Pathology of hypertrophic cardiomyopathy

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This communication will concentrate on the morphological recognition and diagnosis of this condition.

The classical change at macroscopic examination of the heart is asymmetric hypertrophy of the interventricular septum, the maximal bulge occurring at various sites (Olsen, 1972). A few years ago doubt was cast upon the reliability of this change due to its occurrence in normal as well as congenitally abnormal hearts (Bulkley *et al.*, 1977). There is no doubt that if the asymmetry of the septum is of sufficient severity, for example a ratio between the maximal bulge and the free left ventricular wall exceeding two, a diagnosis can be made on macroscopic examination alone (Olsen, 1971).

Not infrequently, the changes may not be as severe or may even be absent, a symmetric form being recognized with increasing frequency. Recourse to histological examination then becomes mandatory.

Microscopical changes include: severe hypertrophy, disarray, the fibres often displaying a whorled arrangement, bizarre shaped nuclei often surrounded by a clear zone and varying degrees of cellular interstitial fibrosis (Van Noorden *et al.*, 1971). Some overlap between the changes occurring in hypertrophy due to known causes and that occurring in hypertrophic cardiomyopathy exist and several years ago the histological HOCM index was developed, assessing the various morphological features semi-quantitatively (Van Noorden *et al.*, 1971). More recently, controversy has arisen as to whether disarray of myocardial fibres is pathognomonic of the condition or at least highly characteristic. It has been shown that if disorganisation of myocardial fibres is wide-spread involving 5% or more of the septum, that this represents a specific histological marker of this disease (Maron & Roberts, 1979). It is, however, unwise to single out one feature and only if the other characteristic changes are considered in combination with dis-

array can a diagnosis be firmly established (Olsen, 1982).

Histological distinction in the distribution of abnormally arranged myocardial fibres in patients in whom 'obstruction' was or was not present during life has been shown to be unreliable (Olsen, 1983).

Of all histochemical analyses on tissue obtained either as part of the surgical intervention to relieve 'obstruction' or by biptome, severe accumulation of glycogen is of diagnostic value (Van Noorden *et al.*, 1971). All other investigations including succinic dehydrogenase non-specific esterases or phosphatases reflect the severe hypertrophy and although greater increases than in secondary hypertrophy are observed they are insufficient for diagnostic purposes.

Ultrastructural changes, which include disarray of myofibrils, frequent abnormal intercellular junctions as well as focal accumulation of mitochondria to a severe degree, also permit confirmation of the diagnosis. Caution should, however, be exercised in placing reliance on ultrastructural changes alone, but as in the histological evaluation when these changes are widespread they can be interpreted as characteristic findings (Olsen, 1980).

An animal model has been established which on administration of triac, the acetic acid analogue of triiodothyronine, to pregnant rats produces changes in new born rats ultrastructurally mimicking those found in the hearts of man (Olsen *et al.*, 1977). By using a variety of therapeutic and other agents together with triac it has been shown that triac exerts its effect on the cell membrane and this in turn permits influx of calcium ions leading to abnormalities in contraction (Olsen, in press). These findings, in addition to having established an animal model for hypertrophic cardiomyopathy, have also demonstrated a likely mechanism for disarray.

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