

DILATED CARDIOMYOPATHY

Dilated cardiomyopathy: an introduction to pathology and pathogenesis

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The patient who presents with a poorly functioning dilated left ventricle (LV) without evidence of coronary artery or valve disease presents conceptual and management problems that the label dilated cardiomyopathy does little to resolve. This section of the supplement describes what is currently known about the pathogenesis, pathology, and clinical management of such patients.

The pathology of the condition is easily described. Any combination of four histological features is present (table). The myocytes show evidence of hypertrophy in that the nuclei are enlarged with an increased DNA concentration indicating polyploidy. The width of the myocytes is, however, not increased and in many instances is even decreased. Left ventricular hypertrophy with no increase in the width of the myocytes has been called attenuation. The shape of the myocytes reflects the ventricular dilatation, but it is not certain whether their length is increased—that is, myocyte volume is increased—or whether there has been slippage between adjacent layers of myocytes. Under light microscopy the myocytes often appear empty and vacuolated because their myofibrillary content is reduced. The loss of contractile filaments is associated with declining ventricular function. Fibrosis is usually interstitial and later surrounds individual myocytes. The number of T lymphocytes present within the myocardium may be increased.

Such straightforward descriptions mask an extraordinary case to case variability. Some patients have no fibrosis: others have quite coarse scarring. A few hearts show such slight histological abnormality that a pathologist examining such a heart removed at transplantation may wonder whether the clinical diagnosis was correct.

The presence of increased numbers of T lymphocytes raises the question of what is the relation of acute myocarditis to dilated cardiomyopathy in humans. The Dallas nomenclature for reading myocardial biopsies lays down clear guidelines on the morphological distinction between acute myocarditis and dilated cardiomyopathy. In acute myocarditis there is evidence of myocyte damage with an increase in T lymphocytes within the myocardial interstitial tissues but no myocyte hypertrophy or fibrosis—a definition that emphasises the acute nature of the process. In contrast, in dilated cardiomyopathy there is myocyte hypertrophy and fibrosis. This definition obscures the fact that T lymphocytes can also be increased in dilated cardiomyopathy. At present, data on the numbers of T lympho-

cytes are limited by the use of rather ill defined quantification methods. For example the number of cells per high power microscopic field is quoted without defining the area of that field. Centres where formal counts have been done, however, show that in dilated cardiomyopathy there can be anything from no increase in T lymphocytes to a very large increase. In about a third of cases there are so many T lymphocytes that the patient could equally well be regarded as having chronic myocarditis. Further evidence for the entity of chronic myocarditis comes from the expression of class II histocompatibility antigens and of adhesion molecules such as ICAM1 on endothelial cells in the myocardium.

The pathogenic mechanisms of dilated cardiomyopathy are as heterogeneous as its pathological features. Regrettably there is no direct match between pathology and pathogenesis. For example, the pathologist cannot distinguish between alcoholic cardiomyopathy and cardiomyopathy with other causes.

There are many potential causes of dilated cardiomyopathy but few are common. Epidemiological and clinical evidence strongly links alcohol to dilated cardiomyopathy, probably through a direct toxic effect on the myocyte. This subject is not discussed here because we assume that such cases are not idiopathic. We accept that this is an oversimplification because many patients hide their drinking habits, the level of drinking that is normal or safe is uncertain, and alcohol may potentiate viral or autoimmune damage.

Familial dilated cardiomyopathy is also heterogeneous. It can be the result of inherited mitochondrial genomic abnormalities. In general such defects cause concomitant skeletal muscle problems and are strongly associated with abnormal conduction rather than abnormal contraction. It would be surprising, however, if there were not a few mitochondrial genetic defects masquerading as idiopathic dilated cardiomyopathy. Much the same applies to skeletal myopathies. In general the cardiac involvement is subsidiary and minor but there are exceptions. Dystrophin has been shown to be reduced in the myocardium in at least one family with pure dilated cardiomyopathy in the absence of important skeletal muscle problems.

In general, however, this supplement is concerned with idiopathic dilated cardiomyopathy where no clear cause or extra-cardiac abnormality is detected. The pathogenesis, prognosis, and treatment are all reviewed.

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*Pathological features of
dilated cardiomyopathy*

- Increased LV mass
- Decreased LV wall thickness
- Myocyte hypertrophy:
 - Increased nuclear DNA content
 - Normal or reduced myocyte width
- Interstitial fibrosis
- Myocyte myofibrillary loss
- Increased number of interstitial lymphocytes

LV, left ventricular.