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ELECTRON-MICROSCOPIC AUTORADIOGRAPHY OF RNA SYNTHESIS IN THE INJURED MYOCARDIUM

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A burn of the wall of the left ventricle was produced in newborn rats. Synthesis of RNA in the muscle cells of the heart at a distance from the site of the burn was investigated by electron-microscopic autoradiography 24 h after injury. The tissue was fixed 2 and 6 h after injection of uridine-^{3}H. The density of distribution of silver grains above the nucleus and cytoplasm of the cardiomyocytes was lower in the experimental animals than in the controls.

KEY WORDS: burn of myocardium; RNA synthesis; electron-microscopic autoradiography.

The ability of the heart to regenerate at the cellular level is very limited [2]. The main method of structural compensation of the myocardium after loss of part of it is by hyperplasia of the ultrastructures in the residual muscle cells [4]. This method of repair is known as intracellular regeneration. The view is held that in the early period of ontogeny, while natural mitotic division of the heart muscle cells is still taking place, the myocardium can replace a lost area by the intensification of this division [3, 7]. Experiments have shown [1] that an increase in mitotic activity of the muscle cells in newborn rats after injury does not continue throughout the period of healing of the heart. One year later elongated scars were found in all the rats at the site of injury. It must accordingly be concluded that in newborn animals in the period of mitotic division of the muscle cells, structural replacement takes place on a basis of intracellular regeneration. The experiments described below were carried out to study this mechanism.

EXPERIMENTAL METHOD

A measured burn of the heart was produced in newborn rats by applying the hot end of a broken needle for 1 sec to the wall of the left ventricle. The animals were given an injection of uridine-5-^{3}H in a dose of 2 mCi 24 h after injury and were killed 2 and 6 h after injection of the isotope. Newborn rats of the same litter, receiving the isotope alone and killed simultaneously with the experimental animals, served as the control.

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TABLE 1. Results of Electron-Autoradiographic Analysis of Density of Distribution of Silver Grains above Nucleus and Cytoplasm of Cardiomyocytes

Animal No.	Group of animals	Period of circulation of isotope, h	Number of cells studied	Density above nucleus	P	Density above cytoplasm	P	Ratio of densities: nucleus/ cytoplasm
869	Experimental	2	21	5,04		0,67		7,5
869	Control	2	19	12,39	<0,01	0,88	<0,01	14,1
870	"	2	46	16,41		1,56		10,5
871	Experimental	6	58	3,76		0,19		19,8
872	"	6	80	5,39		0,43		12,5
873	Control	6	29	7,40	<0,01	0,49	<0,05	15,1
874	"	6	48	6,81		0,56		12,2

Legend. P calculated by comparing samples of all cells investigated from experimental and control animals.

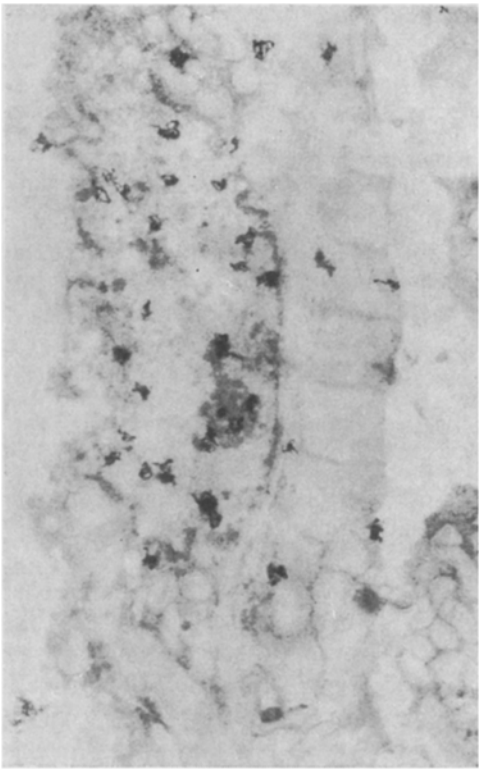

Fig. 1. Electron-microscopic autoradiograph of heart muscle cell fixed 2 h after injection of uridine-^{3}H. Control. Many grains of silver can be seen above nucleolus, nucleus, and cytoplasm. 12,000×.

Pieces for electron-autoradiographic investigation were cut from a portion of the wall of the left ventricle at a distance from the site of injury, fixed with 2.5% glutaraldehyde and 1% osmium tetroxide solutions, and embedded in Epon. A monolayer of type M emulsion was applied to the electron-microscopic sections and, after exposure for 1-2 months and development, the sections were examined in the JEM-100B electron microscope. The density of distribution of silver grains above the nucleus and cytoplasm was determined in electron-microscopic autoradiographs of the heart muscle cells. For this purpose the number of grains of silver found above the appropriate structure was divided by the area of that structure, calculated by weighing its projection on paper.

