

EFFECTS OF SOLUBLE IMMUNE COMPLEXES FROM DIABETICS ON PLATELET AGGREGATION AND RELEASE. J. Colwell, J. Van Zile, M. Kilpatrick, and G. Virella. VA Medical Center, Department of Basic and Clinical Immunology and Microbiology, and Endocrinology-Metabolism-Nutrition Division, Medical University of South Carolina, Charleston, South Carolina.

Soluble immune complexes (IC) can be detected in the serum of diabetic patients in frequencies ranging from 25 to 46%, depending on the screening technique used. Insulin-treated diabetics show a high frequency of insulin-anti-insulin IC (61% vs 4% in non-insulin treated patients) while other non-specific screening techniques show similar positivity frequencies in these two populations of diabetics. Soluble IC were isolated from the sera of 6 patients (5 under insulin treatment) using several combinations of polyethylene glycol precipitation, gel filtration and affinity chromatography. Sera from two normal donors was processed similarly and trace amounts of protein were recovered and used as controls. Platelet aggregation and release of ATP were studied with a Chronolog Lumi-aggregometer using platelet-rich plasma and low concentrations of ADP. All preparations of purified IC were found to induce platelet aggregation and ATP release of ADP sensitized platelets, while similarly obtained preparations from normal sera were inactive. Previous investigations had shown that sera from some diabetic patients contain factor(s) with platelet-activating properties. The present experiments suggest that soluble IC may be at least one of the factors.

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PLATELET REGENERATION TIME IN DIABETICS WITH AND WITHOUT RETINOPATHY. H. Tindall, R.C. Paton, M. Zuzel and G.P. McNicol. University Department of Medicine, The General Infirmary, Leeds LS1 3EX, U.K.

Platelet regeneration time was measured by a modification of the Stuart technique which depends on progressive reappearance of the capacity to synthesize malondialdehyde (MDA) in response to thrombin stimulation following aspirin ingestion. The subjects of the study were 40 normal subjects and 40 patients with insulin-dependent diabetes mellitus for more than 10 years. The presence or absence of retinopathy was independently assessed in a diabetic eye clinic and severe retinopathy was found in 20 patients. The mean platelet regeneration time in normal subjects was 9.98 ± 0.22 days (mean \pm SEM). In diabetic patients without retinopathy the platelet regeneration time was significantly ($p < 0.001$) shortened (7.38 ± 0.14 days) and a further shortening occurred in those patients with retinopathy (6.80 ± 0.18 days), but with the number of subjects studied the difference between these two groups was not statistically significant. MDA produced in response to thrombin-stimulation of platelets was 235.5 ± 12.8 pmole/ 10^8 platelets in controls with significantly ($p < 0.001$) less in diabetics with retinopathy at 156.7 ± 17.5 pmole/ 10^8 platelets. In 10 diabetic patients a standard oral glucose tolerance test was performed with blood taken for MDA at the same time as plasma glucose levels. There was no correlation between plasma glucose and the concentration of MDA produced. These results show that patients with longstanding insulin-dependent diabetes have an accelerated platelet regeneration time even in the absence of overt retinal microvascular complications.

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The influence of microangiopathy in Diabetics with antiplatelet drugs. G. Bremer, O. Richter, E. Jacobi, T. Koschinsky. Department of medicine C, Diab. Institute, University Disseldorf, West-Germany. It is well known that microangiopathy is associated with shortened platelet survival. Therefore a pilot study was performed to test several anti-platelet drugs with respect to their ability to increase platelet survival. The study was confined to 18 patients with long standing Diabetes mellitus and microangiopathy of I.- II. degree, exhibiting platelet survival times less than 7 days. The patients were treated with antiplatelet drugs. Dipyridamole with several combination of Acetylsalicylic acid (ASA) and Sulfinpyrazon.

1. 225 mg Dipyridamole and 990 mg ASA per day,
2. 225 mg Dipyridamole and 300 mg ASA per day,
3. 150 mg Dipyridamole and 150 mg Sulfinpyrazon per day.

Platelet survival was determined by the method described by Harker. The resultant survival curves were analysed by a computer program written by Murphy and Francis which is based on the multiple hit model for platelet survival.

The results of the study are: After 10 days treatment the platelet survival was markedly increased under each of the combination. If one assumes that there exists a causal relationship between microangiopathy and platelet survival, a long-term treatment by antiplatelet drugs may be a prophylaxis against microangiopathy in diabetics.

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CHANGE IN TXB₂, MDA AND AMP LEVELS DURING ARTIFICIAL PANCREAS TREATMENT ON DIABETIC PATIENTS. C. Braun, C. Guimont, Ph. Voisin, D. Rousselle, P. Drouin and J.F. Stoltz. Groupe d'hémorhéologie, Centre de Transfusion Sanguine et Méd. G, CHU Nancy, France.

A study carried out on 9 insulin-dependent diabetic patients undergoing continuous blood glucose control by means of ex-vivo insulin injection (artificial pancreas - Biosator) has revealed: a relationship between the synthetic capacity of TX A₂ (proaggregating molecule) by the platelet and the blood glucose level prior to feed back control. Concurrently, an identical relationship is observed in the case of platelet AMPc levels.

After 24 hours of artificial pancreas treatment, it is noted that the greater the effectiveness of the treatment, the greater the increase in the synthetic capacity of TX A₂. This observation is confirmed after 48 hours of treatment.

Further, the relationship between MDA and Thromboxane B₂ synthesized from the same precursory molecules is reversed during treatment.

On the basis of these results we may assume that there is a disturbance in the regulation mechanisms of platelet synthesis during diabetes, but that these mechanisms are partly reversible after artificial pancreas treatment.