# TRANSIENT CORONARY SPASM IN THE GENESIS OF MYOCARDIAL INFARCTION

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Ischemic myocardial damage is a central problem for cardiologists and for about 100 years it has been studied from all aspects in acute experiments with permanent occlusion of the coronary artery. The results of these experimental studies have been extrapolated to clinical medicine, for the clinical and postmortem diagnosis of myocardial infarction, the determination of the time of its occurrence, and so on. However, a model with permanent occlusion of the coronary artery reflects only one variant of the development of a myocardial infarct, which is due to thrombosis or embolism of a branch of the coronary artery. A basically different model of ischemic myocardial damage has been suggested by Jennings and Ganote [6], on the basis of temporary single occlusion of the coronary artery followed by reperfusion. This variant is observed in cases of spontaneous coronary thrombolysis. A similar clinical situation arises during drug-induced thrombolysis or after surgical thrombectomy. However, even this model of myocardial infarction, while undoubtedly more appropriate, in our view reflects by no means the most frequent variant of its development.

The aim of the present investigation was to test our hypothesis [5] that irreversible ischemic damage to the heart muscle can develop as a result of transient coronary spasm (TCS), using an experimental model developed [1] for this purpose.

## EXPERIMENTAL METHOD

Experiments were carried out on 12 male chinchilla rabbits weighing 3.5-4 kg. All manipulations on the animals were performed under hexobarbital anesthesia, with artificial ventilation of the lungs with atmospheric air.

The model of TCS was described previously [1]. A branch of the left descending coronary artery was surrounded by a length of Kapron tape 10-15 μ wide. One end was fixed in one hole of a plastic plate and applied from above, the other end, which was passed freely into the hole, could be tightened by an amount necessary to cause complete occlusion of the blood flow, and later reverted to its original position for perfusion. The volume blood flow was monitored by means of rheographic electrodes, made by ourselves from wire insulated on one side with Kapron, which was passed around the artery distally to the site of occlusion, and an RPG 2-02 rheoplethysmograph. Three animals were used in the experiments of series I (control), and a mock operation without TSC was performed on them; in the three rabbits of series II, coronary spasm (CS) lasting 1 min was created 3 times, within intervals of 5 min between them, and in series III CS for 5 min was produced in six animals, followed by a reperfusion period of 5 min. All the animals were under continuous electrocardiographic monitoring for 2 h. All the rabbits were kept under observation for 1.5 h of the reperfusion period after TSC, at the end of which the heart was removed from the chest in a one-stage operation and placed in a bath containing ice until it completely stopped beating, after which it was fixed in cold 10% formalin by Lillie's method. Serial paraffin sections of the ischemic and intact zones of the myocardium were stained with hematoxylin and eosin and examined in random samples in polarized light.

## EXPERIMENTAL RESULTS

In the myocardium of animals of the control group 14-17% of cardiomyocytes showed changes characteristic of contracture, namely increased anisotropy, and reduction and disappearance

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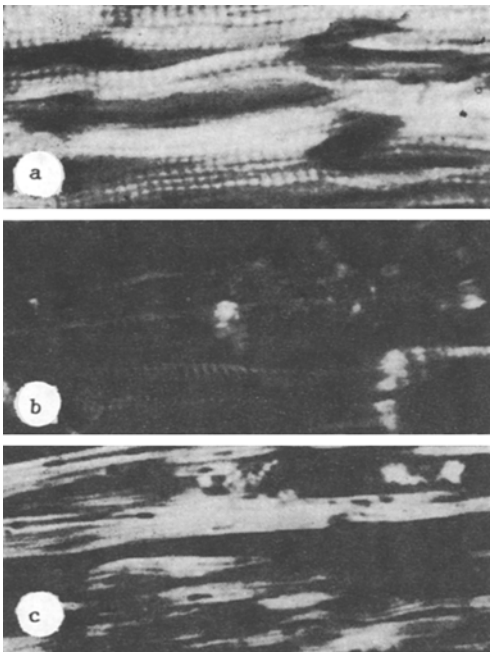


Fig. 1. Changes due to contracture on myocardium in TCS (photographed in polarized light). a) Control: increased anisotropy of A disks; reduction and absence of I disks, 800×; b) intact myocardium of dying animal (experiment of series III): subsegmental contractures (pale bands), 700×; c) myocardium in territory supplied by coronary artery in spasm: primary cloudy-swelling degeneration (top right), irreversible damage due to contracture (top center), residual cardiomyocytes (bottom), 300×.

of the I disks (Fig. 1a). A virtually identical picture was observed in the intact zone of the myocardium of rabbits in the experiments of series II and III. A slight degree of tachycardia was observed on the ECG of the animals of series I.

