ELECTROCARDIOGRAPHIC EXAMINATION OF THE HEART IN RATS AFTER INJURY TO THE MYOCARDIUM

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Regeneration of the myocardium in rats was shown to be possible in our collective work [2]. We studied this process in a combined manner, using the methods of experimental morphology, biochemistry, physiology and histology.

The aim of the present work was to trace the progress of the changes in the electrocardiogram during healing of the myocardium after injury and also during stimulation of the process of regeneration with biological preparations.

The electrocardiogram of normal rats has been studied by many workers [4-6, 7, 8]. It differs from the electrocardiogram of other animals by the definite stability of its main waves. It is not possible to take an electrocardiogram from an unanesthetized rat on account of muscle tremor in the rats which are restless when placed in an outstretched position, and furthermore the type of anesthesia (urethane, ether etc.) also affects the character of the electrocardiogram.

In the experiment we used 100 adult (male) white rats, weighing from 250 to 400 g. Electrocardiograms of 39 of these were studied in experiments with injury. The electrocardiograms were taken under urethane anethesia (3-5 ml of a 5% solution given intraperitoneally). The rat was secured to the table by its paws with soft tape, in the prone position. The electrodes used were fine hypodermic needles, inserted under the skin of the limbs. Electrocardiograms were taken with a type EKP 4 electrocardiograph (EMA factory). Film was fed at the rate of 80 mm/sec. Electrocardiograms were taken with leads I, II and III, but since with lead I the R wave was extremely low and all the other waves were completely absent, lead II and III elecrocardiograms were selected for study (Fig. 1). (in this and in all succeeding experiments the curves shown are from lead II).

The rate of the undamaged heart in the adult anesthetized rat varied from 360 to 480 beats per minute. The amplitude of the waves in the normal electrocardiogram of the rat is considerable less than in man. In the normal rat the P-Q interval from the beginning of the P wave to the beginning of the Q wave, corresponding to the atrioventricular conductivity, is 0.050-0.065 seconds. No realtionship was found between the length of this interval and the rate of the heart. The QRS complex – the time for the spread of excitation through the myocardium of the venticles – in the same conditions was 0.018-0.020 seconds. Here also no relationship was established between the duration and form of the QRS complex and the rate of the heart. The QT segment – the ventricular complex of the electrocardiogram – varied in different animals between limits of 0.063 and 0.110 seconds.

The length of this particular interval depends on the rate of the heart just as is observed in the human electrocardiogram. The amplitude of the waves was characteristically as follows: the P wave was positive in all cases in leads II and III, and the variational deviations of the P wave were within normal limits; the R wave also was always positive and its height in lead II was 0.14-0.36 mv and in lead III – 0.10-0.25 mv; the height of the T wave varied from a smoothed out plateau to a well marked positive crest; the S wave in lead III was present in 37.5% of cases, but in lead II in only 10.2%. The Q wave was not found at all.

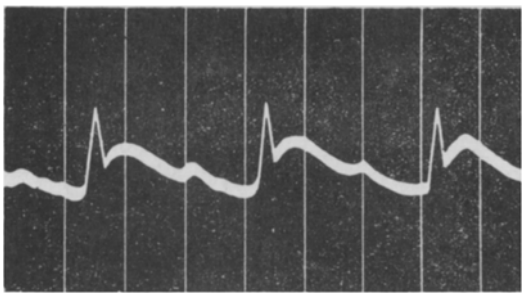

Fig. 1. Electrocardiogram of the healthy rat.

The rats selected for the experiment mainly had a normal type of electrocardiogram. As a result 33 of the 39 showed a normal type, three showed signs of left and three of right axis deviation. The type of electrocardiogram was determined by the height of the main waves in leads II and III. The normal electrocardiogram was studied in rats which had been under our observation for a long time. The electrocardiogram was normally taken in each animal 2 or 3 times in the 2 weeks before operation.

The operation was carried out as follows. The animal was anesthetized with urethane, the fur removed from the operation field, and the heart exposed with sterile precautions in the fourth intercostal space. An artificial respiration apparatus was used. Air was passed into the trachea through a cannula. The beating heart was momentarily damaged with a diathermocoagulation; a whitish spot with a diameter of 4 mm on the average appeared on its surface. The apex of the cone of necrotic tissue, similar to that seen in an infarct, was at a depth of 3-5 mm in the myocardium. The wound was sutured in layers, and an electrocardiogram taken immediately afterwards. Subsequently electrocardiograms were taken 1, 3, 6, 10, 15, 20, 30, 40, 50, 60, 80, 100, 120 and 160 days after the operation.

