

## EXTENT OF METABOLIC CHANGES DURING ISCHEMIA

R. Schröer, F. Nüdemberg, K. Rudolphi. Hoechst

AG Werk Albert, Pharmaceutical Division,  
W. Germany

Ischemic conditions in limbs can be provoked by occlusion with inflatable cuffs. The period of development of ischemia to an extent where muscle exercise is no longer possible is drastically shortened by muscle exercise itself. Blood obtained by venepuncture of the forearm under these conditions showed no differences in pH,  $pO_2$ ,  $pCO_2$ , and lactate and glucose levels in comparison with the blood taken before occlusion. A special technique of blood sampling under low flow flushing conditions was developed, by which blood reflecting the ischemic state is obtained nearly without dilution from the cubital vein. This is demonstrated by measurements of pH,  $pO_2$ ,  $pCO_2$ , lactate concentration and osmolarity, which, under the latter conditions, revealed changes of about 0.3 pH units, 20 mm Hg, 80 mm Hg, 90 mg/dl, and 30 mosm/l respectively. The extent of local changes of these parameters in the microcirculation of muscle tissue in the state of ischemic pain is suggested to be of the same order of magnitude.

EFFECT OF EXERCISE ON PLATELET FUNCTION IN PATIENTS WITH INTERMITTENT CLAUDICATION. William H. Baker, Jawed Fareed, Harry L. Messmore, Judith Kniffin, Grace Squillaci and Marcia Foides. Loyola University Medical Center, Maywood, Illinois 60153 USA.

Activation of platelets as measured by monitoring thromboxane  $B_2$  levels, release specific proteins and quantitation of endogenous platelet aggregates has been reported in patients with angina pectoris. To study the relationship between the platelet-activation and intermittent claudication, 14 patients with demonstrated peripheral atherosclerosis were exercised to tolerance. Segmental limb pressures and platelet function studies were performed both pre and post exercise. A continuous EKG was recorded. All patients exhibited a drop in segmental limb pressures coinciding with complaints of claudication which was consistent with peripheral atherosclerosis. No significant alteration in the platelet release and aggregation pattern was noted in samples obtained prior to and immediately after exercise. Autoaggregation as measured by luminescence (luciferase-coupled) aggregometry to measure spontaneous ADP release and release specific proteins such as  $\beta$  thromboglobulin and platelet factor 4 also remained unchanged. Interestingly although 6 of 14 patients showed an abnormal exercise EKG, no angina pectoris was experienced. Although endogenous activation of platelets has been linked with anginal pain, the present study shows that platelet activation as studied by aggregation, release proteins and thromboxane measurement is not associated with intermittent claudication. The reduction in limb blood flow as evidenced by the drop in segmental pressures is most likely due to anatomic pathology rather than platelet mediated rheologic or vasospastic mechanisms.

THE EFFECTS OF AGE AND THROMBOTIC STROKE UPON PLASMA CONCENTRATIONS OF FIBRINOGEN DERIVATIVES AND PLATELET RELEASE. D.A. Lane, M.J. Gawel, S. Wolff, H. Ireland, and F. Clifford Rose. Departments of Haematology and Neurology, Charing Cross Hospital and Medical School, London, U.K.

An investigation has been made of the activation of coagulation and fibrinolytic systems and platelets in normal individuals and in patients who have had cerebral infarction probably caused by thromboembolism. Thrombin and plasmin activities and platelet releasing stimuli were measured using double antibody techniques directed towards fibrinopeptide A (FpA), fibrinogen fragment B $\beta$ 1-42 and  $\beta$  thromboglobulin ( $\beta$ TG), respectively. Normal healthy laboratory controls (n = 20) of mean age 29 yr, range 18-46, had mean FpA, B $\beta$ 1-42 and  $\beta$ TG plasma concentrations of 1.06, 1.59 and 0.80 pmol/ml respectively. 95% of these normal results were within the range 1.50, 3.50 and 1.30 pmol/ml, respectively. Patients (n = 47) who had had computer assisted tomographical demonstrable stroke at least 1 month, but mostly greater than 1 yr, prior to examination had mean FpA, B $\beta$ 1-42 and  $\beta$ TG levels of 2.81, 4.44 and 2.09 pmol/ml. Some of these patients (n = 15) received sulphinpyrazone (800 mg daily) and their plasma levels were not appreciably different, 3.17, 5.48 and 2.18 pmol/ml respectively. The age of all patients, mean 65 yr, range 53-83, was considerably higher than the laboratory controls and therefore apparently healthy age and sex matched controls (n = 14) were studied. Mean FpA, B $\beta$ 1-42 and  $\beta$ TG of this older control group were 2.1, 3.0 and 1.48 pmol/ml, respectively. It is concluded that (a) in normal apparently healthy individuals plasma concentrations of FpA, B $\beta$ 1-42 and  $\beta$ TG rise with age, suggesting increased activation of coagulation and fibrinolytic systems and platelets (b) following thrombotic stroke the three systems are further activated and remain so for many months (c) sulphinpyrazone does not alter this activation.

CLINICAL AND EXPERIMENTAL STUDIES ON FBG HETEROGENEITY AND FIBRINOGENOLYSIS —ESPECIALLY IN DIC AND UK TREATMENT M. Yamauchi, H. Takei, T. Seiya, Y. Oguma, T. Murakoshi, H. Nagata and H. Hasegawa. First Department of Internal Medicine, Hokkaido University School of Medicine, Sapporo, Hokkaido, Japan.

By means of SDS-PAGE (3.3% gel), Fbg heterogeneity originated from partial degradation of A $\alpha$  chain was studied. Comparison of electrophoretic patterns of plasma and corresponding serum made it possible to identify 2 major Fbg bands designated as high-molecular-weight Fbg (HMW, MW 350,000) and low-molecular-weight Fbg (LMW, MW 310,000). LMW comprised 28 $\pm$ 2% (mean $\pm$ S.D) of total Fbg (HMW+LMW) in healthy subjects. The elevation of fibrinolytic activity did not accompany the increase of percentages of LMW in various diseases, even in cirrhotic patients whose levels of  $\alpha_2$ PI were low. In DIC patients percentages of LMW were decreased extremely (12 $\pm$ 6%, mean $\pm$ SD). Samples from animal experimental models of DIC exhibited the same pattern of Fbg heterogeneity as that of DIC patients.

UK was added to the purified Fbg in vitro. On the earliest stage of the fibrinogenolysis, 2 bands appeared newly on SDS-PAGE, while the bands of HMW and LMW were decreased. One of these new bands (Band 1) corresponded with a major component of Fraction I-9 of Mosesson. It was located in the slightly anodal position (MW 300,000) from LMW band. Another band (MW 270,000) migrated between Band 1 and the band of Frag X. The same pattern of Fbg heterogeneity was observed in patients receiving large dose of UK. After cessation of UK treatment these new bands disappeared, while the bands of HMW was increased extremely.

These findings suggest that HMW is a freshly synthesized Fbg and that unknown mechanism without plasmin may present for the conversion HMW to LMW.