HYPERPLASTIC PROCESSES IN MITOCHONDRIA OF HEART-MUSCLE CELLS AFTER ADMINISTRATION OF TOXIC DOSES OF ADRENALIN

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Hyperplastic processes in mitochondria of heart-muscle cells of albino rats during administration of toxic doses of adrenalin were studied experimentally. Electron-microscopic investigation revealed three types of mitochondria. Those of the first type had dimensions and structure characteristic of myocardial muscle cells. Those of the second type had an extremely dense, finely granular matrix and many cristae per unit area. Mitochondria of the third type had two "compartments" differing in the density of their matrix and the arrangement and number of their cristae under a common outer membrane. It is postulated that the ultrastructural differences between the mitochondria of these three types reflect their functional state.

KEY WORDS: Structure of mitochondria; rat myocardium; adrenalin.

Toxic doses of adrenalin are known to damage the myocardium and to cause contractual changes in the myofibrils and focal necrosis [2, 4, 13]. Deformation, swelling, and destruction of the mitochondria are observedunder these circumstances in the muscle cells [2, 10, 14, 19]. Meanwhile, during the first day after administration of adrenalin, the structure of most muscle cells is completely restored. According to Tsellarius and Semenova [13], this process begins with recovery of the mitochondrial apparatus.

The object of this investigation was to study hyperplastic processes in the mitochondria of heart-muscle cells during administration of adrenalin.

EXPERIMENTAL METHOD

The myocardium of 36 albino rats, in which signs of cardiovascular failure developed on the second day after a single injection of adrenalin, was studied experimentally. Adrenalin hydrochloride was injected intramuscularly (into the thigh) as a 1:1000 solution in a dose of 3 mg/kg. Pieces of myocardium from the left ventricle were fixed in 1% OsO_4 solution by Caulfield's method and embedded in Araldite. Electron micrographs were obtained with the IEM-100V microscope.

EXPERIMENTAL RESULTS

Electron-microscopic study of the heart-muscle cells revealed degenerative changes reflecting basically a disturbance of lipid metabolism. Meanwhile, in most cells signs of intracellular regeneration were observed: marked hyperplasia in the mitochondria and the formation of new mitochondria.

Mainly two types of mitochondria, differing sharply in structure (Fig. 1a), were found in many cells containing numerous lipid droplets.

The mitochondria of the first type, 1.5-2 μ in diameter, had the usual structure for rat myocardial muscle cells: parallel or oblique in their arrangement, several curved cristae, and a pale electron-trans-

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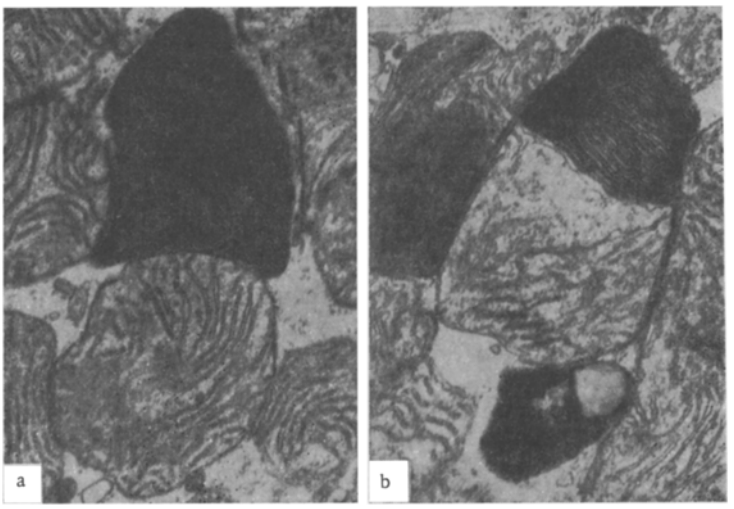

Fig. 1. Mitochondria of myocardial muscle cells of rat receiving toxic dose of adrenalin (65,000 ×); a) two different morphological types of mitochondria; b) mitochondrion consisting of two parts, differing in structure.

