PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

REFLEXES FROM THE INTESTINAL CHEMORECEPTORS ON THE HEART IN EXPERIMENTAL MYOCARDITIS (FROM EKG DATA)

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In spite of the fact that there have been many clinical and experimental observations regarding the reflex influences from the gastro-intestinal tract on the heart [2,5,7,8,9,10,16,20,21,22], the problem of these influences still needs further study. In particular, very little attention has been paid until now to the reflexes from the chemoreceptors of the gastro-intestinal tract on the heart. Yet our clinical observations have led us to the impression that, in the presence of pathology of the cardio-vascular system or the gastro-intestinal tract, the reflex influences from the chemoreceptors of the latter could be a direct cause of changes in cardiac activity [3,6].

In the literature available to us we found only two papers in which the reflexes from the chemoreceptors of the stomach and rectum on the heart were studied with electrocardiographic (EKG) data under the conditions of a series of experiments on dogs. In these papers it was shown that in the presence of experimental myocarditis, gastritis and proctitis, the reflexes from the chemoreceptors of the stomach and rectum on the heart become more evident.

In order to confirm our clinical observations, we considered it necessary to set up experiments with perfusion of an area of the gastro-intestinal tract, since perfusion of an organ which is connected with the system by nerves only is the most exact method of judging the reflex influences of its chemoreceptors.

In the preceding paper [6], we showed that in the presence of pathosis in the gastro-intestinal tract of cats under conditions of perfusion, evident reflex changes of the heart (according to EKG data) could be obtained when the chemoreceptors of the intestines were stimulated with acetyl choline.

The present work was undertaken in order to study the reflex influences from the gastro-intestinal tract on the heart when it is in a pathological state.

EXPERIMENTAL METHODS

The experiments were set up on cats in which experimental myocarditis was caused by the usual methods [1, 12, 13]; caffeine benzoate, using 0.25 mg per 1 kg of the animal's weight, was administered intravenously 4-6 times in succession to the animals and then two minutes later 0.1% solution of adrenaline hydrochloride, using 0.2 ml per 1 kg of the animal's weight. Critical experiments (under urethane narcosis) were set up 3-8 weeks after beginning the injections. The ileal area and, in part, the small intestine, which kept only a nerve connection with the system, were perfused with oxygenated Tyrode's solution by V. N. Chernigovsky's method [18]; the arterial pressure in the carotid artery and respiration through a cannula inserted in the trachea were

recorded on a kymograph. Electrocardiographs were taken with the EKP-4 apparatus from the three standard leads (needle electrodes) before the operation to isolate the intestines, after the operation, after the initiation of perfusion and then when the stimulant was administered during the experiment. Acetyl choline in a dosage of 10-20-50 γ served as the stimulant of the chemoreceptors. After the experiment, the animal's hearts were subjected to histological examination.

EXPERIMENTAL RESULTS

In all, 61 experiments were set up: 36 on control cats and 25 on cats with experimental myocarditis. Histological examination of the cats with experimental myocarditis revealed degenerative changes of the cardiac muscle to some extent in an overwhelming number of cases. These changes were evidenced as homogenization of the muscle fibers, —a loss of cross-sectional outlines. Sometimes the muscle acquired a granular appearance; individual fibers were in a condition of degeneration. Control examination of the cardiac muscle of healthy cats after the experiment showed that the described changes did not occur during the experiment with perfusion of the intestine.*

The EKG of normal (healthy) cats, taken before the beginning of the operation for the isolation of the intestines, has pronounced positive R and T waves in the II and III leads and a small S wave in the same leads; the I lead usually has a low voltage for all the waves. EKG changes (primarily of the T wave: it became isoelectric or negative in two-three leads) were found to some extent in 14 of the 25 cats with experimental myocarditis even before the intestines were isolated. The operation for isolating the intestines did not cause any substantial EKG changes. As regards the effect of the perfusion itself (with Tyrode's solution), it caused considerable EKG changes in two cats with experimental myocarditis which remained throughout the entire experiment (in one case the isoelectric wave T_{II-III} became negative, in the other a considerable depression of the negative T_{II-III} wave occurred). In other cases the electrocardiograph did not change in responce to perfusion. When acetyl choline was brought into the intestines in the indicated dosages, no substantial changes were observed in the EKG of healthy cats (usually a distinct pressor reflex was registered on the kymograph at the same time); only in 7 cats out of 36 were small changes of the T wave observed, evidenced as its small elevation or depression (not over 1 mm). The reflex nature of these changes was proved by the fact that acetyl choline did not cause the indicated changes after the administration of 1 ml of a 1% solution of novocaine into blood vessels of the intestines.

EKG changes were noted in 12 cats out of the 25 with experimental myocarditis when acetyl choline was perfused, while in 10 cases these changes were noticeable: extrasystole (single extrasystoles, bigeminy, group politopic (multiple-beat) extrasystoles) appeared or the T wave was changed substantially, becoming isoelectric or negative instead of positive and, in some cases positive from negative; in one case a lowering of the S-T line was observed in the EKG.

