

P-06-40 CAPILLARY PERMEABILITY TO ALBUMIN IN DIABETIC RAT MYOCARDIUM

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To clarify the mechanism for the well known increase in microvascular permeability that occurs with diabetes mellitus, we investigated capillary permeability to albumin in diabetic myocardium using albumin-gold complexes (Alb-Au: 7nm). Hearts from 28-week streptozotocin-induced diabetic and age-matched control rats were perfused with Krebs-Henseleit buffer containing Alb-Au for 5 or 20 min, fixed and processed for electron microscopy. In control animals, Alb-Au particles were found preferentially bound to the luminal plasmalemmal vesicles. Alb-Au particles were transported across the capillary endothelium via plasmalemmal vesicle and did not penetrate the intercellular junctions in both groups. In diabetic animals, the labeling of luminal vesicles was more extensive and more pronounced after 5 min of perfusion when compared to controls (% of labeled luminal vesicles :92.9% vs. 22.7%). The plasma membrane proper was also heavily labeled in diabetic animals. After 20 min, vesicular transport (transcytosis) of Alb-Au was significantly increased in diabetic myocardium when compared to controls (% of labeled vesicles opening to abluminal front:25.9% vs. 1.3%). We conclude that capillary permeability to albumin is markedly increased in diabetic myocardium due to enhanced vesicular transport. This may play an important role in the pathogenesis of diabetic cardiomyopathy.

P-06-41 ACE-INHIBITION SUPPRESSES THE DIABETIC NEUROPATHY IN MYOCARDIUM.

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Diabetes leads to cardiomyopathy and progressive neuropathy in rats. To study the role of catecholamines and the influence of captopril (Cap) on sympathetic nerve fibres in diabetes, control (C) and spontaneously diabetic BB-(DB) rats were treated with Cap for 6 months. Histofluorescent visualisation and morphometric quantification of intraneuronal catecholamines were performed by a digitalized analyzing system. As compared to controls catecholamine fluorescence was significantly reduced by diabetes to 69% ($p < 0.05$). Additionally, ultrastructural observation revealed severe morphological changes such as axonal degeneration indicating neuropathy of intracardiac fibres. ACE-inhibitors prevented the reduction in catecholamine fluorescence (94%, not significantly different from controls) as well as the ultrastructural alterations typical for diabetic neuropathy in myocardium. We conclude that the autonomic neuropathy of the heart in diabetes results from an over-stimulation of the autonomous nervous system in diabetes presumably induced by an altered enddiastolic relaxation.

P-06-42 METABOLIC IMPAIRMENT OF MITOCHONDRIAL FUNCTION IN DIABETIC RAT HEART AND EFFECT OF INSULIN TREATMENT

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We studied impairment of mitochondrial respiratory activity in streptozotocin (STZ) -induced diabetic rat heart with reference to insulin treatment. Experimental diabetes mellitus was induced in male Wistar rats by single intravenous injection of STZ at 65 mg/kg (D group). Insulin was injected for 3 weeks before sacrifice (I group) in a part of D group. Cardiac mitochondria (MT) from 2 to 16 weeks after STZ injection were prepared by method of Sordahl. Age matched normal rats were used as control (C group). Respiration and electron transport system activities of MT were measured. State 3, complex I and DNP-ATPase activities decreased significantly in D group, but these reductions recovered in I group. Mild fine structural alternations such as swelling of MT were observed from D group. However, these morphologic changes were slight in I group. These results suggest that disturbance of energy production in MT of diabetic myocardium are occurred by impairment of oxidative phosphorylation due to depression of complex I and DNP-ATPase activities. These metabolic changes are one causes of congestive heart failure noted as diabetic cardiomyopathy and are proved to be reversible with insulin treatment.