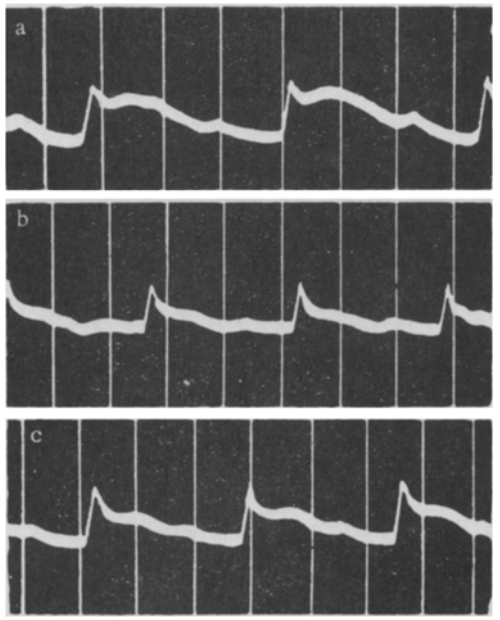

Fig. 2. Electrocardiogram of a rat at different intervals after injury to the heart.
a) Acute stage; b) subacute stage;
c) stage of scar formation.

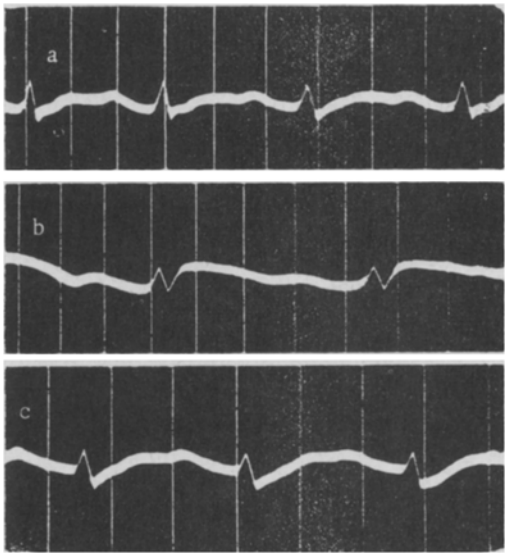

Fig. 3. Electrocardiogram of a rat during experimental injury to the heart and the subsequent injection of a hydrolyzate of cardiac muscle.
a) Normal b) acute stage; c) stage of scar formation.

In a control series in which the heart was damaged without any additional treatment, on the basis of the characteristic changes in the electrocardiogram 3 stages of injury were established. In experiments on rabbits [1] in which the coronary arteries were ligated, characteristic changes in the electrocardiogram were also found at certain times after operation.

In our experiments the acute stage (Fig. 2, a) begins immediately after operation. In this period the following characteristic signs are observed on the electrocardiogram: the RS-T interval is markedly displaced upwards, forming a monophasic curve; the T wave is "gigantic" and positive; the S wave if present normally is deepend; the rate is considerably slowed: 310-340 beats per minute; the atrioventricular conduction is retarded and PQ

measures 0.062-0.080 seconds. The electrical systole of the ventricles of the heart is lengthened and QT measures 0.100-0.137 seconds. The changes continue for several hours, and in some animals for 2-3 days after the operation. During this period the animals are very weak and a large proportion of them die in the course of it. In the weakest rats the heart rate falls to 180 per minute. After only 24 hours, in the majority of animals the character of the electrocardiogram is sharply altered, changing over from the acute to the subacute stage (see Fig. 2, b). The T wave, instead of being "gigantic," is smoothed out an may even become slightly negative. The RS-T interval is left in isolation and the rhythm becomes slightly quicker than normal: 420-500 beats per minute. The PQ interval measures 0.050-0.062 seconds and QT 0.062-0.081 seconds. The amplitude of R is increased; R_{II} measures 0.17-0.14 mv, R_{III} is 0.17-0.50 mv. The subacute stage lasts for 4 to 8 days. With reestablishment of RS-T on its original line, the longest stage begins – the stage of scar formation, which lasts for different lengths of time in different animals. The rate of the heart attains the normal value; the length of the PQ and QT intervals hardly differs from normal. The amplitude of the R wave is reduced. At later periods of the stage of scar formation the electrocardiogram may approach closer to normal. In two of the seven cases in the control series the electrocardiogram returned to normal in one animal after 30 days and in the other 40 days after operation. However, after 50 days and continuing until the 160th day, their electrocariogram once more returned to that of the stage of scar formation.

In the stage of scar formation (see Fig. 2, c) the electrocardiogram differs from normal by the shape of the T wave, which merges with the P wave at a height above the base line. The PQ interval is displaced upwards at an angle to the base line. The R wave is diminished in height, and its apex is blunter than normal.

