## 0200

SCANNING ELECTRON MICROSCOPIC EVALUATION OF DIMETHYL SULFOXIDE, BARBITURATE OR STEROID ANTIPLATELET AGGREGATION PROPERTIES. M. Dujovny, R. Segal, N. Kossovsky. Department of Neurological Surgery, University of Pittsburgh School of Medicine and V.A. Medical Center, Pittsburgh, PA, U.S.A.

Despite advances in instrumentation, suture material, and operative techniques, thrombus formation at the anastomotic site remains a major factor in compromising surgical results in cerebral revascularization. Dimethyl sulfoxide (DMSO), methyl prednisone, thiopental, and pentobarbital are drugs that have been shown both clinically and experimentally to have protective effects in focal cerebral ischemia, and also to possess antiplatelet properties. We undertook a study on the carotid arteries of 72 Sprague-Dawley rats to assess the effect of the above drugs on microvascular thrombus formation. The control group consisted of 24 arteries, 12 that had an aneurysm clip applied for 1 hour, and 12 that had an arteriotomy and suture repair; no pharmacological agent was administered to this group. The experimental group was sub-divided into 2 major subgroups: Group A consisted of a total of 24 arteries subjected to aneurysm clip application for 1 hour; Group B consisted of a total of 24 arteries subjected to arteriotomy and suture. In both experimental groups, 6 animals were treated with one of the following pharmacological agents that was infused IV over a period of 1 hour: DMSO 2 mg/Kg; methyl prednisone 40 mg/Kg, thiopental 90 mg/Kg, pentobarbital 90 mg/Kg. The tissue was recovered 15 minutes after arterial segment reperfusion and prepared for Scanning Electron Microscopy (SEM). The specimens treated with DMSO, despite showing fracture of the endothelial layer with exposure of the sub-endothelium, had minimal thrombus formation. Specimens treated with the barbiturates showed less thrombus formation than the control group, but not comparable to the effect obtained with DMSO. The methyl prednisone group showed no difference compared to the control group.

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VASCULAR AND PLATELET EFFECTS OF SYNTHETIC ANALOGUES OF PROSTACYCLIN. BY F.I.Pareti, P.M.Mannucci, S.Vanasia, C.Gandolfi, N.Mongielli and D.C.B.Mills. Centro Angelo Bianchi Bonomi, Universita di Milano; Farmitalia Carlo Erba, Milano; and the Thrombosis Research Center, Temple University, Philadelphia.

A series of synthetic analogues of prostacyclin (PGI2) have been compared for their ability to increase the formation of cyclic AMP and to inhibit the aggregation of human platelets, and for relaxation of isolated bovine coronary arteries and lowering of the blood pressure of concious rats. The most active inhibitors of aggregation were derivatives of PGI2 with a triple bond at C14:15. There was good aggreement between the inhibition of platelet aggregation and elevation of cyclic AMP in platelets, and both effects were enhanced by phosphodiesterase inhibitors. The most active compounds of the series were K13415 (14,15-didehydro 20-methyl PGI2), and a carbocyclic analog, FCE21258 (5e-14,15-didehydro carbo PGI2) which were both more active than PGI2 itself. In addition, the carbocyclic compounds were stable at neutral pH. Compounds K13817 (14,15-didehydro 16-methyl PGI2) and FCE21292 (5e-14,15 didehydro 20-methyl carbo PGI2) were similar in activity to PGI2 as platelet inhibitors, but had less vasodilator and depressor activity. The results show considerable differences in the structural specificities of the platelet and vascular activities of PGI2.