EFFECT OF HYPERCHYLOMICRONEMIA
AND HYPERPREBETALIPOPROTEINEMIA ON THE VASCULAR
WALL IN RATS OF VARIOUS AGES

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The effect of hyperchylomicronemia and hyperprebetalipoproteinemia on the vascular wall was studied in rats aged 6-10 and 26-30 months. The animals were given an intravenous injection of blood serum from rats which themselves had previously been injected intraperitoneally with Triton WR1339. Inclusions of chylomicrons and lipoproteins of very low density were found electron-microscopically in the endothelium of the old rats only. Swelling of the Golgi complex and mitochondria and dilatation of the cisternae of the endoplasmic reticulum in the endothelial cells of the young rats indicated activation of intracellular metabolism. The study of biosynthesis of certain classes of lipids in the aorta under these conditions showed inhibition of biosynthesis of free cholesterol, the intensity of which was the same in rats of different ages. Increased phospholipid biosynthesis was observed only in the young animals.

KEY WORDS: age; vascular wall; hyperchylomicronemia and hyperprebetalipoproteinemia; lipid biosynthesis

In the modern view the development of atherosclerotic lesions of the walls of blood vessels is due largely to the character of disturbances in lipid and lipoprotein metabolism in the blood, namely in the type of hyperlipoproteinemia. Types IIa, IIb, and IV, characterized by a high level of cholesterol and low-density lipoproteins (β-lipoproteins), are generally regarded as the most atherogenic [1, 4]. A problem not yet finally settled is the atherogenicity of other types of hyperlipoproteinemias, characterized by elevation of the blood level of very low density lipoproteins (VLDL) and chylomicrons (ChM). Several workers state that ChM cannot penetrate through the endothelium and are split up in the blood stream or on the surface of the endothelial cells [9, 10]. However, Foroglou-Kerameos [7] and Mjos et al. [8], using electron microscopy, found formations resembling VLDL and ChM in character in the endothelial cells and subendothelial space under the conditions of hyperlipidemia. When the role of these classes of lipoproteins in cardiovascular pathology is assessed it must be remembered that a high frequency of hypertriglyceridemia and disturbance of tolerance to exogenous glucose are regular phenomena which accompany the development of atherosclerotic lesions, especially in old age, and they may be reflected in particular by changes in VLDL and ChM metabolism.

The object of the present investigation was to study the character of the effect of hyperprebetalipoproteinemia and hyperchylomicronemia on the vascular wall in animals of different ages.

EXPERIMENTAL METHOD

Experiments were carried out on 68 rats. Hyperlipidemia was produced in young animals by intraperitoneal injection of Triton WR1339 in a dose of 500 mg/kg body weight. Analysis of changes in lipid and lipoprotein metabolism developing under these circumstances in the blood (from the standpoint of the type of hyperlipoproteinemia [4]) showed that they belonged to type V, i.e., hyperchylomicronemia and hyperprebetalipoproteinemia [3]. In the basic experiments, to rule out the possibility of the local effect of Triton on the vascular wall, lipemic blood serum from "Triton" animals was injected intravenously into young (6-10 months) and old (26-30 months) rats (1 ml/100 g body weight). Under these circumstances, biochemical determination of total cholesterol, triglycerides, total lipids, and the combined fraction of lipoproteins (α < 1.063; β-lipoproteins, prebetalipoproteins, and chylomicrons) was carried out after animals of different ages had been injected with blood serum containing the same concentration of lipids and lipoproteins (the concentration of the latter was 1246 mg%).

The biosynthesis of the individual classes of lipids in the tissues of the aorta was determined in vitro by the method described in [3]. An electron-microscopic technique was used.

The significance of the results was assessed statistically [2].

**EXPERIMENTAL RESULTS**

Part of an endothelial cell from the aorta of an old rat is illustrated on the electron micrograph in Fig. 1. The large vacuoles 0.3-1.5 μ in diameter, filled with amorphous electron-dense material, appeared a few minutes after injection of the lipemic serum. They could also be found when the vessel wall was examined after 1 h. Similar inclusions have been found in the endothelium of the coronary arteries of animals. Casley-Smith [5], who compared the structure of isolated ChM and of ChM in the mammary gland, showed that these complexes acquire this appearance in tissue sections. Meanwhile, in the control old animals no such formations were observed in the endothelium (Fig. 2).

After injection of lipemic blood serum into the young animals no electron-dense inclusions of lipid-protein complexes could be found in the endothelial cells (Fig. 3). Nevertheless, swelling of the Golgi complex and mitochondria and dilatation of the cisternae of the endoplasmic reticulum, which were observed under these circumstances, are evidence of activation of intracellular metabolism, possibly in connection with the action of the injected lipoproteins on the vessel wall. An argument in support of this explanation is given by the results of a study of the biosynthesis of certain classes of lipids (phospholipids, triglycerides, cholesterol esters, and free cholesterol) in the aortic tissue of experimental rats of different ages, which was carried out 1 h before the experiments began.

As Table 1 shows, under normal conditions differences were observed only in the biosynthesis of free cholesterol in the vessel wall between the rats aged 6-10 and 26-30 months. The significance of the small decrease in the specific activity of the remaining classes of lipids studied during aging could not, however, be confirmed by statistical analysis.