Electron Microscopical Findings in Hypertrophied Human Ventricle

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The normal ultrastructure of the human myocardium is fairly well documented (Porter and Bonneville, 1963; Stenger and Spiro, 1961; Burdette and Ashford, 1963; Lannigan and Zaki, 1966) and some of the prominent subcellular changes have also been described (Burgos and Rodriguez-Echandta, 1966; Alexander, 1967).

We should like here to present the ultrastructural features observed in hypertrophied hearts from subjects whose only complaint was tightness in the chest during heavy exercise. They showed clinical and radiological signs of cardiac hypertrophy due to outflow tract stenosis, later confirmed at open heart operations. These patients were not in heart failure, nor had they received any treatment.

For the purposes of comparison the electron microscopical studies were made of the myocardia of two children who had nearly normal hearts. One was a boy of 12 years with moderate subvalvular aortic stenosis, and the other a girl of 12 years with a small atrial septal defect. Neither had appreciable ventricular hypertrophy. The cardiac condition of these children was discovered at routine school medical examination, and they were of normal growth and fully active.

MATERIAL AND METHOD

The biopsies were taken from the anterior surface of the right ventricle in the children, and the hypertrophied ventricles in the adults when the pericardium was opened at the time of operation. A 2 × 3 mm. wedge-shaped specimen was taken and immediately transferred to a dish containing 5 per cent glutaraldehyde and was cut into thin slices. These were post-fixed in osmic acid, embedded in Epon, sectioned by a Reichart's ultratome, stained with uranyl acetate and lead citrate, and studied with a Hitachi HS-7S electron microscope.

RESULTS

Fig. 1 and 2 show the structure of the myocardium from the two control hearts. The muscle cells are delimited by the sarcolemma, which itself is externally bound by a thinly granulated basement membrane. There are numerous pinocytotic vesicles at different stages of formation from the surface.

The cells are separated along their longitudinal axis by the intercalated discs (Fig. 2).

Inside the cell there are rows of myofibrils, separated one from another by columns of mitochondria or "sarcosomes". The myofibrils consist of many sarcomeres which are the functional units of the heart. Each sarcomere stretches between two Z-lines. The mitochondria are arranged in a regular pattern and are abundant in the myocardium. The proximity of the energy-producing organelles (mitochondria) to energy-consuming elements (i.e. sarcomeres) is a good example of co-ordinated cellular function. Their approximate 1:1 column ratio is shown in Fig. 1.

The sarcoplasmic reticulum, which plays an important role in the coupling of excitation and contraction as well as relaxation of the heart muscle and is thought to be in direct communication with the interstitial spaces, is usually found near the Z-lines (Fig. 2).

In the cells of the hypertrophied heart (Fig. 3) the number of mitochondria is increased, and there are more myofibrils than in the controls (see Fig. 1). Finger-like processes protrude from the cell surface into the interstitial space (Fig. 4). These "cardiac villi" are crowded with mitochondria (Fig. 5). There is active pinocytosis on their surface, and some villi contain vacuoles, apparently formed by the coalition of pinocytotic vacuoles.

DISCUSSION

The ultrastructural alterations in myocardial hypertrophy have been the subject of several papers.

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FIG. 1.—A section of right ventricle. ($\times 11,700$.) Normal appearances of human cardiac muscle. Base-ment membrane (bm), interstitial space (is), mitochondrion (m), pinocytotic vesicle (pv), sarcolemma (s), Z-line (z).

FIG. 2.—Normal human cardiac muscle ($\times 17,300$), showing intercalated disc (id) and sarcoplasmic reticulum (sr).

Richter and Kellner (1963) in their study of the hypertrophied human heart observed that there was no change in the geometrical disposition of the actin-myosin filaments. They suggested that hypertrophy was due to possible increase in the number of filaments in the existing myofibrils as well as an increase in the total number of myofibrils. Carney and Brown (1964), in rats with experimentally produced left ventricular hypertrophy, concluded that the mean diameter of the "thick" cardiac myofilaments was the same as in the normal rat left ventricle. They suggested that hypertrophy was due to an increase in the number of thick myofilaments resulting in increase in the size of the myofibrils.

Meerson *et al.* (1964) analysed the various phases of myocardial hypertrophy in rats from the time when the demand for increased work begins until heart failure results. They distinguished three stages. During the first stage there is an increase in the size and the number of mitochondria, after an initial destructive phase. This priority in the production of mitochondria by the cell is apparently

due to its DNA-dependant RNA, which acts more rapidly than the DNA-dependant synthesis of any other RNA.

The second stage is characterized by increase in number and size of the myofibrils. Therefore, a balanced distribution of function per unit structure is achieved.

During the third or final stage there is a disturbance of nucleic acid production, derangement of normal structure, and disturbance of functional activity. Clinically in the third stage the heart has begun to fail.

Clinically and histologically the cases presented in this paper demonstrate the features of a second stage (compensated) hypertrophy.

The increase in number and size of mitochondria and myofilaments is in agreement with findings of Meerson and his colleagues. The formation of villi protruding from the cell surface probably indicates the need of the cell for an increased absorptive surface, and the very active pinocytosis confirms that absorption is proceeding.

FIG. 3.—A section of hypertrophied left ventricle ($\times 19,920$), showing increase in the number of mitochondria (m) and the volume of myofibril (my).

SUMMARY

The salient ultrastructural features of hypertrophied human myocardium are presented. They are as follows.

(1) Increase in the number of mitochondria and myofibrils in the cell. (2) Increase in the absorptive surface area by villus formation of the sarcolemma, with multiple pinocytotic vacuoles, and mitochondria in these finger-like processes.

FIG. 4

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FIG. 5

FIG. 4 and 5.—Hypertrophied left ventricle. ($\times 20,000$.) Finger-like processes (cardiac villi (cv)) protruding into the interstitial space. Vacuole (v), myofibril (my), glycogen granules (g), mitochondria (m).

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