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0966 EXPERIMENTAL ATHEROSCLEROSIS: SURFACE ULTRASTRUCTURAL STUDIES IN THE RABBIT AORTA

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Numerous techniques have been employed in the study of experimental atherosclerosis. This study employs critical point drying, cryofracture and transmission and and scanning electron microscopic studies of experimental atherosclerosis in New Zealand white rabbits. Rabbits were maintained on a diet containing 1% cholesterol and 5% Wesson oil and had serum cholesterol levels of 1800 to 2100 mg/dl. Animals were sacrificed at 100 days, 181 days, 217 days, 225 days and 246 days after starting the atherogenic diet. Animals were fixed by perfusion, using Tyrode's solution followed by Trump's fixative. Most severe lesions were in the ascending aorta. Least severe lesions were in the common iliac arteries. Very early lesions had widened intimal spaces containing free lipid and smooth muscle cells containing lipid vacuoles. These lesions had distinct borders or were irregular and diffuse. More severe lesions had micro-ulcers at irregular borders. Endothelium over the surface of such lesions was variable and usually intact. An occasional cell with microvilli was observed. By cryofracture cells contained lipid vacuoles with multiple intercommunications. In later lesions cholesterol clefts were also seen. Lipid vacuoles were also observed in endothelial cells and in smooth muscle cells of the superficial media. It seems reasonable to conclude that lipid is transported into the subendothelial intimal space and there taken up by smooth muscle cells.

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0967 EFFECTS OF DIETARY FATTY ACIDS ON PLATELET AGGREGATION AND PLATELET THROMBOXANE B_2 PRODUCTION IN THE RABBIT.

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Semisynthetic isocaloric diets containing 25% of either butter or corn oil were fed to male rabbits for periods of 21 days and 2½ months. Platelet aggregation induced by threshold concentrations of collagen and sodium arachidonate and the conversion of labelled arachidonic acid were then studied. Response of platelets from butter-fed animals was considerably higher to arachidonate, whereas the thresholds for collagen-induced aggregation were similar in both groups of animals. Conversion of labelled arachidonic acid to thromboxane B_2, studied at different substrate concentrations in washed platelets, was significantly higher, at low substrate concentration, at 21 days in the butter fed group, and the difference was still present after 2½ months of treatment. Conversion of arachidonic acid to the hydroxy fatty acids by lipoxygenase activity was not affected by the dietary treatments. In conclusion, the metabolic conversion of exogenous arachidonic acid to thromboxane B_2 appears to be selectively affected by the type of dietary fatty acids and this effect is associated with changes in the response of platelets to aggregating concentrations of arachidonic acid.

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0968 HYPOTHETICAL ROLE OF HEPARAN SULPHATE (HS) IN ATHEROGENESIS

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Evidence indicates that the following factors are concerned with atherogenesis: Blood flow, thrombosis, endothelial injury, lipid and protein accumulation in the intima. The initiating mechanism is unknown. Several investigators have observed thrombus formation on structurally normal intima. The changes in the intima starting the process may, however, be biochemical rather than structural. HS is a weak heparin-like anticoagulant attached to the external endothelial cell surface. HS may be liberated by a platelet endoglycosidase, and may be inactivated by platelet factor 4 or beta-lipo-proteins. Assuming platelet damage because of the flow pattern, platelet aggregation and release reaction may result in inactivation of endothelial bound HS, thus favouring local thrombosis. High levels of beta-lipo-proteins in the circulating blood may add to this effect. Released platelet substances may increase vascular permeability counting for the plasma components found in atherosclerotic lesions. Exogeneous heparin binds to the intima, probably by substituting HS at the endothelial cell surface. Long term heparin prophylaxis may hypothetically prevent or retard advancing atherosclerosis. Heparin fractions, possibly with less side effects, could be of value.