

PLASMA LIPIDS, LIPOPROTEINS, AND CHOLESTEROL ESTERIFICATION INDEX  
OF THE AMERICAN MINK *Mustela vison*

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Mammals of different species are known to differ in their susceptibility to the development of spontaneous atherosclerosis and its experimental model. In man and animals in which spontaneous atherosclerosis is observed (monkeys and pigs), the predominant localization of cholesterol is in lipoproteins of low and very low density (LDLP and VLDLP, respectively). Conversely, in animals resistant to the development of both spontaneous and experimental atherosclerosis (rats, cats, dogs, susliks) cholesterol is localized mainly in high-density lipoproteins (HDLP) [1].

The study of the causes of this species specificity would, in our opinion, assist with the understanding of the mechanism of atherosclerosis. As test object in the investigation described below the American mink *Mustela vison* was chosen, because there have been few studies of this species of animal, which is interesting in connection with the biochemistry of lipid metabolism, and the results have been contradictory [11, 15].

#### EXPERIMENTAL METHOD

Experiments were carried out on male American mink aged 6 months. The animals were starved for 24 h before sacrifice. Plasma was prepared with EDTA (1 mg/ml). To estimate activity of lecithin-cholesterol acyltransferase (LCAT) the plasma was incubated for 4 h at 37°C and the concentrations of free and esterified cholesterol determined before and after incubation. Activity of the enzyme was expressed as the increase in content of cholesterol esters in mg/h of incubation/liter plasma.

Plasma lipids were extracted according to [6] and fractionated by thin-layer chromatography on silica-gel in a system of hexane-diethyl ether-glacial acetic acid (80:20:1). Total cholesterol was determined as in [3]. Cholesterol of HDLP (HDLP C) was determined in the supernatant after precipitation of VLDLP and LDLP from the plasma by heparin in the presence of manganese ions [8]. The content of triglycerides was studied as in [12]. Three-layer disc electrophoresis of the plasma lipoproteins in polyacrylamide gel (PAG) was carried out in Magracheva's modification [2].

#### EXPERIMENTAL RESULTS

In the overwhelming majority of animals (the mean results are given in Table 1) the total plasma cholesterol concentration exceeded 200 mg/dl. The mean value (232 mg/dl) is significantly higher than the corresponding figure for cats, rats, guinea pigs, and rabbits [1, 14]. The HDLP C level in mink was very high — mean 187 mg/dl. In man, and also in animals in which atherosclerosis can be reproduced comparatively easily in the laboratory or arises spontaneously, this parameter was much lower (35–70 mg/dl in man, 42–64 mg/dl in monkeys, 24–51 mg/dl in pigs, 10–23 mg/dl in rabbits, 3–7 mg/dl in guinea pigs) [1]. HDLP C

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TABLE 1. Plasma Lipids and Lipoproteins of *Mustela vison* ( $M \pm m$ ,  $n = 30$ )

LCAT activity, mg cholesterol esters/h of incubation/liter plasma	Total plasma cholesterol, mg/dl	Plasma tri-glycerides, mg/dl	HDLP cholesterol, mg/dl	(LDLP C + VLDLP C)/HDLP C	Relative percentages of main classes of lipoproteins revealed by electrophoresis in PAG		
					$\alpha$ -LP	$\beta$ -LP	Pre- $\beta$ -LP
$79,0 \pm 7,2$	$232,0 \pm 13,5$	$158,0 \pm 10,8$	$188,0 \pm 9,3$	0,3	$85,0 \pm 2,3$	$12,0 \pm 1,1$	$3,0 \pm 0,3$

in mink accounts for on average 80% of the total cholesterol concentration, whereas in man it accounts on average for 25%, in monkeys for 46%, pigs 38%, rabbits 36%, and in guinea pigs for 10%. The results of electrophoresis in PAG showed the presence on average of 85% of  $\alpha$ -lipoproteins ( $\alpha$ -LP) in mink, 12% of  $\beta$ -LP, and about 3% of pre- $\beta$ -LP. The concentrations of phospholipids and triglycerides in the mink blood plasma averaged 403 and 158 mg/ml, respectively.

