**MECHANISMS OF CARDIAC DYSFUNCTION IN DIABETIC CARDIOMYOPATHY**

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Chronic diabetes is known to be associated with the development of cardiomyopathy, metabolic derangement and cardiac dysfunction. By employing an experimental model of streptozotocin-induced diabetic cardiomyopathy, we have shown that cardiac dysfunction in this condition may be due to the activation of sympathetic nervous system and calcium-handling abnormalities in cardiomyocytes. Experiments in our laboratory have also demonstrated the involvement of renin-angiotensin system and oxidative stress in diabetes-induced cardiac dysfunction. Since platelet aggregation is enhanced in diabetic cardiomyopathy, we tested the effect of an antiplatelet agent, sarpogrelate

(a 5-HT2A antagonist), on depressed cardiac function in streptozotocin-induced diabetes. Treatment of diabetic rats with sarpogrelate for 8 weeks was observed to attenuate cardiac dysfunction and changes in the protein content of glucose transporters

(GLUT 1 and GLUT 4) in the myocardium. Furthermore, the depressed level of plasma insulin, unlike the elevated level of plasma glucose, in diabetic animals was partially restored by sarpogrelate treatment. These results suggest that elevated levels of plasma 5-HT, as a consequence of platelet aggregation, may play an important role in inducing defects in glucose utilization and cardiac dysfunction in diabetes.