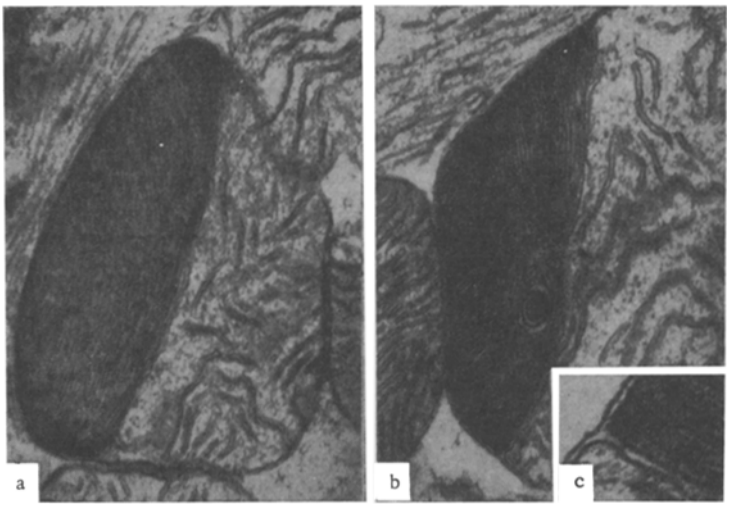

Fig. 2. Mitochondria differing in arrangement and in packing density of cristae. a) Perpendicular and oblique arrangement of cristae in two parts of a mitochondrion (100,000 ×); b) difference in density of matrix and structure of cristae in two parts of mitochondria (100,000 ×); c) fragment: common outer membrane for two parts of a mitochondrion (300,000 ×).

lucent matrix. The number of cristae in the mitochondria was 10-15. The cristae were arranged at varied distances from each other.

Mitochondria of the second type were rather smaller (diameter 0.9-1.8 μ), and they were distinguished by an extremely dense, finely granular osmiophilic matrix. The cristae were always strictly parallel to one another and their number per unit area was 2-3 times greater than in ordinary mitochondria.

Meanwhile, mitochondria consisting of two different parts, a denser part and a more swollen and loosely packed part, were frequently seen in the heart-muscle cells (Fig. 1b). These mitochondria had what looked like two "compartments" separated by the membranes of a single septum, beneath a common outer membrane (Figs. 1b and 2). Characteristically the cristae in the two different parts of the mitochondrion were often arranged perpendicularly or obliquely to each other (Fig. 2a). The membranes of the cristae were clearly outlined in the "dense" parts of the mitochondrion and the matrix was finely granular

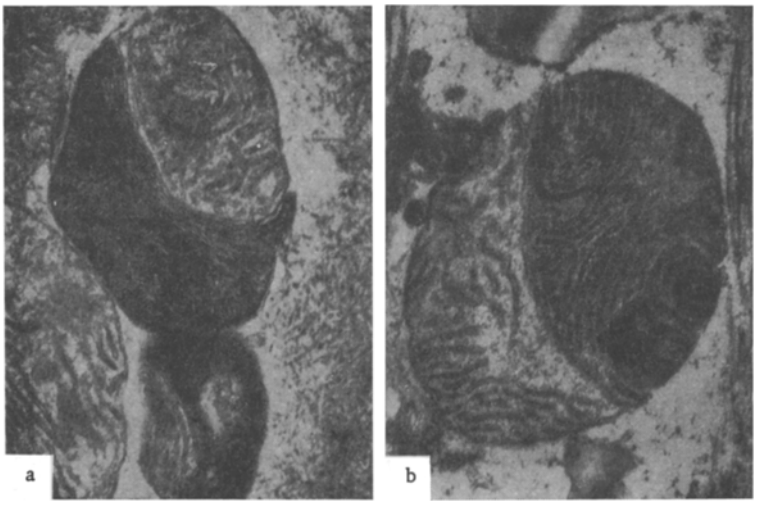

Fig. 3. Division and "budding" forms of mitochondria (80,000 ×) a) rupture of outer membrane of mitochondrion; b) intramitochondrial "buds".

and strongly osmiophilic. Cristae of the "loose" part of the mitochondrion were curved, twisted, and extremely haphazardly arranged (Fig. 2b). Often the membranes of the cristae in this part of the mitochondrion had blurred and indistinct outlines. The part of the mitochondrion with a pale matrix and with loosely packed cristae was in a swollen or even fragmented state. Sometimes rupture of the common outer membrane and commencing separation of the two parts of the mitochondrion could be seen (Fig. 3a). Inside some mitochondria there were distinctive membraneous structures resembling tiny mitochondria in their appearance (Fig. 3b). These intramitochondrial "buds" as a rule were bounded by two membranes and contained 2–4 septa.

