## 0305
**08:45 h**

THE FATE OF SURFACE BOUND HEPARIN AND THE LONG TERM THROMBORESISTANCE OF HEPARINIZED MATERIALS. M.F.A. Goosen, M.V. Sefton and M.W.C. Hatton. Department of Chemical Engineering and Applied Chemistry, University of Toronto, Toronto, Ontario, Canada; and Plasma Proteins Research Laboratory, Department of Pathology, McMaster University, Hamilton, Ontario, Canada.

Displacement by plasma of radiolabeled thrombin and radiolabeled thrombin-antithrombin III inactive complex from a heparinized surface (heparin-PVA) was measured and found to be significant. For example, 63% of the thrombin and 90% of the complex that could not be removed by PBS alone was displaced by heat defibrinated plasma. Preliminary characterization (molecular weight, antithrombin III content) suggests that the eluting product consists largely of thrombin-antithrombin III complex and post complex antithrombin III. Heparin polyvinyl alcohol (PVA) gel beads were prepared by acetal coupling of the heparin to PVA using glutaraldehyde with $MgCl_2$ catalysis. Although permanently bound to the PVA (heparin removal rate was $1.67 \times 10^{-2}$ mg/g gel·min), the heparin retained at least part of its activity in thrombin time, recalcification time, chromogenic substrate and AV shunt assays. Thus, heparin need not be lost from a surface to impart thromboresistance. Our results further suggest that the resulting surface bound thrombin-antithrombin III complex can be displaced from the surface by a component or components of plasma (antithrombin III?) indicating that the surface bound heparin does not become saturated with inactive complex. These results support the argument that heparinization can be an important means of preparing the materials needed for the development of improved cardio-circulatory assist devices and blood handling procedures.

## 0306
**09:00 h**

FACTORS AFFECTING THROMBUS FORMATION ON SURFACES. J.S. Schultz, S.M. Lindenauer, and J. Penner. Engineering College and Medical School, University of Michigan, Ann Arbor, Michigan.

An ex-vivo test device consisting of a flow-through cylinder with a rotatable central rod has been developed for evaluating thrombus formation on surfaces. The rod can be coated with polymers, or segments of blood vessels can be placed on the rod. Blood access to the device is obtained by means of a A-V shunt, using dogs as the test animal. Measurement of platelet, fibrinogen, and red cell content characterizes thrombus composition on the rod and provides several indicies of the coagulation systems involved in thrombus development.

Tests of more than a dozen biomaterials showed that thrombus amount and composition on surfaces differ many fold under similar flow conditions. Increases in shear from 100 $sec^{-1}$ to 200 $sec^{-1}$ on the rod surface, by increasing the rotation rate of the rod, resulted in virtually complete reduction of rbc attachment, corresponding to a 75% inhibition of fibrinogen deposition while platelet attachment was only reduced by 50%. This demonstrates that shear has a differential effect on the various components of the clotting system.

The use of systemic drugs like aspirin and heparin showed that the effects on thrombus formation are quite different for materials with various degrees of thrombogenicity. Also it was demonstrated that when the same polymer material was cast from two different solvents to obtain variations in surface morphology the thrombogenicity was quite different.

A direct comparison of the thrombogenicity of biomaterials and vascular endothelium is possible by placing an everted piece of vein on the coated rod.

Tests showed that silastic and vein endothelium were similar with respect to platelet and frbrinogen deposition. This ex-vivo procedure provides an opportunity to assess the antithrombogenic effect of drugs applied directly to the surface of the excised vessel segment.

## 0307
**09:15 h**

VON WILLEBRAND FACTOR AND PLATELET DEPOSITION ON ARTIFICIALS SURFACES. P. Maisonneuve*, C. Pusineri**, J.P. Farges**, Y.Sultan*. *Hôpital Cochin-Paris. **Rhone Poulenc - Lyon.

