A PLASMA FACTOR WHICH STIMULATES PROSTACYCLIN FORMATION IS INCREASED IN DIABETES. M. Johnson, A. H. Reese and H. E. Harrison. Department of Bacteriology, 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. Rat and human cell-free plasma from 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 (0.03±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. Passa. Department of Endocrinology and Metabolism, Hôpital St. Louis and Department of Embryology, UER Biomedical Stas-Pêres, Paris, France.

Reduced levels of prostaglandin Ip (PGIP) may contribute to the platelet hyper-reactivity and vascular complications found in diabetes mellitus. This study compared PGIP2 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 non-diabetic 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 KIU/ml bovine thrombin. After 2 min incubation, the supernatant was tested for i)PGI₂-like activity on ADP-induced platelet aggregation, results expressed as % inhibition and ii) 6-keto-PGF₁α by radio-immunoassay, results expressed as nmoles/ml. There was a significant correlation between PGI₂-like activity and 6-keto-PGF₁α levels (r 0.78, p<0.001). The liberation of PGF₁₂ from endothelial cells from different umbilical cords varied, but both PGI₂-like activity and 6-keto-PGF₁α were significantly lower in supernatants from cells cultured in the presence of diabetic compared to control serum. PGF₁₂ production was not significantly different in cells cultured with serum from hypophysectomized and non-hypophysectomized diabetics. These results suggest that serum from diabetics with proliferative retinopathy contains factors which impair the release or production of PGF₁₂ by endothelial cells and that this effect is not mediated by the pituitary.

DETERMINATION OF MALONDIALDEHYDE IN NORMAL AND DIABETIC PREGNANCIES. I. Bakkoci, G. Gerö, J. Demeter and I. O. G. Department of Obstetrics and Gynecology, Postgraduate Medical School, Budapest, H.

It is known that platelet hyperaggregation observed in diabetic patients is, at least in part, due to an increased activity of the endoperoxide-thromboxane or arachidonic acid pathway. It was interesting to determine the platelet malondialdehyde (MDA) production in normal and diabetic pregnancies. Following individuals have been studied: I/ twenty-five healthy non-pregnant volunteers; II/ thirty women in third trimester of non-complicated pregnancies; III/ twenty two diabetic pregnant women without retinopathy; IV/ fifteen diabetic pregnant women with retinopathy. Platelet MDA production following N-ethyl-maleimide induced aggregation was measured according to Stuart et al. The mean value of MDA production was similar in volunteers and normal pregnant women (SDM, 7.07±.73 nmol MDA per 10⁷ platelets; 7.22±0.61). The mean MDA production in diabetic women without retinopathy was slightly but non-significantly higher than in normal pregnant women (5.7±1.02; p>0.05). The corresponding value in diabetic women with retinopathy was significantly higher than the values in the other three groups (6.47±0.82; p<0.01). These data suggest that the activation of prostaglandin synthetic pathway measured by MDA is significantly increased in diabetic pregnancy complicated by retinopathy. The increase of platelet prostaglandin synthesis in diabetic pregnancy might play an important role in initiating and/or promoting the small-vessel complications of placenta.