SOME ASPECTS OF BILIARY FIBRINOLYSIS IN MAN. S.Oshiba, T.Ariga, H.Sawai and H.Imai. Department of Physiology, Nihon University School of Medicine, Tokyo, Japan.

The co-existence of a biliary plasminogen activator, bilokinase, and a streptokinase responsive factor, so-called proactivator, has recently been demonstrated in the bile of several mammalian species including man by Oshiba et al. (The 16th International Congress of Hematology, Kyoto, 1976). Our further investigations have revealed certain characteristic biliary fibrinolysis in man which differ from those in other species. Human bile was obtained from patients with cholelithiasis who had received a surgical operation. The bilokinase activity and proactivator activity in the bile were measured in either the original form or in a quantitatively extracted form.

The main results were as follows: (1) The bilokinase activity of human bile was weak in comparison with that of certain other species. (2) Proactivator in human bile showed the highest activity, and the levels in the other species were generally less than the bilokinase activity. Thus, the activity ratio of proactivator to bilokinase in human bile far exceeded that in the other species. (3) Human bile proactivator and plasma proactivator demonstrated different affinity chromatographic behavior on lysine-sepharose. (4) There was apparently no significant relationship between biliary and plasma fibrinolysis.

EXPERIMENTAL STUDY OF A PLATELET ANTIAGGREGATING AGENT - APPLICATION TO TICLOPIDINE.

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The authors consider the various methods suitable for in vivo study of the anti-aggregating properties of a new drug - Ticlopidine :

- study of photometric ADP-induced aggregation and screen filtration pressure in vivo in the rabbit treated per os for 5 days with doses of 25 and 50 mg/kg/d. This gave average inhibitions of 30 % and 45 % respectively.

- study of circulating platelet aggregates using the method of Wu and Hoak after continuous infusion of ADP or of thrombin. The principle of the method involves definition of an aggregation index : the ratio between the platelet counts in the two specimens (EDTA + formol 1 % + EDTA alone).

The average results showed : control group index 0.9 -after infusion of ADP 0.57- after infusion of ADP under the influence of Ticlopidine (50 and 100 mg/kg/d) 0.66 to 0.78.

- the mechanism of action of the drug was studied using crossed aggregation experiments and by the study of interference with ionised or ionisable groups of the platelet membrane (isotope method, electrophoresis in liquid phase).

In parallel with these experiments, studies in vivo in the rabbit and in patients (obliterative arterial disease, Raynaud's syndrome) are in progress : interference with membrane groups, rheological properties (viscosity, rouleau formation, erythrocyte deformability) and biochemical properties (erythrocyte glycolysis enzymes).

NEW METHOD FOR ASSESSMENT OF PLASMA VON WILLEBRAND FACTOR. T. Sano, T. Motomiya, N. Mashimo and H. Yamazaki. Aoyama Tokyo Metropolitan Hospital, Tokyo Medical and Dental University and Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan.

As much interests have been focused on von Willebrand factor (vWF) in diabetes melitus and atherosclerosis, request to determine vWF has been increasing recently. Two methods for assessment of plasma vWF level, without platelet aggregometer, were devised. 1) Platelet-rich plasma (PRP) sensitivity to ristocetin-induced platelet aggregation (RIPA): PRP was separated without centrifugation from citrated blood. Serially two-fold diluted ristocetin (16 to 16×10^{-2} mg/ml) was prepared in a Cooke Microtiter tray and PRP (25 μ l each) was added to each concentration of ristocetin. Then the ristocetin-PRP mixture was agitated for 15 seconds using a Kowa Kizai Micromixer and the minimum effective final concentration of ristocetin to give platelet aggregation was obtained microscopically and this was defined as PRP sensitivity to RIPA. This method is convenient for screening test. 2) vWF assay: Serially two-fold diluted plasma (2 to 1024 times, in Tris-saline pH 7.2 containing 12 mg/ml bovine serum albumin), fixed and washed platelet suspension (6×10^7 / μ l, Macfarlane et al. 1975) and 3 mg/ml ristocetin were mixed (25 μ l each) in a microtiter tray and agitated for 15 seconds. The maximal plasma dilution to induce platelet aggregation was obtained microscopically and defined as the titer of plasma vWF. In normal subjects, minimum effective ristocetin concentration (PRP sensitivity to RIPA) was around 1 to 0.5 mg/ml and maximal plasma dilution to give platelet aggregation (vWF titer) was around 16 to 32 times. The present methods have a good reproducibility and are performed easily without aggregometer and thought to be useful clinically.