INTRODUCTION AND AIM OF THE WORK

It is well known that ischemic heart diseases, especially acute myocardial infarction, are responsible for a high percentage of deaths particularly in well developed counteries. Clinically it is known that the infarct size is an important determinant of prognosis in patients with acute myocardial infarction (Geltman et al., 1979). The hospital mortality of patients with large infarcts is several folds greater than it is in patients with small infarcts (Holmans et al., 1978).

In experimental animals the fate of injured ischemic tissue may be affected favourably by interventions that restore perfusion, reduce myocardial oxygen requirements, inhibit accumulation or facilitate washout of noxious metabolites, augment the availability of substrate for anaerobic metabolism or blunt the effect of mediators of injury such as calcium and metabolites.

Myocardial injury induced by ischemia is associated with complexes of calcium in the tissue detectable by electrone microscope. The interaction between myocardial ischemia and myoplasmic $[Ca^{++}]$ is complex. Ischemia, however produced, is characterised by a reduction of

myocardial ATP stores, which interferes with transsarcolemmal [Na^+- K^+] exchange, which in turn elevates intracellular [Na^+], raising intracellular [Ca^{++}] through an enhanced Na^+- Ca^{++} exchange. Lowered ATP stores also reduce Ca^{++} uptake by the sarcoplasmic reticulum and reduce the extrusion of Ca^{++} from cells. The resultant raised intracellular [Ca^{++}] causes mitochondrial Ca^{++} overload which depresses ATP usage and activate sarcolemmal phospholipases which release membrane phospholipid degradation products whose detergent properties impair the integrity of the cell membrane (Sedlis et al., 1983 and Corr et al., 1982a).

The hypothesis that entry of calcium into the ischemic cells may be harmful is based on the observation that after a period of myocardial ischemia and subsequent reperfusion the accumulation of excess calcium in the mitochondria may interfere with their capacity to generate ATP. The destructive chain of metabolic events provoked by increased intracellular [Ca^{++}] appears to be responsible, at least in part, for the death of cells in the ischemic myocardium.

Henry and associates, in 1977, found that during one hour of myocardial ischemia, the left ventricle

undergoes progressive ischemic contracture, with development of an elevated ventricular diastolic pressure and a fourfold increase in mitochondrial calcium. With subsequent reperfusion, both myocardial systolic function and relaxation remains abnormal and a further marked increase in calcium accumulation occurs.

Reperfusion injury, by definition, refers to cell death (or damage) caused by reperfusion (Hearse, 1977 and Jennings et al., 1985a), in contrast to cell death (or damage) caused by the preceeding ischemic episode.

It has been demonstrated that prostaglandin synthesis by the heart is increased after ischemia, although the significance of this observation has never been elucidated (Kraemer et al., 1976 amd Brandt et al., 1984)

The aim of our study was to prove or disprove the reperfusion injury, to detecte the best time for reperfusion starting by 30 minutes after ischemia, the time after which reperfusion is to be useless with or without adjuvant interventions and to show the role of calcium in the reperfusion injury. If calcium flux

across the specific calcium channels is a major source of intracellular calcium overload, thus, calcium antagonists might prevent or delay ischemic cell death.

We were aiming also to study the role of one of the prostaglandins secreted by the heart during reperfusion,prostgalndin $F_{2\alpha}$, (Karmazyn, 1986).