Deposition of purified $^{125}I$. Von Willebrand factor (VWF) and $^{51}Cr$ platelets on well characterized artificial surfaces (Rhone Poulenc Lab.) were studied in the in vitro circulation system of Baumgartner. Free silica silicone rubber, cationic and anionic polyelectrolyte complexe (PEC) were directly synthetised on the central rode of the perfusion chamber. Concentration of $^{125}I$ VWF varying from 80 µg/ml to $1{,}5.10^{3}$ µg/ml were circulated for 10 mn at a shear rate of 800 $sec^{-1}$. On all surfaces VWF deposition is correlated with the VWF concentration in the circulating solution. With regard to the nature of the surfaces : whatever the concentration of VWF, silicones fixed hundred times less than PEC and among PEC the positively charged surfaces fixed 3 times more VWF than negatively charged PEC.

Similarly $^{51}Cr$ platelets resuspended in whole blood were studied in the same system at the same shear rate after 10 mn of circulation. It was found that platelet adherence on the various types of surfaces paralleled VWF deposition. In contrast no correlation between $^{125}I$ Fibrinogen and platelet fixation on the surfaces was found.

In another series of experiments the role of VWF on platelet adhesion to surfaces was tested. It was observed that fixation of normal platelets resuspended in the blood of a severe VW patient was identical to the fixation of platelets resuspended in normal blood. And this was verified after 1, 3, 5 and 10 mn of circulation, assuming that platelet fixation, at least in these experimental conditions, is independent of the presence of VWF in the system and that the plateau is reached before the first minute of contact. It is more likely that the amount of VWF, fibrinogen and the number of platelets deposited on a surface are related to the intrinsic properties of this surface and characterize the surfaces. These results showed that, platelets and VW factor do not interact on artificial surfaces as it has been demonstrated for the subendothelium of the vessel wall.

## 0308
**09:45 h**

THE INFLUENCE OF MATERIALS AND PLATELET INHIBITION ON THE THROMBOGENICITY OF ARTERIAL GRAFTS IN MAN. C.N. McCollum, H.C. Norcott, R.J. Hawker, M. Goldman, E. Snape, Z. Drolc. Queen Elizabeth Medical Centre, Birmingham, UK.

Prosthetic arterial grafts often thrombose when used to bypass diseased small arteries due to the deposition of laminated platelet thrombus. The rate of 111-Indium labelled platelet accumulation on autogenous vein, polytetrafluoroethylene (PTFE, Gore-Tex) and double velour Dacron (Microvel) has been investigated in patients and the influence of aspirin and dipyridamole (ASA/DPM) evaluated.

Two days before surgery 40 patients undergoing femoropopliteal bypass were started randomly and double blind, on either ASA 300 mgm + DPM 75 mgm tds or placebo. One week postoperatively autologous 111-Indium labelled platelets were injected and isotope emissions over the graft and contralateral leg counted for 7 days. Graft thrombogenicity was calculated as the daily rise in the ratio of counts, graft/contralateral thigh.

Three placebo and one ASA/DPM prosthetic grafts occluded prior to study. Thrombogenicity (mean $\pm$ SEM) was greatest in the Dacron grafts at 0.22 $\pm$ 0.03 on placebo (n=7) and 0.16 $\pm$ 0.03 on ASA/DPM (n=5) ($p < 0.05$). The effect of therapy however, was most striking in reducing thrombogenicity of PTFE grafts from 0.17 $\pm$ 0.03 (n=4) to 0.06 $\pm$ 0.01 (n=7) ($p < 0.02$). The thrombogenicity of 0.03 $\pm$ 0.005 was so low in the 13 vein grafts that the effect of therapy could not be determined.

The 111-Indium platelet technique described may be used to quantitate in vivo platelet deposition. In man the combination of ASA/DPM reduced the rate of thrombus formation on prosthetic materials. PTFE grafts with ASA/DPM therapy most nearly approach the low thrombogenicity of vein.