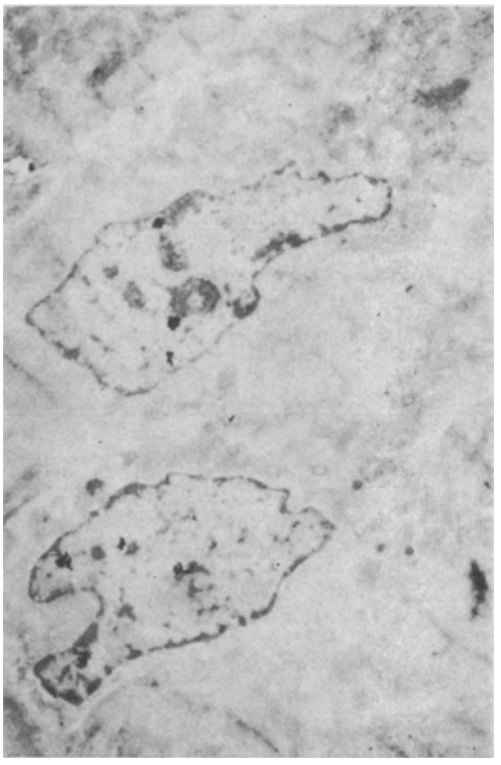

Fig. 2. Electron-microscopic autoradiograph of heart muscle cells fixed 6 h after injection of uridine-^{3}H. Experiment. Three or four grains of silver above nuclei of cardiomyocytes. Cytoplasm does not contain label. 7000×.

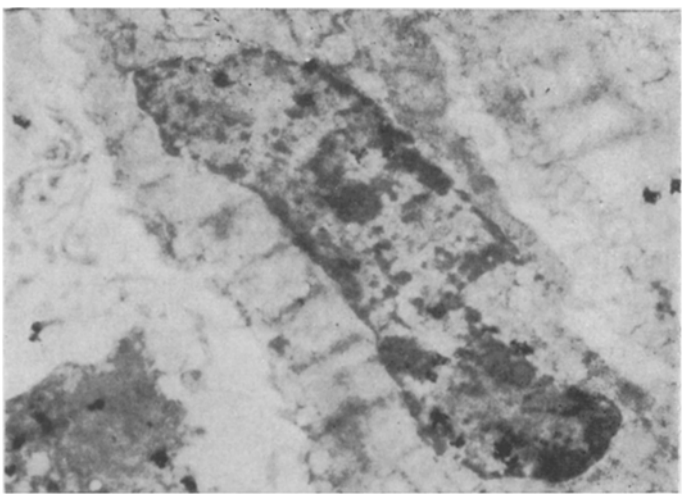

Fig. 3. Electron-microscopic autoradiograph of heart muscle cell fixed 6 h after injection of uridine-^{3}H. Control. Many grains of silver in nucleus distributed in perichromatin zone (on boundary between dispersed and condensed chromatin). A few grains present above cytoplasm also. 12,000×.

EXPERIMENTAL RESULTS

On the grounds that regenerative processes start in an organ immediately after its injury, we expected to find an increase in the intensity of intracellular synthesis, especially the synthesis of ribonucleoproteins, in the muscle cells of those parts of the heart which remained undamaged. However, 24 h after injury, the quantity of label in the cardiomyocytes of rats on which a measured burn of the heart was inflicted was less than in control rats of the same litter (Table 1; Figs. 1-3). This is evidence that toward the end of the first day after injury RNA synthesis was reduced in the muscle cells. It must evidently be assumed that the decrease in RNA synthesis may reflect a higher intensity of division of the heart muscle cells in the experimental rats, for newly formed cells have a greater and not a lesser need to increase the synthesis of their ultrastructures and, consequently, they require increased RNA synthesis. It is also known that during the period of DNA replication, RNA synthesis is increased [5, 6, 8]. The main activity of the heart muscle cells 24 h after injury is evidently directed toward maintenance of the contractile function. The restricted energy supply evidently does not allow the cells to use more energy for self-reproduction at a time when there are increased demands on their contractile activity. There is therefore a redistribution of the energy reserves, so that a higher proportion of them are used to maintain external function and a smaller proportion to maintain synthetic processes. This is reflected in the decrease in RNA synthesis. This period of 24 h is thus the acute period during which functional and structural compensation take place through the intensification of activity of ultrastructures which existed before injury. Any attempt to form an apparatus of protein synthesis de novo is inhibited in this period.

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