

INFLUENCE OF IMIDAZOLE CARBOXAMIDE ON PLATELET FUNCTION. P. Kubisz, P. Klener and S. Cronberg. Division of Hematology, University Hospital, Oran, Algeria, Hemostasis Laboratory, Departmental Hospital, Čadca, Czechoslovakia, Division of Hematology, Charles University Hospital, Prague, Czechoslovakia and Department of Infectious Diseases, General Hospital, Malmö, Sweden.

Imidazol carboxamide (DTIC, NSC-45388) is a cytostatic drug used in the treatment of malignant melanoma under the trade name of Dacarbazine<sup>®</sup>, MSD. Its influence on platelet function, blood coagulation and fibrinolysis was investigated in vitro. At a concentration of 160 µg/ml it inhibited the increase in light transmission induced in platelet-rich plasma by standardized freezing and thawing. It also retarded the retraction of reptilase clots. This therefore indicated a stabilizing effect on the platelets at this dosage.

At a concentration of 40 µg/ml the drug did not significantly influence the platelet function in vitro. This concentration corresponds to therapeutic plasma levels.

At current dosage of the drug any bleeding tendency due to platelet dysfunction therefore seems unlikely.

INFLUENCE OF LOW DOSE HEPARIN AND OF ACETYSALICYLIC ACID ON ALTERATIONS OF THE HEMOSTATIC MECHANISM BY VENOUS OCCLUSION. H. Vinazzer and D. Loew. Blood Coagulation Laboratory, Linz, Austria. Venous occlusion was used as a model to examine the action of antithrombotic substances. In 15 healthy volunteers, a blood pressure cuff attached to an arm was inflated to 90 mm Hg for 15 minutes. Blood was collected from an antecubital vein prior to and at the end of occlusion. Parameters of coagulation, of fibrinolysis, and of platelet function were examined.

At the end of occlusion, factors XIa and Xa were demonstrable in intact plasma. There was also a diminution of plasminogen and a shortening of the euglobulin lysis time. Collagen induced platelet aggregation was increased. Platelet factor 4 (PF 4) was diminished in platelets, and was demonstrable in plasma after occlusion.

Three groups were formed from these volunteers. Group 1 received 1500 mg acetylsalicylic acid (ASA) per day, group 2 was injected 5000 units heparin s.c. at 12 hr intervals, and group 3 received both drugs. After one week of therapy, blood samples were again collected before and after occlusion. In the ASA group, platelet aggregation was diminished. This was not altered by occlusion. PF 4 was neither diminished in platelets nor was it demonstrable in plasma. There was no influence on plasminogen and factors XIa and Xa were not demonstrable in plasma after occlusion. There was no PF 4 in plasma though PF 4 in platelets was diminished. Platelet aggregation was not influenced. In the heparin plus ASA group, factors XIa and Xa as well as plasma PF 4 were missing after occlusion. PF 4 in platelets was not diminished whilst platelet aggregation was inhibited.

These experiments demonstrate a mutual support of ASA and heparin in the prevention of alterations of the hemostatic mechanism which are likely to provoke an increased thrombotic tendency.

PROSTAGLANDIN-ENDOPEROXIDES AND CYCLIC 3'-5'-AMP IN PLATELETS OF PATIENTS WITH HYPERCOAGULABILITY AND SHOCK. F.R. Matthias. Dept. of Int. Medicine, Justus Liebig University, Giessen, Germany.

To get more insight in platelet function of patients suffering from insufficiency of the circulation together with intravascular fibrin formation as a sign of a stimulated coagulation system, the following parameters were determined: 1. the prostaglandin-endoperoxide formation of platelets in response to N-ethylmaleimide and collagen measured as malondialdehyde; 2. the c-AMP content of platelets and plasma according to the Gilman method; 3. the stimulating effect of prostaglandin E<sub>1</sub> on the platelets adenylate-cyclase activity; 4. the collagen induced platelet aggregation.

Platelet aggregation was reduced. The prostaglandin-endoperoxide formation was unchanged or elevated in comparison to normal donors. Plasma c-AMP was increased, whereas the platelet c-AMP content was unaltered. Adenylate cyclase activity in response to prostaglandin E<sub>1</sub> was reduced. Platelet function recovered concomitantly with the improvement of the circulation and the clotting parameters.