MYOCYTE INJURY AND ALTERED VASCULAR FUNCTION IN DEVELOPING MYOCARDIAL INFARCTS

By

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The cicada's song:
Sentinel insentient
Of imminent death.

Matsuro Basho (1644-1694)

ABSTRACT

The temporal and spatial relationships between altered vascular function and cardiac muscle cell injury at the margins of developing myocardial infarcts were investigated, because such knowledge might provide potential for intervention in the evolution of myocardial infarcts and limitation of their size.

Regional myocardial ischaemia was modelled in isolated rabbit hearts subjected to ligation of the ventral interventricular branch of the left coronary artery (0,30,60,120 or 240 minutes duration), the remainder of the heart being continuously perfused with oxygenated Krebs-Henseleit buffer solution.

After the experimental ischaemic period, the whole heart was fixed by perfusion with phosphate-buffered 2.5% glutaraldehyde which, in preliminary studies, was shown not only to preserve the morphological appearance of cardiac muscle cells, but also to stabilise the distribution of flow through the myocardial blood vessels in the pattern pertaining immediately prior to fixation.

Polymerising acrylic resin (L.R. White) was then injected into the vessels of the ischaemic and non-ischaemic regions simultaneously at identical pressures. Resin injected into the ischaemic region contained lead dioxide whilst that injected into the other vessels contained Fat Red 7B dye to allow identification of the source of supply

of blood vessels within the heart.

Cryofracture, freeze-drying and imaging by scanning electron microscopy (SEM) with a backscattered electron detector and low vacuum specimen chamber conditions were used. This made possible examination of transmural segments of myocardium spanning the margins of the ischaemic and control ventricular myocardium containing blood vessels filled by resin.

SEM showed severe injury of cardiac muscle cells after 60 minutes of ischaemia, as characterised by separation and swelling of some organelles. Earlier ischaemic changes in some cells (focal increase in prominence of t-tubules and sarcoplasmic reticulum) were seen after 30 minutes. There was a transmural progression in development of irreversible injury from the subendocardium to the epicardium between 60 and 120 minutes corresponding to the "wavefront phenonenon". The lateral margins did not show such marked progression and were typically sharply demarcated on a cell-to-cell basis after 60 minutes.

An increase in the proportion of functional capillary pathways (from 55% to 85%) in early (30 minutes) ischaemia was succeeded by a profound perfusion defect, corresponding to the "no-reflow" phenomenon, which had a very close temporal and spatial association with severe injury of cardiac muscle cells. Loss of patency was associated with increased proportions of collapsed, compressed capillaries and swollen myocardial cells.

This study demonstrated that there is a significant region of myocardium which for a period shows intermediate degrees of myocyte injury (and is thus potentially salvageable) in the subepicardial portion of the developing infarct. Contrary to the claims of various authors similar potentially salvageable lateral "border zones" were neither large nor non-existent. Within 150 microns of the typically abrupt boundary, small discontinuous areas (<20% of this region) showed intermediate degrees of injury, and there was also an increased proportion of non-functional capillaries which were not collapsed or compressed, resulting in a 'low-flow' zone.

This narrow lateral zone requires further investigation to determine whether it is static, and thus of negligible size, or whether it moves in advance of infarction and is thus pathogenetically significant.

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Sage M.D., J.B. Gavin and P.B. Herdson (1982) Scanning electron microscopy of lateral border zones of regional infarcts in isolated rabbit hearts. J Mol Cell Cardiol 14 : Suppl 2 : 12 (abstract)

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From the conference of the New Zealand Society for Electron Microscopy

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