

# CYTOCHROME c CONTENT IN THE HEART OF RABBITS WITH EXPERIMENTAL MYOCARDITIS

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Cytochrome c is a component of the respiratory electron transfer chain in the mitochondria and takes part in the formation of high-energy ATP bonds [1-4]. Experiments have shown [5] that in the zone of a myocardial infarct in man the cytochrome c content is only half that found in tissue from a healthy part of the same heart. In experimental hypoxia and myocardial infarction in dogs the cytochrome c content in the heart shows regular changes, increasing in the zone of hypoxia during the first hour after ligation of the coronary artery and decreasing in the necrotic focus in later periods after the operation [6].

The object of the present investigation was to study the cytochrome c content in the heart muscle of rabbits with toxic myocarditis.

## EXPERIMENTAL METHOD

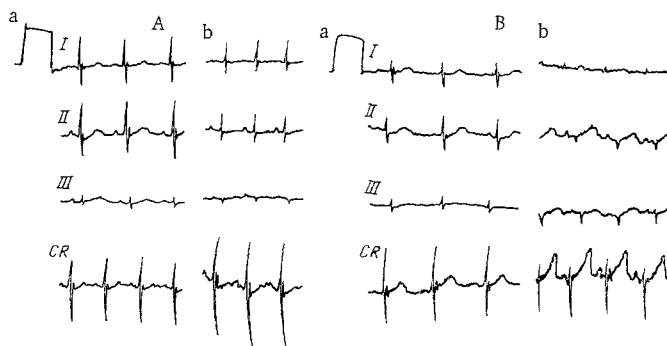
Experiments were carried out on 31 rabbits of both sexes weighing 2.5-3 kg. Fourteen control animals were used. Myocarditis was produced in 17 rabbits by one or two intravenous injections of streptococcal toxin (batch 70, N. F. Gamaleya Institute of Epidemiology and Microbiology, Academy of Medical Sciences of the USSR) in a dose of 0.2-0.5 ml at an interval of 14 days. As a first step the animals were sensitized by subcutaneous injection of normal horse serum. The development of myocarditis was judged from changes in the electrocardiogram (ECG) and the morphological picture of the myocardium. The animals were sacrificed in the acute and subacute periods of development of myocarditis. The cytochrome c content in the tissue of the left ventricle was determined by the method of Rosenthal and Drabkin [6]. The weight of tissue taken for analysis was 2 g; the extinction (E) of the solutions at 550 and 535 m $\mu$  was measured in 1 cm quartz cells on a type SF-4 spectrophotometer and the values obtained were used for calculating the tissue content of cytochrome c in mg%. Some tissue from the left and right ventricles was investigated histologically in sections stained with hematoxylin-eosin and picrofuchsin.

## EXPERIMENTAL RESULTS

The content of cytochrome c in tissue from the left ventricle of the control rabbits varied from 4.7 to 16.2 mg%, with a mean value of  $8.7 \pm 0.3$  mg%. No appreciable abnormalities were found on the ECG of the control rabbits. Marked changes in the ECG of the experimental animals were found after injection of streptococcal toxin. Depending on their character and degree the ECG disturbances of the experimental rabbits could be divided into two groups. In the animals of group 1 (7 rabbits) the ECG changes took the form of a decrease in voltage of the P, R, and T waves, a slight displacement of the S-T interval below the isoelectric line, and a deepening of the S wave. In most cases the changes affected lead 1 or 2 (see figure, A). In the animals of group 2 (10 rabbits) a general lowering of voltage of the ECG waves was observed in all leads, with inversion and reduplication of the R wave and considerable depression of the S-T interval in leads 3 or 4. The T wave disappeared in some cases, while in others it became negative or biphasic, and in the chest leads a giant T wave (bigger than the R wave) sometimes appeared. The P and T waves were smoothed out and widened. In lead 3 a pathological S wave appeared. In 3 animals, normal ventricular complexes alternated with deformed and inverted complexes. In these cases the R wave was widened, and its sloping leading edge led into a giant T wave (see figure, B). The changes observed continued for a long time and increased in severity.

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Changes in ECG of rabbits with toxic myocarditis. A) Rabbit of group 1; B) group 2; a) initial ECG; b) ECG in myocarditis.

Investigation of tissue from the left ventricle of the animals of group 1 revealed no changes in the cytochrome c content by comparison with that found in the control rabbits. The cytochrome c content in the myocardium of the rabbits of this group varied from 6.1 to 11.7 mg%, mean  $8.5 \pm 0.8$  mg%. The cytochrome c content in the rabbits of group 2 varied from 12.6 to 19.2 mg%, mean  $17.1 \pm 0.6$  mg%, i.e., it was considerably higher than its content in the myocardium of the rabbits of group 1 and the control animals ( $P < 0.001$ ).

On histological investigation of the heart in rabbits of both groups, changes were found in the walls of the blood vessels and in the muscle fibers. The blood vessel walls were thickened, loosened in structure, tortuous and infiltrated, and clusters of cells and sclerotic foci were observed around the vessels. Multiple small collections of leukocytes could be seen in the substance of the myocardium of the left and right ventricles. Degeneration and necrosis of the muscle fibers were of slight degree. No correlation could be seen between the severity of the morphological changes in the myocardium and the degree of changes in the ECG and cytochrome c content in the myocardium.

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