CONTRACTIONS TO PLATELETS IN AORTAS OF CONTROL AND CHOLESTEROL-FED RABBITS. T.J. Verheuren, M.J. Van Dien and A.G. Herman. Division of Pharmacology, University of Antwerp (UIA), Universiteitsplein 1, B-2610 Wilrijk, Belgium.

Atherosclerotic aortas obtained from cholesterol-fed rabbits show a decreased responsiveness to norepinephrine and an increased responsiveness to low concentrations of serotonin and an unaltered responsiveness to prostaglandins. In vitro contractions induced by aggregating platelets are largely due to serotonin liberated during the aggregation. The present study was designed to compare the contractile responses to aggregating platelets in aortas obtained from control and cholesterol-fed rabbits. Segments of the aortic arch of the rabbits were then mounted in organ chambers for isometric tension recording.

In both the control and the atherosclerotic aortas increasing concentrations of platelets evoked contractions: the contractions obtained with the lower concentrations of platelets were significantly greater in the atherosclerotic tissues. The maximal responses and the ED50-values were comparable in both groups of blood vessels. No significant differences were observed when platelets obtained from control or hypercholesterolemic rabbits were compared. In the control and the atherosclerotic aortas the thromboxane receptor antagonist BM13505 at 2 x 10^-5M did not significantly affect the contractions to platelets obtained from either control or cholesterol-fed rabbits. The serotonin receptor antagonist ketanserin 5 x 10^-8M nearly abolished the responses to platelets in both groups of aortas.

These experiments illustrate that (1) the contractions induced by rabbit platelets in control and atherosclerotic aortas are mediated by serotonin and (2) the responses to platelets, as those to serotonin, are augmented in the atherosclerotic preparations.

DIET, HAEMOSTASIS AND THROMBOSIS

THE EFFECT OF TWO CHOLESTEROL-LOWERING AGENTS ON PLATELETS IN PATIENTS WITH HYPERCHOLESTEROLAEMIA. A. Norby, T. Simonsen, K. Lyngmo and B. Svensson, Dept. of Medicine, University Hospital, Tromsø, Norway.

Twenty-one subjects with type IIA hyperlipoproteinaemia, receiving dietary treatment were given Synvasin (MK-733), a HMG-CoA reductase inhibitor, 40 mg or Cholestyramin (Quetran) 2A g daily for a period of 12 weeks. Serum lipids, platelet cholesterol, phospholipids and fatty acid composition and platelet function were measured before and after the intake of the two drugs.

Both drugs reduced serum total cholesterol with approximately 30%. No significant changes were observed in platelet lipid concentrations or in the primary bleeding time. Collagen induced aggregation and thromboxane (TXA2) production were reduced, whereas thrombin induced aggregation and TXA2 production were unaffected. This study shows that both a cholesterol synthase inhibitor and Cholestyramin reduce the total serum cholesterol concentration and also reduce platelet aggregation and thromboxane synthesis without changing the platelet cholesterol content or the cholesterol/ phospholipid ratio. The effect on serum lipids and platelet function may indicate a beneficial effect of both drugs on arterial disease in patients with hypercholesterolaemia.

RAPID AND STRONG PLATELET REACTIONS AND COAGULATION CAUSED BY INJURY OF PROLIFERATING INTIMAL SMOOTH MUSCLE CELLS. L. Jørgensen (1,2), A.G. Grøthe (2). M.J. Verheuren (3) and R.J. Maitland. Department of Forensic Medicine, University of Oslo, Oslo, Norway (1), Institute of Medical Biology, University of Tromsø, Tromsø, Norway (2) and Department of Pathology, McMaster University, Hamilton, Ont., Canada (3).

We have shown that while one balloon catheter injury to rabbit aortae results in formation of a monolayer of platelets on the de-endothelialized surface, a second identical injury 7 days later gives rise to platelet-fibrin thrombi as observed at 30 minutes after the re-injury. The enhanced thrombogenicity the second time was related to damage of the neointima which had formed during the intervening days. It was unclear whether it was due to damage of the cells or of the interstitium. In order to further explore the mechanisms of the enhanced thrombogenicity following re-injury we observed by SEM and TIM the sequence of reactions before and during the first seconds and minutes after the second injury. The neointima was distributed around and opposite the branch orifices; the remainder of the luminal surface consisted of uncovered subendothelium. Within 10-30 seconds after the re-injury some of the neointimal cells were partly detached, and a few platelets and fibrin-like strands were in contact with them. Within 1-5 minutes many platelets single and in groups, with or without fibrin strands, had gathered in association with injured smooth muscle cells. The re-injured subendothelium remained uncovered the first 10-30 seconds; at 1-5 minutes a complete monolayer of swollen platelets had formed, but no fibrin was observed. These observations confirm that injury to neointima causes increased thrombogenicity. Since the first platelet reactions and coagulation are associated with injured neointimal cells, it is likely that injury to these cells precipitates these reactions.