

ROLE OF VERAPAMIL (CALCIUM BLOCKER) IN THE REDUCTION OF PLATELET DEPOSITION IN GORE-TEX GRAFTS IN DOGS. V. Fuster, M.K. Dewanjee, K. Murphy, R.E. Vlietstra, P. Didisheim, M.P. Kaye. Mayo Clinic, Rochester, Minnesota, U.S.A.

Platelet calcium appears to be essential in platelet activation. Accordingly, Verapamil (a channel calcium blocker) was tested "in vivo" as a possible platelet inhibitor agent. Fifteen dogs underwent bilateral femoral artery grafting with one polytetrafluoroethylene (Gore-Tex) and one autologous vein graft. Peroperatively, five dogs were infused continuously with Verapamil (6 µg/kg/min) and 9 dogs were left untreated and the arterial prostheses were surgically implanted. Using autologous Indium-111-labeled platelets injected 24 hours prior to surgery as a platelet marker, grafts were removed 1 hour following resumption of blood flow. Radioactivity per unit weight of Gore-Tex, vein and blood were determined with a gamma counter and the relative radioactivity with respect to the internal reference standard of blood is tabulated below:

	Gore-Tex Blood	Vein Blood	Gore-Tex Vein
Control	19.70±5.40	3.02±1.77	11.20±4.11
Verapamil (I.V.)	2.52±2.88	1.39±0.89	1.35±1.17

Verapamil-treated dogs showed a significant reduction in the "in vivo" platelet deposition on Gore-Tex and autologous venous grafts. Preliminary data indicates that "in vitro" platelet aggregation with soluble calf skin collagen (515 µg/ml) and ADP (2-100 µM) is not different between control and drug-treated dogs.

Calcium channel blockers may be promising "in vivo" platelet inhibitor agents; in addition, they may provide further understanding of the different processes involved in "in vivo" and "in vitro" platelet activation.

EVALUATION OF PHARMACOLOGIC INHIBITORS OF PLATELET FUNCTION IN BABOONS. S. R. Hanson and L. A. Harker, Department of Medicine (Hematology), University of Washington, Seattle, Washington, USA.

The ability of aspirin (ASA), dipyridamole (DIP), sulfinpyrazone (SP) and combinations of these agents to prevent arteriovenous cannula thromboembolism in baboons has been assessed by measuring the destruction of autologous ⁵¹Cr-platelets. In 24 studies with untreated baboons (10-12 kg), thrombogenic polyurethane femoral A-V cannulae (Biorner, 50 cm, 4 mm i.d.) consumed $22.5 \pm 4.5 \times 10^6$ platelets/cm²-day. In animals with identical shunts, the efficacy of various antithrombotic treatment regimens was determined by measuring the percent reduction in platelet consumption (PC) compared to untreated control values. All drugs were given to at least four animals by oral administration twice daily.

ASA, 3-100 mg/kg/day, did not significantly reduce PC ($p > 0.02$). SP in doses of 10, 50 and 100 mg/kg/day reduced PC by 7, 48, and 97% respectively. DIP, 1, 2.5, 5, 10 mg/kg/day, reduced PC by 14, 34, 51, and 99% and was significantly more effective than SP ($p < 10^{-5}$). ASA (10, 15, 20 mg/kg/day) given with DIP (2.5 mg/kg/day) reduced PC by 47, 67, and 94% demonstrating significant and dose dependent potentiation of DIP by ASA. ASA (10 mg/kg) potentiated DIP (2.5 mg/kg/day) less effectively when given only with the first dose of DIP, or when given twice daily but two hours after administration of DIP ($p < 0.01$). In both cases PC was reduced about 67% (vs. 94% for simultaneous administration twice daily). DIP (2.5 mg/kg/day) plus SP (10, 20, 40 mg/kg/day) reduced PC by 50, 51, and 72% in an additive fashion without potentiation. Similarly SP (20 mg/kg/day) given with DIP (2.5 mg/kg/day) plus ASA (10 mg/kg/day) reduced PC by 65% in an additive manner.

It is concluded that PC is more effectively reduced by DIP than either SP or ASA. DIP is potentiated by ASA but not SP. DIP and ASA should be administered simultaneously in multiple daily doses.

COMPARATIVE THROMBOGENICITY AND HEALING OF VASCULAR PROSTHESES. G.P. Clagett, G.M. Graeber, H. Hufnagel, R. Carter, W. Gregory, M. Robinowitz, J.M. Langloss, Y. Maddox, and P. Ramwell. Division of Surgery, Walter Reed Army Institute of Research, Washington, D.C., U.S.A.

Thrombogenicity and healing characteristics were evaluated for 3 commonly used vascular prostheses: expanded polytetrafluoroethylene (PTFE), knitted Dacron (KD), and velour knitted Dacron (VKD). Adult mongrel dogs were randomly allocated to receive thoracoabdominal aortic prostheses (6 animals for each type prosthesis) according to a randomized block design. Prostheses were 28-32 cm in length and 10 mm in diameter. Platelet survival (PS) studies were performed pre-op and every 6-8 weeks post-op for 1 year. PS data were subjected to analysis of variance and are shown ($\bar{X} \pm \text{SEM}$) below:

	PTFE	KD	VKD	F, P Value
PS (Days)				
Pre-Op	4.82±0.40	5.01±0.30	4.23±0.44	N.S.
Post-Op (6 weeks)	4.11±0.39	4.02±0.19	2.31±0.20	4.96, <0.032

PS, normal in each group pre-op, was shortened by all prostheses post-op; however, VKD reduced PS significantly more than KD and PTFE. At the end of 1 year, PS in animals with KD returned to normal but remained shortened in those with VKD and PTFE. Animals with VKD had the shortest PS throughout. Prostheses were then removed to assess coverage of luminal surface with prostacyclin-producing pseudointima. KD demonstrated the most complete coverage (90.6±5.5% of surface area) followed by VKD (56.3±9.6%) and PTFE (34.0±5.3%), $p < 0.02$. These studies demonstrate that important differences exist among vascular prosthetic materials in initial reactivity with platelets following implantation and in subsequent rate and degree of healing.

THE DURATION OF THROMBOTIC ACTIVITY IN MATURING PROSTHETIC VASCULAR GRAFTS IN MAN. M. Goldman, D. Simpson, R.J. Hawker, H. Norcott, Z. Droic, C.N. McCollum, Queen Elizabeth Medical Centre, Birmingham, UK.

Prosthetic graft occlusion is most frequent in the early postoperative period when the luminal surface is highly thrombogenic. It is generally believed that graft maturation ultimately results in a non-thrombogenic surface. The accumulation of 111-Indium labelled autologous platelets in Dacron aorto-femoral grafts has been measured one week following surgery and at intervals of 3 months to 1 year.

Platelets from 9 patients were labelled with 111-In-oxine and reinjected. Isotope emissions over the graft and a reference site (aortic arch) were measured daily for 7 days and gamma camera images taken on alternate days. Graft thrombogenicity was calculated as the daily rise in the ratio of emissions graft/reference.

All grafts, regardless of age, accumulated platelets and were imaged by gamma camera. Mean thrombogenicity ($\pm \text{SEM}$) one week after surgery was 0.207 ± 0.037 compared with 0.08 ± 0.025 at follow-up ($p < 0.01$). The platelet survival during the early study was reduced at 6.805 ± 0.61 days but had recovered to a near normal value of 8.57 ± 0.78 days ($p < 0.001$) at follow up.

Although at a reduced rate, platelet accumulation still occurs on Dacron grafts 1 year following surgery despite the presence of normal platelet survival times.