Hyperlipidemia and inhibition of lipoprotein lipase occur in rabbits after exposure to lethal or not lethal levels of whole-body ionizing radiation (1,2) and after antimitotic agent injection (cyclophosphamide) (3). However, the interrelationships of hyperlipidemia and the lipoprotein metabolism disorders remain obscure.

It is well known actually that some apolipoproteins exhibit an inhibiting or an activating effect on this enzyme. The CII apolipoprotein is generally agreed to be the most potent activator of lipoprotein lipase from different sources (4,5). Apo CI and apo CIII have been reported to inhibit CII activated lipoprotein lipase (4,5).

The example of these apolipoproteins had lead us to explore the influence of other apolipoproteins such as those displayed after antimitotic treatment.

Treated animals receive a maximal dose representing 1/2 LD 50 (65 mg/Kg) of cyclophosphamide in the ear marginal vein. 16 h after injection, blood was drawn by intracardiac puncture into EDTA. Lipoproteins of the different classes were isolated and purified by sequential ultracentrifugation. Subfractionation of VLDL was carried out by heparin-sepharose chromatography as described by Huff and Telford (6).

Apolipoproteins were fractionated by chromatography on Ultrogel AcA 54 and by preparative electrofocusing according to the procedure of Marcel et al. (7).

Hepatic triacylglycerol lipase and lipoprotein lipase were fractionated from control and treated rabbit post-heparin plasma by affinity chromatography on heparin Sepharose (8). Post-heparin lipolytic activity was measured according to Nilsson-Ehle and Schotz (9).

Cholesteryl ester transfer activity was determined according to Marcel et al. (10).

I. Rabbit lipoprotein modifications induced by antimitotic agent

Among these drugs, cyclophosphamide is frequently used in chemotherapy. Its injection induces in rabbit a hypertriglyceridemia and a hypercholesterolemia and provokes modifications of lipoproteins: VLDL increase and HDL decrease. Lipid composition of these VLDL and HDL shows cholesteryl ester- and triacylglycerol-rich VLDL and HDL poor in esterified cholesterol but relatively enriched in triacylglycerol.
Fig. 1: Electron photomicrograph of cyclophosphamide-induced lipoproteins negatively stained with 2% potassium phosphotungstate. Distribution of particles diameters in photographic prints.
A, VLDL of control rabbit; B, VLDL of treated rabbit; C, HDL of control rabbit; D, HDL of treated rabbit.