These results agree with data obtained previously by other workers who studied some blood plasma lipids of mink receiving different diets [11, 15]. To characterize the "atherogenicity" of the blood plasma lipoprotein spectrum the quotient (LDLP C + VLDLP C)/HDLP C was calculated. The value of this quotient for mink averaged 0.3, close to its values for the blood plasma of dogs (0.3), susliks (0.6), rats (0.4), and cats (0.5), i.e., animals resistant to the development of both spontaneous and experimental atherosclerosis and it differs considerably from the corresponding quotient in man (3.9), monkeys (1.2), pigs (1.6), rabbits (1.6), and guinea pigs (9.0), animals in which atherosclerosis can be reproduced relatively easily under laboratory conditions or arises spontaneously [1].

Evidence has recently been obtained of negative correlation between the HDLP cholesterol level in the blood plasma and the frequency of appearance of atherosclerotic lesions in the vessels. It has been suggested that hyper- $\alpha$ -cholesteremia is an antirisk factor in the development of atherosclerosis and ischemic heart disease [4, 10].

In connection with the facts described above it seems likely that the high blood concentration of HDLP in mink prevents the accumulation of lipids in the vessel walls through intensive elimination of cholesterol. Neither microscopic nor macroscopic foci of lipid infiltration have been found in the aorta and coronary arteries of mink of different ages receiving an ordinary and a high-cholesterol diet [15].

The degradation rate of VLDLP and LDLP in mink blood plasma may perhaps be significantly higher than that for the atherogenic lipoproteins of the blood plasma of man and of animals predisposed to the development of both spontaneous and experimental atherosclerosis. We know, in particular, that complete turnover of the VLDLP in human blood plasma takes 4-6 h [13], whereas complete turnover of rat VLDLP takes only 6-8 min [5].

The American mink is characterized by unique concentration of neutral lipids and lipoproteins, and it is thus a very interesting object with which to study some of the mechanisms of atherogenesis.

#### LITERATURE CITED

1. T. N. Lovyagina, "Lipoproteins and atherosclerosis," Author's Abstract of Doctoral Dissertation, Leningrad (1974).
2. E. Ya. Magracheva, Vopr. Med. Khim., 19, 652 (1973).
3. L. L. Abel, B. B. Levy, B. B. Brodie, et al., J. Biol. Chem., 195, 357 (1952).
4. K. Berg, A. L. Borresen, and G. Dahlin, Lancet, 1, 499 (1976).
5. O. Faergeman, T. Sata, J. P. Kone, et al., J. Clin. Invest., 55, 1210 (1975).
6. J. Folch, M. Lees, and G. H. Sloane-Stanley, J. Biol. Chem., 226, 497 (1975).
7. H. B. Lofland and T. B. Clarkson, Proc. Soc. Exp. Biol. (New York), 103, 238 (1960).
8. Manual of Laboratory Operation: Lipid Research Clinics Program, Vol. 1, Washington (1974).
9. I. F. McKenzie and P. J. Nestel, J. Clin. Invest., 47, 1685 (1968).
10. G. L. Miller and N. E. Miller, Lancet, 1, 16 (1975).
11. P. Narasimhalu, R. J. Berzile, and M. Lepage, Can. J. Animal Sci., 58, 191 (1978).
12. B. B. Nerry and C. S. Fings, Clin. Chem., 19, 1201 (1973).
13. G. Sigurdson, A. Nicoll, and B. Lewis, J. Clin. Invest., 56, 1481 (1975).
14. K. T. Stokke, Atherosclerosis, 19, 393 (1974).
15. D. B. Zilversmit, T. B. Clarkson, and L. B. Hughest, Atherosclerosis, 26, 97 (1977).