Electron-microscopic study of the mitochondria of heart-muscle cells after administration of adrenalin thus revealed the appearance of mitochondria with sharply different structure: different in the optical density of their matrix and in the number and arrangement of their cristae. The ultrastructural features of the mitochondria described above evidently reflect their functional state by determining the level of intracellular regeneration.

If the results described above are compared with those of biochemical investigations some parallels can be drawn for the relationship between the structure and function of these organelles.

Mitochondria isolated from the tissue consist chiefly of two conformational types – condensed and orthodox mitochondria [15, 16]. Condensed mitochondria have a dense, finely granular osmiophilic matrix, widened cristae, and a high respiratory quotient, and they contain more than twice as much RNA as mitochondria of the orthodox type [1, 5]. Mitochondria with a compact structure and continuous outer membrane with clearly marked cristae have been shown to be in a state of firm coupling of respiration and phosphorylation and to have a high content of ATP [8]. Kozel'tsov and Khoroshkov [7], who studied the mitochondria of the "heavy" fraction, analogous in structure to condensed mitochondria, also describe the high respiratory activity of mitochondria of this type and their ability to incorporate thymidine-C^{14} and leucine-C^{14} and to synthesize DNA and various proteins. Mitochondria with a pale matrix and only a few cristae (orthodox mitochondria), on the other hand, are characterized by processes of uncoupling of oxidation and phosphorylation, a low respiratory quotient, much less active incorporation of thymidine-C^{14} and leucine-C^{14}, inability to synthesize DNA, and a low rate of protein synthesis [7, 9]. Beketova [1] considers that mitochondria of the condensed type are in a state of energy accumulation, whereas the orthodox type are characterized by a state of functional overstress. Mitin and Beketova [9] showed correlation between the structure of mitochondria in the tissue and definite configurational types of isolated mitochondria.

The mitochondria with a dense, finely-granular, osmiophilic matrix and with a large number of densely packed cristae, parallel to each other, observed in these investigations evidently correspond in their functional characteristics to condensed mitochondria, and they have a high level of synthetic processes and a high degree of coupling of respiration and phosphorylation. Mitochondria with a pale matrix and loosely packed cristae, on the other hand, correspond to the orthodox type and are in a state of energy production and functional stress.

The distinguishing features of mitochondria consisting of two parts of different structure, and containing intramitochondrial "buds," are connected with active metabolic processes. Sarkisov [11] states that hyperplastic processes can take place in mitochondria, and he considers that under conditions when rapid formation of new mitochondria and replacement of damaged mitochondria by them do not take place, the structure of the damaged mitochondria can be restored through regeneration of their component parts, i.e., through intraorganoidal (intramitochondrial) regeneration. Adrenalin is known to evoke profound changes in the metabolism of the muscle cells in the myocardium and, in particular, changes in lipid and phospholipid metabolism [6]. Activation of lipolysis and, correspondingly, of the mitochondrial phospholipase A, by adrenalin, may lead to changes in phospholipids of the mitochondrial membranes [12, 17, 18], and this limits the formation of new mitochondria by transverse division or budding. At the same time it has been shown that the fraction of structural proteins of the mitochondria (inner and outer membranes) has a stimulant action on template activity of mitochondrial DNA, and thereby promotes template synthesis of RNA [3].

The presence of mitochondria with a dense osmiophilic matrix, with numerous cristae, and consisting of different structural divisions is evidence of the marked hyperplastic processes taking place as the result of the action of adrenalin.

In that case a special type of intraorganoidal regeneration can evidently take place – regeneration through activation of intramitochondrial synthesis and, in particular, high activation of synthesis of RNA and proteins in individual sites of the mitochondrial matrix. The increased intensity of protein synthesis is perhaps brought about by the stimulant action of the dissociated protein–lipid component of the mitochondrial membranes. These processes may affect not the whole mitochondrion, but only part of it, with subsequent separation and independent functioning of the organelles.

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