A plasma factor which stimulates prostacyclin formation is increased in diabetes. M. Johnson, A. H. Reese and H. E. Harrison. Department of Biotics, ICI Pharmaceuticals Division, Macclesfield, England.

Vascular prostacyclin (PGI₂) generation is decreased in diabetes in experimental animals and in man. In this study, we have investigated the possibility that levels of a plasma factor(s) modifying PGI₂ production are abnormal in diabetes. Diabetic and control rats were washed in Krebs buffer to reduce endogenous PGI₂ formation. Addition of rat or human cell-free plasma stimulated PGI₂ release by the "exhausted" vascular rings, and this activity was still present after freezing and thawing. The stimulation of PGI₂ synthesis by control tissue was significantly greater (p<0.001) with plasma from diabetic animals (0.25±0.04ng/mg) than from controls (0.05±0.02ng/mg). Similarly, plasma from diabetic volunteers showed increased (p<0.05) PGI₂-stimulatory activity. Diabetic tissue was less responsive than control tissue to stimulation by diabetic plasma, and the difference between diabetic and control plasma was not apparent. This suggests that the abnormal vascular PGI₂ synthesis in diabetes may be due to a defect in the vessel wall and not to lack of stimulatory plasma factors.

PGI₂ production in human endothelial cells cultured in diabetic and nondiabetic serum. R.C. Paton, R. Guillot and Ph. Passy, Department of Endocrinology and Metabolism, Hopital St. Louis and Department of Embryology, UER Biomedical Ste-Péres, Paris, France.

Reduced levels of prostaglandin I₂ (PGI₂) may contribute to the platelet hyper-reactivity and vascular complications found in diabetes mellitus. This study compared PGI₂ production (PGI₂-like activity and 6-keto-PGF₁α levels) by vascular endothelial cells cultured in the presence of serum from 15 diabetic with proliferative retinopathy (5 treated by surgical hypophysectomy) and 15 sex-matched nondiabetic controls. Endothelial cells from human umbilical veins were cultured in M199 with either 20% diabetic or control serum. At confluence, cultures were washed and stimulated with 0.1 KU/ml bovine thrombin. After 2 min incubation, the supernatant was tested for PGI₂-like activity on ADP-induced platelet aggregation, results expressed as % inhibition and II) 6-keto-PGF₁α by radioimmunoassay, results expressed as pmol/ml. There was a significant correlation between PGI₂-like activity and 6-keto-PGF₁α levels (r 0.78, p<0.001). The liberation of PGI₂ from endothelial cells from different umbilical cords varied, but both PGI₂-like activity and 6-keto-PGF₁α were significantly lower in supernatant from cells cultured in the presence of diabetic compared to control serum. PGI₂ production was not significantly different in cells cultured with serum from hypophysectomized and nonhypophysectomized diabetics. In these results suggest that serum from diabetics with proliferative retinopathy contains factors which impair the release or production of PGI₂ by endothelial cells and that this effect is not mediated by the pituitary.

Increased platelet aggregation and decreased sensitivity of platelets to synthesized prostacyclin in alloxan-diabetic rabbits. K. Yamada, T. Yoda, Y. Goto, T. Hirata and K. Serizawa. The Third Department of Internal Medicine, Tohoku University School of Medicine, Sendai, Japan.

Platelet aggregation and sensitivity of platelets to prostacyclin were examined with a view to clarify platelet function in alloxan-diabetic rabbits. Diabetic rabbits were obtained by intravenous injection of alloxan (100mg/kg body weight) and range of plasma glucose in these diabetic rabbits was 350-500mg/100ml. Blood was collected from the central artery of the ear of normal and alloxan-diabetic rabbits. Platelet aggregation was measured turbidometrically as rate of light transmission at maximal aggregation to light transmission of platelet poor plasma by a NKK aggregometer (Tokyo, Japan). Platelet aggregation was measured by ADP with each final concentration of 0.5, 1.0, 2.0 and 5.0 μM. Sensitivity of platelets to synthesized prostacyclin (Ono Pharma Co., Tokyo, Japan) was represented as prostacyclin concentration of fifty percent inhibition of ADP-induced platelet aggregation. Platelet aggregation rate in normal and alloxan-diabetic rabbits was as follows: 8.4±1.1, 22.8±1.5% (0.5 μM), 22.3±1.5, 37.6±1.6% (1.0 μM), 31.6±1.4, 54.3±1.8% (2.0 μM), 51.6±2.2, 66.1±2.7% (5.0 μM). Platelet aggregation was measured by ADP with each final concentration of 0.5, 1.0, 2.0 and 5.0 μM. Sensitivity of platelets to synthesized prostacyclin (Ono Pharma Co., Tokyo, Japan) was represented as prostacyclin concentration of fifty percent inhibition of ADP-induced platelet aggregation in normal and alloxan-diabetic rabbits as follows: 8.4±1.1, 22.8±1.5% (0.5 μM), 22.3±1.5, 37.6±1.6% (1.0 μM), 31.6±1.4, 54.3±1.8% (2.0 μM), 51.6±2.2, 66.1±2.7% (5.0 μM). Platelet aggregation was measured by ADP with each final concentration of 0.5, 1.0, 2.0 and 5.0 μM. Sensitivity of platelets to synthesized prostacyclin (Ono Pharma Co., Tokyo, Japan) was represented as prostacyclin concentration of fifty percent inhibition of ADP-induced platelet aggregation. Platelet aggregation rate in normal and alloxan-diabetic rabbits was as follows: 8.4±1.1, 22.8±1.5% (0.5 μM), 22.3±1.5, 37.6±1.6% (1.0 μM), 31.6±1.4, 54.3±1.8% (2.0 μM), 51.6±2.2, 66.1±2.7% (5.0 μM).