In the experiments of series II slight elevation of the ST segment was recorded after the first CS, falling again toward the time of the second CS, but without reaching the initial level. During the second CS the ST segment rose and remained virtually unchanged in the reperfusion period. The greatest rise of the segment took place during the third CS, when paroxysms of tachycardia also appeared; the rhythm was restored in the reperfusion period and the ST segment fell (without reaching its initial level), stabilized by the 20th minute of reperfusion, and thereafter remained unchanged until the end of the investigation. Reduction of the I disks in most cardiomyocytes, changes in the myofibrils due to contracture, and found in 21-24% of contractile cells, and single cells with primary cloudy-swelling degeneration were characteristic of the ischemic zone of the myocardium in this series of experiments. Thus TCS even of short duration (model of a transient attack of angina) may be the cause of development of microfocal cardiosclerosis, and later of hypertrophy, as one variant of structural (plastic) adaptation to loss of a structural–functional unit [3].

In the experiments of series III the morphological and ECG pictures were rather different. Disturbances of rhythm were progressive in character, conduction was impaired, and in one case the animal died from ventricular fibrillation (Fig. 1b). Lowering of the ST segment was not observed in any of the reperfusion periods, and it rose progressively from one CS to another. Moreover, throughout the 1.5-h period of reperfusion and until the end of the experiment, the height of the segment was virtually not reduced. In the zone of myocardial ischemia in this series of experiments, changes due to contracture were identified and were irreversible in character in 35-50% of cases (Fig. 1c). Groups of cardiomyocytes with primary cloudy-swelling degeneration and irreversible contracture, characterized by a single ansotropic conglomerate [4], were distributed mainly in mosaic pattern throughout the section of the myocardium. Thus this variant of TCS can be used as a model for the induction of microfocal myocardial infarction, or of the acute coronary insufficiency that is so frequently found.

The results differ from those described by Ol'binskaya and Litvitskii [2]. In our view the reason is differences in the technique of inducing TCS and the time of the reperfusion on period. Further investigations are evidently needed, in which the emphasis laid on the duration of CS will have to be switched to the interval between them, and the reperfusion time and frequency of TCS reduced. Further efforts at improving the experimental model of ischemic myocardial damage will also have to be aimed at creating a remotely controlled TCS with strict monitoring to ensure total or partial reduction of the coronary blood flow and its restoration in order to make the experimental and real conditions as close as possible and, above all, to make anesthesia and artificial ventilation of the lungs unnecessary.

The discovery of damage to the myofibrillary apparatus due to contracture indicates a disturbance of cardiomyocyte function. Metabolites of arachidonic acid and endoperoxidases evidently are involved in the genesis of the disturbance of sarcolemmal function, for the ability of ischemia to activate phospholipase $A_2$ is well known, and the pathogenic effect of this activation can be realized only if oxygen (i.e., reperfusion) is present.

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# EFFECT OF STIMULATION ON REGENERATION OF GASTROCNEMIUS MUSCLE IN OLD RATS AFTER X-RAY IRRADIATION


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KEY WORDS: skeletal muscles; old rats; regeneration; x-ray irradiation; laser therapy


This investigation is a continuation of research into methods of stimulating repair processes in irradiated muscles of old animals. Considerable recovery of regenerative capacity of the irradiated gastrocnemius muscle of young, sexually mature, and old rats was demonstrated previously under the influence both of laser irradiation and of transplantation of minced unirradiated muscle tissue into the region of injury of the gastrocnemius muscle [1, 5]. However, in old animals, areas of dense connective tissue are formed in the region of injury to the gastrocnemius muscle only after treatment with helium–neon radiation, and they limit growth of muscle fibers restored after x-ray irradiation. In the case of transplantation of unirradiated minced muscle tissue the positive effect was reduced in the late stages of regeneration: the number of muscle fibers in the central zone of the defect was reduced compared with the zone located near the muscle stumps. To potentiate the stimulating action on the regenerative capacity of skeletal muscles of old rats, irradiated with ionizing radiation, transplantation of the unirradiated minced muscle tissue was carried out simultaneously with laser therapy.

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