THE EFFECTS OF TWO NEW ANTITHROMBOTIC AGENTS (IMIDAZOQUINAZOLINONES) ON PLATELET SHAPE AND AGGREGATION. S.S. Tang and M.M. Frojmovic, Department of Physiology, McGill University, Montreal, Quebec, Canada.

Recently, one member of a new series of compounds was reported as a potent, nontoxic and long lasting antithrombotic agent, based on in vitro and in vivo animal tests (Bristol Labs; Hemming et al. J. Pharmacol. Exp. Ther. 194, 435). We here report on the effects of this compound, 6-methyl-1,2,3,5-tetrahydroimidazo [2,1-b] quinazolin-2-one hydrochloride monohydrate (BL-3459), and its metabolically more stable 6,7-dichloro analogue (BL-4162), on rabbit and human platelet shape change and aggregation, and compare them with other agents known to affect platelet adenosine 3':5'-cyclic monophosphate (cAMP). In aggregometer studies with citrated (0.29%) platelet-rich plasma (PRP), both BL-compounds were found to inhibit platelet shape change and aggregation induced by ADP, thrombin, serotonin and adrenaline-serotonin. Typically for human PRP, aggregation induced by 10 µM ADP was inhibited by 90% with 10 µM BL-4162 or 0.1 µM prostaglandin E_1 (PGE_1), and by 60% with 10 µM BL-3459. In corresponding rabbit PRP tests, 60% inhibition was caused equally by 1 µM BL-3459 or BL-4162, and by 0.05 µM PGE_1. Both BL-compounds, like methylxanthines, were found to potentiate the inhibitory effect of PGE_1 on platelet aggregation but did not potentiate the action of methylxanthines. Moreover, they both slightly increased the basal level of rabbit cAMP and potentiated the elevation of cAMP by PGE_1. These BL-compounds are potent inhibitors of human and rabbit shape change and aggregation and appear to act by a mechanism distinct from that of PGE_1.

AN ACQUIRED PLATELET STORAGE POOL DEFICIENCY IN PATIENTS WITH SEVERE VALVULAR HEART DISEASE. C.B. Harbury and C.A. Galvan. Stanford University School of Medicine.

The purpose of this study was to assess whether patients with severe valvular disease damage their platelets in vivo and acquire a platelet storage pool deficiency. Forty-three preoperative valve patients, 43 coronary artery bypass patients (CABG) and 22 concurrent normal controls were studied. Platelets were counted by phase and ZBI Coulter Counter. Total and releasable platelet ADP and ATP was measured by the luciferase assay (Holmsen). Nucleotides are expressed in nanomoles per 10^8 platelets. Analysis is by a non paired t test. Releasable ADP: control = 2.35 ± 0.6, valve 1.86 ± 0.5 $t = 3.35$, $p<0.01$, a significant difference. Releasable ATP: control = 1.7 ± 0.4, valve 1.2 ± 0.4 $t = 4.05$ $p < 0.01$ a significant difference. Total ADP control = 3.3 ± 0.5, valve 2.6 ± 0.6, $t = 4.12$, $p <0.01$ a significant difference. Total ATP control = 5.7 ± 0.8 valve = 5.3 ± 1.1. This is not a significantly lower value $t = 1.07$. CABG patients were not significantly different from controls, but were significantly different from valve patients. Twenty-six valve patients were studied postoperatively, 10 had received platelet transfusions and were excluded from quantitative assessments. Estimated blood loss (OREBL) valve =1556 cc, CABG = 734 cc, $p<0.001$. Transfused red cells (RBCTx) valve = 8.5u, CABG 6.5 u, $p<0.01$. Postoperative chest tube drainage (CTD) above and below 400 cc, CABG vs valve $\chi^2 = 5.12$, $p< 0.02$. Ten valves and 2 CABG received platelet transfusions. If these are included and considered bleeders $\chi^2 = 11.01$ $p<0.001$. These patients with severe valvular heart disease appear to have a mild acquired platelet storage pool deficiency and a significantly greater bleeding tendency at surgery.

PLATELET COAGULANT ACTIVITIES IN METRIZAMIDE GRADIENT PLATELETS : APPLICATION TO BERNARD-SOULIER AND THROMBOTIC DISORDERS. S. Levy-Toledano, A. Dmoszynska, H. de La Baume, E. Dupuy and J. Caen. Laboratoire d'Hémostase et de Thrombose Expérimentale, Hôpital Saint-Louis, Paris, France.

A new technique for platelet isolation from five ml of total blood on metrizamide gradients has been applied to the study of platelet coagulant activities. Assay methods have been described : contact product forming activity (CPFA), collagen induced coagulant activity (CICA) and platelet factor three (PF3) have been measured in the metrizamide gradient platelets (MGP) and found similar to that of platelets in platelet rich plasma (PRP).

Platelet coagulant activities of the MGP have been measured in patients with hemorragic tendencies like Bernard-Soulier (B-S) patients or those with thrombotic tendencies including diabetics with or without vascular complications or patients with transient ischemic attacks (TIA). CICA was not found in all the 3 patients with B-S syndrome. 3 of the 10 diabetics showed an increased CPFA activity while 5 showed an increased CICA activity contrasting with the normal activities found in diabetics without vascular complications ; PF3 activity is increased in the two groups of diabetics. 3 patients of the 7 with TIA had an increased CPFA as well CICA.

The results suggest that these activities may play some role in diabetics with vascular complications and in some cases with TIA.