The effect of lysolecithin on sarcolemmal permeability during ischaemia

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91 THE IMPORTANCE OF ADP AS A REGULATOR OF MYOCARDIAL MITOCHONDRIAL RESPIRATION. **Ref Harmsen, Anne-Marie Seymour and George K. Radda.** Dept. Biochemistry, University of Oxford, OXFORD OX1 3AQ.

To investigate the importance of ADP in the regulation of oxidative phosphorylation, isolated rat hearts (paced at 300bpm) were initially perfused at low work load (60mm Hg perfusion pressure) and then at high work load (120mm Hg), with either 10 mM glucose, pyruvate, acetate or lactate. ATP and phosphocreatine (PCr) levels were monitored continously by ^{31}P-NMR. At the end of the experiment, hearts were freeze-clamped and assayed for ATP, PCr and creatine. [ATP] is constant throughout. [ADP] (μmol/l) were calculated from the phosphocreatine kinase equilibrium ($1.7*10^{-9}$M), with an assumed pH of 7.1.

	Low work load		High work load	
	PCr/ATP	ADP	PCr/ATP	ADP
Glucose	1.78	42	1.65	55
Pyruvate	1.92	28	1.78	40
Lactate	2.24	20	2.26	20
Acetate	2.00	30	2.00	32

We therefore conclude that factors other than ADP are important in regulation of mitochondrial respiration. (Supported by MRC and BHF).

92 THE EFFECT OF ISCHAEMIA AND REPERFUSION ON SARCOLEMMAL PERMEABILITY IN THE ISOLATED RAT HEART. I.S.Harper, A.Lochner, MRC Research Institute for Medical Biophysics, and MRC Centre for Molecular and Cellular Cardiology, University of Stellenbosch Medical School, Tygerberg, South Africa.

To examine the relationship between development of irreversible damage and changes in sarcolemmal membrane permeability, a quantifiable ionic lanthanum probe technique was applied to an isolated rat heart model. Hearts were subjected to total global ischaemia, with or without subsequent reperfusion for 30 minutes, and then perfused (10 min) with an inert La saline to probe membrane permeability. Distribution of La was evaluated with TEM. After 15 minutes of normothermic ichaemic cardiac arrest (NICA) about 70% of the subendocardial myocytes showed intracellular La deposits, indicating increased sarcolemmal permeability. Reperfusion (REP) stimulated full recovery of ultrastructure, exclusion of La from myocytes and allowed mechanical recovery. Effects of NICA and REP were less pronounced in the subepicardium. After 25 minutes of NICA subendocardial myocytes (93%) exhibited intracellular La deposits and severe ultrastructural injury. REP was accompanied by mechanical failure, La influx and increased ultrastructural damage. CONCLUSION: Changes in sarcolemmal permeability occur shortly before mechanical failure and may therefore contribute to the onset of irreversible damage.

93 THE EFFECT OF LYSOLECITHIN ON SARCOLEMMAL PERMEABILITY DURING ISCHAEMIA. I.S.Harper, A.Pentz, A.Lochner, MRC, RIMB, and MRC Centre for Molecular and Cellular Cardiology, University of Stellenbosch Medical School, Tygerberg, South Africa.

Accumulation of lysophosphoglycerides during myocardial ischaemia has been shown to facilitate Ca^{2+} influx, contributing to dysrhythmias and cellular injury. In order to examine the effects of lysophosphoglyceride accumulation on sarcolemmal permeability, isolated rat hearts were perfused with lysolecthin (LL,<10μM) for 20 min, subjected to 15 minutes of global ischaemia and perfused with ionic lanthanum saline either directly or after reperfusion (30 min). Electron microscope detection of La in non-ischaemic tissue showed extracellular localization of La, with intracellular deposits occurring after ischaemia. Non-treated hearts recovered fully during reperfusion and excluded La. In hearts treated with LL, reperfusion after 15 minutes of ischaemia promoted severe cellular damage and contracture. Both reperfused and non-reperfused treated hearts experienced considerable La influx in myocytes indicating increased membrane permeability. The harmful effects of LL were completely reversed by administration of Chlorpromazine (30mg/kg).
Our results suggest that LL accumulation may promote increased sarcolemmal Ca^{2+}-permeability during both ischaemia and reperfusion. Coupled with reduced SR Ca^{2+}-uptake (J Mol Cell Cardiol 18 Suppl 1:214, 1986) this may explain the severe contracture development.