Atherosclerotic aortas obtained from cholesterol-fed rabbits show a decreased responsiveness to noradrenaline, 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^-5 M did not significantly affect the contractions to platelets obtained from either control or cholesterol-fed rabbits. The serotonin receptor antagonist ketanserin at 5 x 10^-8 M 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.

**CONCLUSIONS**

1. Male New Zealand rabbits were fed either a control or a 0.3% cholesterol diet during 16 weeks. Macroscopic and microscopic examination of the luminal surface of the aorta obtained from these animals revealed a substantial amount of fatty streaks in the tissues obtained from the cholesterol-fed rabbits.

2. The serotonin receptor antagonist ketanserin at 5 x 10^-8 M did not significantly affect the contractions to platelets obtained with the lower concentrations of platelets.

3. The serotonin receptor antagonist BM13505 at 2 x 10^-5 M did not significantly affect the contractions to platelets obtained from either control or cholesterol-fed rabbits.

4. The serotonin receptor antagonist ketanserin at 5 x 10^-8 M nearly abolished the responses to platelets in both groups of aortas.

**DIET, HAEMOSTASIS AND THROMBOSIS**

**1002**

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

Twenty-one subjects with type IIA hyperlipoproteinaemia, receiving dietary treatment were given Synvulin (MK-733), a BFin-CoA reductase inhibitor, 40 mg or Cholestyramine (Questran) 24 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 50%. 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 Cholestyramine reduce the total serum cholesterol concentration and also reduce platelet aggregation and thromboxane synthesis without changing the platelet cholesterol content or the platelet 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), H. Møller (1) and B. Svensson (1).

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^-5 M did not significantly affect the contractions to platelets obtained from either control or cholesterol-fed rabbits. The serotonin receptor antagonist ketanserin at 5 x 10^-8 M 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.

**Decreased Responsiveness of Intimal Smooth Muscle Cells to Noradrenaline. T.J. 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 noradrenaline, 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^-5 M did not significantly affect the contractions to platelets obtained from either control or cholesterol-fed rabbits. The serotonin receptor antagonist ketanserin at 5 x 10^-8 M 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.

**Increased Factor VII Activity in the Rabbit Following Diet-Induced Hypercholesterolaemia. A. Mitropoulos (1), S.G. Walter (2), T.I. Menda (1) and M.P. Kadou (2).

The association of Factor VII coagulant activity (VIIc) with plasma lipid concentrations has been a consistent feature of a number of studies in man and points to plasma lipoproteins as determinants of VIIc. To modify plasma lipoprotein concentration and to study the effect of this on VIIc, rabbits were fed a 1%- cholesterol-supplemented diet. Treatment resulted in a many-fold increase in plasma cholesterol concentration with the major fraction of excess cholesterol associated with the very low and intermediate density lipoprotein fractions. VIIc was considerably higher in rabbits fed 1%- cholesterol-supplemented than in rabbits fed the standard diet. In both groups of rabbits, the direction and extent of variation in VIIc coincided with variation in cholesterol concentration so that over time there were significant and positive correlations between VIIc and plasma cholesterol. A method that provides a measure of the total functional factor VII concentration (VIIc) was also used. This assay involves clotting the plasma in the presence of excess tissue factor and therefore the conversion of all VIIc to the more reactive two-chain form of the protein (VIIa). The concentration of VIIa present in the serum was measured from the rate of appearance of excess of [3H]thrombin-blabeled factor X. By day 10 of treatment, and in all further comparisons VIIc was only slightly higher in the group of rabbits fed cholesterol-supplemented diet. This increased in VIIc, too, was due to a higher proportion of VIIa in the plasma of hypercholesterolaemic rabbits rather than to an increase in the concentration of the single-chain protein.