PLATELET AND FIBRIN DEPOSITION ON SUBENDOTHELIUM: OPPOSITE DEPENDENCE ON BLOOD SHEAR RATE.

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The rate of platelet deposition on subendothelium (adhesion + adhesion-induced aggregation) from anticoagulated blood is shear rate ($\sim V/d$) dependent and thus increases with increasing blood flow velocity (V) and decreasing vessel diameter (d). To investigate concomitant fibrin deposition on subendothelium of rabbit aorta was exposed to native blood under controlled flow conditions (Schweiz. Med. Wschr. 106, 1367 (1976)). Native blood was circulated by a roller pump for 3 min from a carotid artery through an annular perfusion chamber (maintained at 37°C) into a jugular vein of a rabbit at flow rates of 5, 20 and 40 ml/min, producing wall shear rates at the exposed subendothelial surface of 500, 2000 and 4000 s^{-1} , respectively. Subendothelium and adhering blood elements were immediately fixed by perfusion of glutaraldehyde avoiding any blood-air interphase. Platelet interaction with subendothelium and fibrin deposition were determined morphometrically. At a shear rate of 500, 2000 and 4000 s^{-1} , 23 ± 3 , 43 ± 4 and 66 ± 3 % (mean $\pm$ SE) of the surface were covered with platelets and 67 ± 12 , 26 ± 12 and 10 ± 4 % with fibrin, respectively. The corresponding values for adhesion-induced aggregation were 12 ± 3 , 38 ± 6 and 56 ± 5 % in native and about 4, 17 ± 5 and 29 ± 4 % in citrated (15mM) blood indicating that even a low citrate concentration inhibits adhesion-induced aggregation. Similar results were obtained with human blood drawn from a cubital vein.

This is direct evidence that fibrin deposition on subendothelium predominates at low (veins), platelet adhesion and aggregation at high (arteries + small vessel) shear rates.

PATTERNS OF DEPOSITION OF BLOOD CELLS ON THE LUMINAL SURFACE OF JUGULAR VEINS INDUCED BY SURGERY OR INFUSION OF VASOACTIVE SUBSTANCES. R.G. Schaub and G.J. Stewart. Temple University Health Sciences Center, Philadelphia, PA 19140.

The deposition of blood cells on canine jugular veins induced by intestinal anastomosis followed by a 4 hour post-operative interval or 4 hour intravenous infusion of vasoactive substances was studied by scanning and transmission electron microscopy (SEM,TEM). The vasoactive compounds infused were serotonin (200 $\mu g/min$), histamine (150 $\mu g/min$), or bradykinin (6 $\mu g/min$). Control dogs were infused with Tyrode's solution alone. Three dogs were used in each group. At the end of the experimental period 90% of blood was removed by total body perfusion. Immediately after asystole the vessels were partially fixed in situ then removed for further processing. The pattern of cellular deposition varied with the experimental group. Control dogs exhibited the least response with only sparse deposition of individual leukocytes and erythrocytes. Anastomosis dogs exhibited the greatest response with extensive deposition of erythrocytes and leukocytes both alone and in association with fibrous material. The response of serotonin infused dogs was limited to deposition of patches of leukocytes with occasional erythrocytes. Both histamine and bradykinin infused dogs exhibited a sparse to moderate deposition of leukocytes and erythrocytes on most of the luminal surface. In addition, these animals also had extensive focal deposition of leukocytes and erythrocytes around valves and inflow areas of feeder vessels. The results suggest: (1) extensive deposition of thrombotic material can occur in the early post-operative period, (2) agents known to alter endothelial permeability can induce moderate general and extensive focal cellular deposition, and (3) the extensive focal deposition induced by histamine and bradykinin infusion was limited to stress areas.

EFFECTS OF INFUSED PRODUCTS OF TISSUE INJURY ON GENERATION OF CIRCULATING FIBRIN MONOMER, CONDITION OF THE ENDOTHELIUM AND DEPOSITION OF BLOOD ELEMENTS ON JUGULAR VEINS IN THE DOG.

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In previous studies we found that major surgery in dogs resulted in generation of fibrin monomer and adhesion of blood cells to veins. In this study we investigated the effects of a 4-hour intravenous infusion of products of tissue injury on early events in deposition of thrombotic material on veins. Substances infused were (per minute): histamine, 150 μg ; serotonin, 200 μg ; bradykinin, 6 μg ; and, thromboplastin, 0.04 ml. Fibrin monomer was measured in pre- and post-infusion plasma. Jugular veins were prepared for scanning electron microscopy after removal of >90% of blood by whole body perfusion prior to asystole. No fibrin monomer was found in pre-infusion plasmas and in 1/4 post-infusion controls at low (1-20) dilution of protamine sulfate. However, monomer was found at higher dilution (1:80, 1:160) in post-infusion plasmas from all treatments. Even in the presence of circulating monomer no fibrin accumulated on the luminal surface of veins. Adhesion of blood cells to vessels was rare in dogs infused with Tyrode's solution or thromboplastin but was common in dogs infused with histamine, serotonin or bradykinin. Adhering cells were mostly leukocytes (PMN, giant cells) and erythrocytes with few platelets. Cells adhered to grossly intact but altered endothelium and to areas of endothelial disruption at side branches and valves. These observations show that: (1) infusion of vasoactive substances caused generation of considerable monomer; (2) in vivo generation of monomer was not sufficient to lead to thrombosis of medium sized veins, (3) infusion of vasoactive substances caused leukocytes and erythrocytes to adhere to altered endothelium.