>
	TG	1,36±0,07 <sup>b,c</sup>	1,95±0,09 <sup>a,b,c</sup>
	Total CS/TG	0,39±0,02 <sup>b,c</sup>	0,31±0,01 <sup>a,b,c</sup>

**Legend.** Differences statistically significant ( $P < 0.05$ ): a) between young and old birds; b) compared with normal; c) between birds receiving CS and DESP (at least nine birds in each group).

5-6 months. Similar age differences have been found in rabbits and rats [1, 7].

Investigation of the lipid content in the aortic tissue of birds 4 months (in the case of CS administration) and 4.5-5 months later (after injection of DESP) showed that lipids accumulated in both experimental models of HLP (Table 2). Higher values of all the lipid indices studied in the aorta were found in the older birds. A fact to which special attention is drawn is that the composition of lipids in the blood vessels of birds with induced HLP differed depending on the experimental conditions (administration of CS or DESP) and also on the type of hyperlipidemia. Hypercholesteremia (after administration of CS) was accompanied by greater deposition of CS in the tissues, whereas hypertriacylglycerolemia (after injection of DESP) led to accumulation of TG. The total CS/TG ratio was statistically significantly raised in the first group of birds and lowered in birds receiving DESP, compared with normal. The age differences were reflected in greater accumulation of total CS and TG in the vessels of the older birds, irrespective of the mode of formation of HLP, and this was reflected also in the more marked macroscopic manifestations of atherosclerosis.

The results thus indicate that, irrespective of the nature of the factor producing hyperlipidemia and the type of disturbances arising in lipid and lipoprotein metabolism, their atherogenicity increased during aging. This situation must be taken into account when the role of HLP as a risk factor in the development of cardiovascular diseases in the late periods of life is assessed. The results are also evidence of the important role of age changes in the blood vessel wall in its vulnerability to atherosclerotic damage, which can be deduced from the more intensive development of atherosclerosis in the older birds after injection of DESP than in the younger birds, despite the equal degree of disturbance of lipid and lipoprotein metabolism of the birds at different ages.

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## PERICARDIAL RESORPTION IN THE GROWING ORGANISM UNDER NORMAL CONDITIONS AND IN EXPERIMENTAL PERICARDITIS

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**KEY WORDS:** pericardial cavity; isotope resorption; experimental pericarditis.

Inflammatory diseases of the pericardium stem from a wide range of etiologic causes [1]. Recently, with the development of cardiac surgery, the incidence of postoperative pericarditis has increased [5]. In pediatric practice pericarditis is rare and, as a rule, it accompanies diseases associated with septicemia and the acute pneumonias, and it considerably aggravates the course of the underlying disease.

There are no data in the literature on the resorptive capacity of the peri-epicardial system in the young growing organism under normal and pathological conditions. The object of this investigation was to determine any differences which may exist in resorption from the peri-epicardial cavity of young animals under normal conditions and in experimental pericarditis [7].

## EXPERIMENTAL METHOD

Experiments were carried out on 26 mongrel puppies 1-3 months, using a technique specially developed by ourselves. Under ether-thiopental anesthesia with controlled respiration a microirrigator was sutured into the pericardial cavity, and one end of it was brought out through a subcutaneous channel in the posterior surface of the animal's neck. Through this irrigator radioactive  $^{131}\text{I}$ -hippuran (M-315), with a short half-life (5-6 days) and half-elimination time (3-4 min), and which is not cumulative in organs or tissues, could be injected into the pericardial cavity [6]. The isotope is resorbed by the terminal portions of the blood and lymphatic systems [4], is excreted from the blood stream by the kidneys, and accumulates in the bladder. The animal was fixed to the operating table in the supine position and the radioactive background was recorded from the region of the heart (the lower border of the counter was at the level of the costal angle) and the region of the urinary bladder (the level of the pubic symphysis) by means of STO-5 and SBT-7 recording counters and a B-3 computer. Both counters were placed 1 cm from the skin surface. To reduce the external background radiation the counters were placed under lead covers. The dose of isotope, with a radioactivity of 0.5 mCi/ml, injected into the animal was 0.5 ml/kg body weight. This dose had no pathogenic action on the tissues, for it was 10-15 times smaller than the minimal dose.

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