PLATELET FUNCTION AND BLOOD LOSS AFTER CARDIOPULMONARY BYPASS. M.D. Rosario, H. Leinberger, A. Suehiro, S. Zeitlin, G. Moore, B. Barker, R.T. Mamiya and J.J. McNamara. Queen's Medical Center, Honolulu, Hawaii, U.S.A.

The relationship between platelet function and bleeding tendency was studied in 42 patients undergoing open heart surgery. Template bleeding time (TBT) and hourly chest tube outflow were measured as indices of bleeding tendency. Platelet function tests included platelet count (PC), aggregation with epinephrine, ADP, and collagen, and a modified platelet slide adhesion test (PSAT) which allowed us to quantitate in vivo the relative amount of more adhesive platelets, i.e., the "spread" forms, as compared to the number of smaller non-adhesive platelets. Post operatively the PC decreased 36% (from 214.1 ± 11.4 K to 136.3 ± 6.8 K, $p<0.001$) in all patients irrespective of the amount of blood loss. Using the PSAT, the product of the % "spread" forms and the PC showed a significant 57% decrease (from 110.5 ± 7.4 K to 47.4 ± 4.6 K, $p<0.001$) which was 19% more than the PC decrease implying that the more adhesive platelets had been expended. TBT increased significantly (7.7 ± 0.5 min. to 17.7 ± 1.3 min., $p<0.001$) and aggregation to epinephrine decreased significantly (60.9 ± 4.8% to 36.0 ± 3.4%, $p<0.001$), but no significant change was noted with ADP or collagen. There was no significant difference in the above parameters between patients bleeding more than 113 cc/hr. from 1 to 5 hrs. post op (N=14) and those bleeding less (N=28). A second study of 16 patients with bleeders having >1000 cc output in the first 4 hrs. post op showed results similar to the first group comparing pre vs. post and bleeders (N=8) vs. non-bleeders. This study indicates that after cardiopulmonary bypass surgery platelet function is frequently compromised and this dysfunction though probably contributing to a bleeding tendency did not correlate well with the magnitude of blood loss.

CONTRIBUTION OF PLATELETS TO THE CARDIOVASCULAR EFFECTS OF ADP IN THE RAT. E. Dejana, M.G. Castelli, G. de Gaetano, A. Bonaccorsi. Istituto di Ricerche Farmacologiche 'Mario Negri', Milano, Italy.

The contribution of platelets to the cardiovascular effects of ADP was investigated in rats in different experimental conditions. Following rapid i.v. bolus injections of ADP(from 0.001 to 0.03 mg/kg b.w.) only a dose-related fall in blood pressure could be detected. Increasing the dose of ADP (up to 1 mg/kg b.w.), platelet fall and changes in cardiac rhythm (bradycardia, A.V. blocks and ectopic beats) became evident. All these phenomena were rapidly reversed. Inhibition of platelet aggregation by a pyrimido-pyrimidine compound (SH 869) or thrombocytopenia induced by Busulfan or antiplatelet antiserum did not significantly protect the animals from the cardiovascular effects of ADP. The fall in blood pressure, however, was reduced. Adenosine, at equimolar concentrations, caused ECG changes similar to those induced by ADP with no platelet aggregation and a less pronounced blood pressure fall. These results suggest that most of the cardiovascular modifications induced by rapid injection of ADP are largely independent of platelets. Platelets appeared to play a more important role when ADP was given for a longer period of time. A slow i.v. infusion of ADP (6 mg/kg b.w. for 10 min) was accompained by platelet fall, cardiovascular collapse and ECG alterations typical of myocardial ischaemia. All these effects persisted throughout the ADP infusion but disappeared soon after its termination. They were almost completely inhibited in rats given SH 869 or made thrombocytopenic.

In conclusion, platelets seem to contribute to the cardiovascular effects of ADP only in certain experimental conditions. In others, the nucleotide's direct effects seem more important.

EFFECTS OF ETHANOL ON PLATELET SEROTONIN METABOLISM. D. H. Cowan and P. Shook. Case Western Reserve University, Cleveland, Ohio, U.S.A.

The metabolism of serotonin (5-HT) in platelets is altered in several mental disorders and by various neurotransmitters. Since ethanol impairs the function of both nerves and platelets, the effect of ethanol on 5-HT metabolism was studied in normal platelets and in platelets from patients ingesting ethanol. Ingestion of ethanol by 3 subjects produced blood ethanol levels of 65-76 mM. Platelet MAO activity in each decreased by 50% and platelet serotonin levels increased 50-100%. Ethanol, incubated with normal platelets in vitro, competitively inhibited MAO activity. With phenylethylamine as substrate, the Km of MAO was 23 μM and the Ki of ethanol was 33 mM. With tyramine, Km and Ki were 94 μM and 571 mM, respectively. 5-HT uptake by platelets increased 50-100% during ethanol ingestion over control values. By contrast in vitro addition of ethanol to normal platelets inhibited initial 5-HT uptake : Km and Ki were 0.0004 mM and 89.6 mM, respectively. The efflux of 5-HT from platelets was 3-5 times control values during ethanol ingestion and with addition of ethanol to normal platelets. Acetaldehyde at a concentration of 2 mM did not alter MAO activity or 5-HT uptake or efflux. The inhibitory effects of ethanol on MAO and 5-HT uptake were not altered by reserpine, aspirin, or tricyclic antidepressants. The results indicate that ethanol substantially alters 5-HT metabolism by human platelets. Inhibition by ethanol of MAO activity and 5-HT transport may contribute to ethanol-induced platelet and neuronal dysfunction.