Assessment of myocardial damage in dilated cardiomyopathy

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Dilated cardiomyopathy is associated with impairment of systolic function. Damage to cardiac myocytes, including disruption of the sarcolemma, can be demonstrated by enhanced myocardial binding of monoclonal antibody to cardiac myosin in a large proportion of patients with dilated cardiomyopathy. Binding of an ¹¹¹In-labelled Fab fragment of antmyosin antibody to myocardium can be quantitated by scintigraphy and compared to uptake by other tissue such as lung. This heart-to-lung ratio has been used to assess the degree of myocardial damage in patients with acute inflammation resulting from myocardial infarction, myocarditis or rejection of the transplanted heart[11]. The histological changes in dilated cardiomyopathy are nonspecific and similar to those in patients with end-stage heart failure from causes such as valve disease, hypertensive heart disease or coronary heart disease. Unlike patients with dilated cardiomyopathy, however, enhanced uptake of antimyosin is not seen in end-stage heart failure due to these other causes.

Enterovirus infection of myocardium has been shown to be associated with myocarditis and the subsequent progression to dilated cardiomyopathy[2,3]. Virus can persist in myocardium to end-stage dilated cardiomyopathy requiring transplantation and its presence is a powerful independent predictor of poor prognosis[24]. In this issue Marti and colleagues[3] address the question of whether the detection of enterovirus in myocardium from patients with dilated cardiomyopathy correlates with enhanced antimyosin uptake, suggestive of continuing myocardial cell damage. Sixteen of 19 (84%) dilated cardiomyopathy patients showed enhanced antimyosin uptake and enterovirus RNA was detected by quantitative slot-blot hybridization in myocardial samples from four of these (25%): this is comparable with the frequency of detection of enterovirus in myocardium in several previous studies of patients with so-called idiopathic dilated cardiomyopathy[6,7]. Virus was not detected in dilated hearts without increased antimyosin binding, or in ten samples of normal myocardium. This may be one example of an insult to the myocardium leading to increased cell permeability and exposure of cardiac myosin. A further consequence may be to elicit the formation of cardiac autoantibodies reported by many groups and presumed to be pathogenic[8,9].

Marti and colleagues demonstrate the value of ¹¹¹In-antimyosin uptake in assessment of myocardial cell damage and support the concept of the pathogenic role of persistent enterovirus infection of myocardium in the development of some cases of dilated cardiomyopathy. It remains to be determined what other aetiologies may be correlated with myocardial damage in dilated cardiomyopathy.

P. J. RICHARDSON
Kings College Hospital,
London, U.K.

References

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Preconditioning of the heart

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The paper by Claey's and co-workers in this issue\textsuperscript{11} draws attention to the important phenomenon of ischaemic preconditioning. This subject has been extensively investigated after the first description by Murry \textit{et al.} in 1986\textsuperscript{22}. In the canine heart, ischaemic preconditioning could be induced by a short period (about 5 min) of ischaemia followed by a period of less than 60–120 min of reperfusion, prior to the actual period of ischaemia, which then caused less damage than was observed in the absence of preconditioning ischaemia. Also, multiple periods of 5 min of ischaemia, each followed by 5 min of reperfusion, induced preconditioning. Ischaemic preconditioning was observed in hearts of several animal species, and proved to be independent of a rapidly recruitable collateral circulation. Preconditioning could also be induced by measures other than coronary occlusion provided the myocardial supply/demand ratio was compromised. From 1990 onwards, several groups have collected evidence that ischaemic preconditioning may also occur in the human heart. In the Thrombolysis In Myocardial Infarction (TIMI)-4 trial, patients who had a history of previous angina at any time before acute myocardial infarction, had lower in-hospital mortality, experienced congestive heart failure or shock less frequently, and had smaller enzymatic infarct sizes than patients without a history of previous angina\textsuperscript{33}. At open heart surgery, Yellon \textit{et al.} demonstrated that brief episodes of aortic cross-clamping followed by reperfusion prior to construction of the proximal anastomoses\textsuperscript{34}.

Balloon occlusion during percutaneous transluminal coronary angioplasty (PTCA) provides a suitable clinical model with which to study preconditioning in vivo. In accordance with the observations of Claey's \textit{et al.}\textsuperscript{11} several investigators have demonstrated that initial repeated balloon inflations followed by reperfusion led to diminished signs of ischaemia during PTCA. However, these observations rely to a large extent on the magnitude of ST elevations which may be influenced by other (metabolic) factors than ischaemia. In addition, in spite of a careful selection of cases the possibility of changes in collateral flow cannot be excluded. Therefore, we must conclude that the results of these clinical studies in man are compatible with a protective effect due to myocardial preconditioning, but cannot be considered to be definite proof of a unique phenomenon.

Interestingly, 'ischaemic preconditioning' of the heart can be induced by several pharmacological compounds. The working hypothesis has emerged that adenosine formed by degradation of adenosine triphosphate during the first period of ischaemia and liberated by ischaemic myocytes, acts as an autacoid and binds to adenosine A\textsubscript{1}-receptors on the sarcolemmal membrane\textsuperscript{35}. A beneficial response is elicited which protects the myocyte against a second period of ischaemia. Infusion of adenosine or adenosine A\textsubscript{1}-receptor agonists could, indeed, diminish myocardial damage of the ischaemic heart\textsuperscript{36}. Likewise,