In the next series of experiments an extract of hydrolysate of cardiac muscle was injected into the animals immediately after operation. The biological preparations were injected 10 times on alternate days [2]. Electrocardiograms were taken under normal conditions and at the same times as in the control series. In this series only two stages could be identified – an acute stage and a stage of scar formation. The subacute stage was probably very much shortened. The duration of the acute stage was different in the different animals. They could be separated into two groups. In the animals in which the acute stage lasted several hours, after only 24 hours the characteristic curve of the stage of scar formation was registered. On subsequent days the stage of scar formation again reverts to the acute stage; finally, after 7 days the stage of scar formation becomes stabilized. The return of the electrocardiogram to normal was not observed in these animals. In the rats of the other group the length of the acute stage (see Fig. 3, b) was increased to 2-3 days. The next stage was that of scar formation and the character of the curve was close to normal. Only 11 days after operation, in 50 per cent of cases the electrocardiogram returned to normal and remained normal until the 30th day after operation (see Fig. 3, c). The characteristics of this stage were the same as in the previous series of experiments. Comparison of the electrocardiograms of the rats in these 2 series of experiments will show that in the series of animals treated with hydrolysate the process of wound healing takes place more rapidly than in the control series. Furthermore, in 50% of these cases, return of the electrocardiogram to normal was observed.

In a third series of experiments the animals were injected with extracts of cardiac muscle [2]. No essential differences in the electrocardiogram in comparison with the controls could be observed. In some animals, 3 days after operation the subacute stage once more returned to acute, and this lasted until 5 days after operation. Later the stage of scar formation appeared and continued until the 160th day after operation without any return to normal.

If the electrocardiographic findings are compared with the histological picture of the experimental hearts, a certain parallel may be observed between the functional and morphological changes in the heart. The histological findings show that [2] in the control series, 20 days after operation, in the region of the injury, foci of regenerating muscle are seen which have become resolved 46 days after the operation, and become converted into a connective tissue scar. We see a similar picture in the electrocardiogram: in some animals 30-40 days after operation the electrocardiogram has become normal, and after 50 days it once more changes into the stage of scar formation. In the experiments with hydrolysate a return of the electrocardiogram to normal from the stage of scar formation is also observed, but this takes place much earlier and is more stable than in the control series. In this series of experiments, only 11 days after operation in 50% of cases a normal electrocardiogram is registered. Histological examination shows that at this same time, on the 10th-13th day after operation, regeneration of muscle fibers is taking place in the focus of injury.

SUMMARY

Three stages of myocardial healing were established in injury of the heart wall in rats (by means of electrodiathermocoagulator) and the following development of an infarct-like focus, i.e. acute, subacute and the stage of of scar formation. Changes in the electrocardiogram correspond to these stages.

In experiments with additional administration of biopreparations stimulating the regeneration after the heart injury the best effect was obtained by using the hydrolysate of the heat muscle. Thus, after the 10-fold administration of this hydrolysate a shortening of the subacute stage and the earlier appearance of the stage of scar formation was noted.

In this series of experiments a stable return of the electrocardiogram to the normal was noted 11 days after the the operation in 50% of the cases.

In comparing the physiological data with the histological one it was established that the normalization of the electrocardiogram corresponds to the time of regeneration of muscles at the site of the injury.

LITERATURE CITED

[1] Kh. Ia. Gorodins'ka, Fiziologichn. Zhur. 2, 1, 53-57 (1956).

[2] L. V. Polezhaev, L. V. Akhabadze, N. A. Zakharova and V. L. Mant'eva, Doklady Akad. Nauk. SSSR, 119, 5 (1958).*

[3] I. A. Sapov, Biull. Eksptl. Biol. i Med. 40, 9, 26-30 (1955).

[4] J. Boros and B. Boros, Cardiologia, 1948, Bd. 13, S 325-251.

[5] J. Buchanan, J. Physiol. 1909, Vol. 72, N. 39.

[6] P. Eggers and H. Schumann, 1940, Bd. 137, S. 710-717.

[7] E. Heise and K. H. Kimbel, Ztschr. Kreislaufforsch. 1955, Bd. 44, S 212-221.

[8] E. Lepeschkin, Das Electrokardiogramm, Dresden-Leipzig, 1947.

[9] P. Lukoschek and J. Thiesen, Ztschr. Kreislaufforsch. 1954, Bd. 43, S. 115-120.

[10] W. Massmann and H. Opitz, Cardiologia, 1954, Bd. 24, N. 1, S. 54-64.

[11] W. Massmann and H. Opitz, Ztschr. ges. exper. Med. 1954, Bd. 124, S. 35-43.

*See English translation.