REPAIR PROCESSES IN THE RABBIT FETAL MYOCARDIUM AFTER MECHANICAL TRAUMA

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An original method of injuring the myocardium in the intrauterine period in rabbits was developed. Healing of the injured part takes place quickly through proliferative activity of the cells. The tissue arising at the site of injury is morphologically very similar to muscle tissue, but special investigations are needed to give the final answer to the question of its nature.

KEY WORDS: intrauterine period; rabbit fetal myocardium; reparative regeneration; mechanical trauma.

Regeneration of heart muscle tissue has been studied chiefly in adult animals and in the early postnatal period. The regenerative power of the myocardium in the intrauterine period has been studied only by the tissue culture method [2-4], although the discovery of the principles governing reparative regeneration of the heart muscle in the intact organism is of the greatest interest.

The object of the present investigation was to develop a method of injuring the fetal myocardium in the intrauterine period and subsequently studying the dynamics of the repair process.

EXPERIMENTAL METHOD

An operation was performed on pregnant rabbits at the 20th-24th day of pregnancy. Under sterile conditions and general anesthesia laparotomy was performed and the uterus with the fetuses was brought into the operation wound. An incision was made in the uterus to reveal the fetal membranes and the fetus inside them. In some cases the fetal membranes were completely removed from the uterine cavity. The fetus was turned in the uterus and fixed by the fingers in a convenient position for puncture. With a steel needle the membranes and the anterior thoracic wall of the fetus were punctured in the midthoracic line at the level of the fourth to seventh intercostal spaces. The needle was fitted with a guard so that the chest wall and heart of the fetus could be punctured without the risk of deeper penetration of the needle. The manipulation needle from a "Rekord" syringe also was used for puncture, in which case a weak solution of nickel sulfate could be injected into the injured area of myocardium. After removal of the needle the membranes were tied with catgut and returned to the uterus, in which the incision also was closed with catgut sutures. Each fetus contained in the uterus was subjected to similar manipulations.

Altogether 92 operations were performed and positive results obtained in 57 cases. In the course of the experiment 247 fetuses were obtained and the periods after injury to the heart ranged from 1 h to 11 days.

The material was fixed in 10% neutral formalin, after which the heart was embedded in toto in paraffin or celloidin. Histotopographical sections were prepared for histological investigation. The sections were stained with hematoxylin–eosin, with picrofuchsin, for acid mucopolysaccharides, for DNA by Feulgen's method, and by the PAS reaction. Nickel in the tissues was determined with dimethylglyoxime [1].

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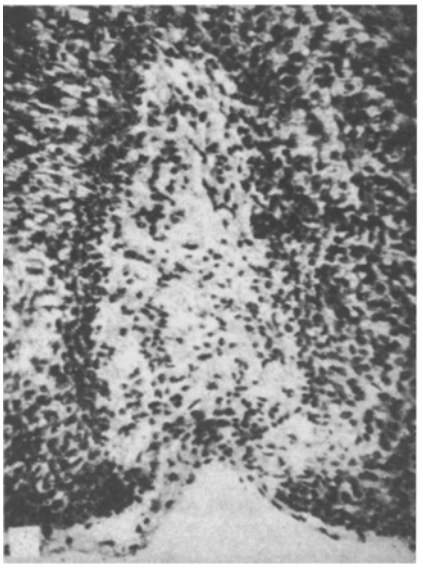

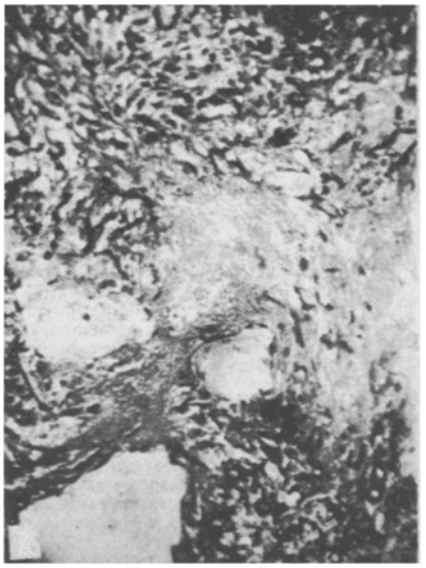

Fig. 1 Fig. 2

Fig. 1. Focus of necrosis of muscle tissue 8 h after trauma. Here and in Fig. 2: hematoxylin–eosin, 400 ×.

Fig. 2. Focus of injury on the third day after trauma; barrier of muscle nuclei can be seen at the periphery of the injured area.

EXPERIMENTAL RESULTS

Deformed, torn muscle fibers and hemorrhages were found at the site of injury 1 h after trauma. The histological picture at the site of injury 8 h after trauma was characterized by extensive areas of necrotic muscle tissue rich in PAS-positive material and containing many erythrocytes (Fig. 1). At the periphery of the necrotic focus sharply altered fibers with partially lysed nuclei were seen. At the periphery of the tissue defect degenerative changes were clearly marked in the residual muscle fibers.

The changes described, with predominance of necrosis of muscle tissue, were observed during the first 24 h after trauma; however, by the end of the first and beginning of the second days, mitotic figures appeared in the muscle fibers at the boundary of the focus of injury. Meanwhile the peripheral portions of the focus of injury were filled with cells with large nuclei. They were very similar to nuclei of muscle cells. No reaction of the connective tissue could be seen in response to necrotic changes in the heart.

Starting on the first to second day proliferation of the cells increased and reached a maximum of intensity on the third day when a barrier of cells was formed about the focus of injury (Fig. 2). The nuclei of these cells varied in size: Cells with hypertophied nuclei were arranged at the periphery of the barrier and cells with smaller nuclei on the inside. The zone of necrosis was smaller by this time. At the periphery of the focus of injury, solitary delicate and thin fibrils, staining yellow with picrofuchsin, appeared. Since there was no reaction of the connective tissue around the focus of injury, the mechanism of absorption of the necrotic muscle tissue is not quite clear.

After mechanical trauma to the fetal heart only proliferative activity of the myocardial cells was thus seen. No myoblasts were found. On the third day after trauma a few solitary muscle buds were found in the residual stumps of the muscle fibers but their number was small.

By the fourth to fifth day the area of injury was completely replaced by newly formed tissue. This could not be called connective tissue, for it stained negatively for acid mucopolysaccharides and yellow with picrofuchsin. This tissue was most probably muscle tissue, although differing from it in some respects: The cell nuclei were hyperchromic, their number was increased, and they were smaller than the average size of the muscle nuclei in the fetal heart.

By the sixth day and later the area of injury differed very little morphologically from the remaining muscle tissue of the heart and only the presence of nickel in the tissue indicated the site of trauma.

These results show that the myocardium of rabbit fetuses aged 20-24 days can regenerate quickly in response to mechanical trauma. Restoration of its structure evidently takes place through the high prolif-

erative activity of the muscle cells. The tissue arising in place of the injured area is similar in many respects to muscle tissue, but further special investigations are necessary to reach a final decision regarding its nature.

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