Most frequently 20 γ, sometimes 10 γ or 50 γ, composed the threshold dose of acetyl choline which caused EKG changes. The development of EKG changes corresponded in time with the pressor reflex registered on the kymograph; in some cases of extrasystole, the EKG changes corresponded to its second, depressor, phase of the double-phased blood pressure reflex.

The changes which occurred in the EKG under the influence of acetyl choline administration disappeared in a few minutes and the EKG took on its usual appearance. Repeated administration of acetyl choline caused the same changes again. Preliminary denervation of the intestinal loop or the administration of novocaine to it brought about a disappearance of the changes in the EKG as well as in the arterial pressure in response to the administration of acetyl choline, which indicates the reflex nature of the above EKG changes (Fig. 1-3).

Pronounced EKG changes in response to the addition of acetyl choline to the perfusate were observed most often in those animals in which EKG changes were observed even before the preparations for perfusion were begun (9 out of 12).

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* I take this opportunity of expressing deep appreciation to Doctor E. E. Kikayon for examining the preparations (I.G.).

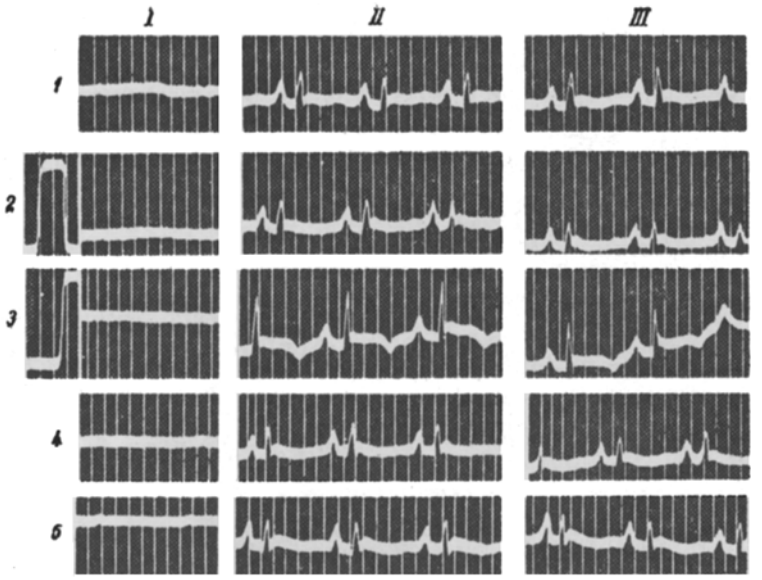

Fig. 1. Electrocardiogram of animal No. 22-experimental myocarditis. 1) before beginning preparation; 2) after beginning perfusion; 3) during administration of 20γ of acetylcholine into the blood vessels of the intestines; 4) 10 minutes after administration of acetyl choline; 5) during administration of 20γ of acetyl choline into the blood vessels of the intestines after preliminary administration of 2 ml of 1% novocaine solution; I, II, III) leads.

Out of 13 cats in which reflex changes of the heart (according to EKG data) were not observed when the chemoreceptors of the intestines were stimulated with acetyl choline, substantial EKG changes were observed in two after perfusion was begun, in 4 cases out of the remaining 11 the EKG was changed before the operation for isolating the intestines was begun, in the 7 remaining cases there were no EKG changes. Thus, the impression is created that reflex changes of the heart occur most frequently in those cats in which EKG changes were registered before the experiment as well. However, it was not possible to observe a direct relationship between the extent of the EKG changes before beginning perfusion and the extent of reflex changes in the cardiac activity under the influence of stimulation of the chemoreceptors of the intestines. No direct relationship was found between the extent of anatomical changes in myocarditis, the EKG changes before the experiment, and its further changes during the experiment.

In agreement with the data in the literature [12, 13], inflammatory and degenerative changes which later lead to the development of cardiosclerosis develop after the administration of caffeine and adrenalin in the myocardium; changes in the external blood vessels of the heart were also observed. Our observations show that EKG changes were present in the experimental cats even before the intestinal operation was begun, indicating affection of the cardiac muscle; a different degree of degenerative changes was found in the cardiac muscle. Investigations, mostly carried out by pharmacologists [12, 13, 14], showed that in animals with experimental myocarditis, the reactions (particularly the cardio-vascular ones) in response to various pharmacological substances change; the animals become more sensitive to some substance, and sometimes their responses to these substances are distorted. The authors explain the increased sensitivity by changes in the state of the autonomic nervous system.

On the other hand, experimental work [5, 11, 17, 20, 23] has shown that in the presence of cardiac pathology, the reflexes from the mechanoreceptors of the gastro-intestinal tract on the heart (according to EKG data) become pathological.

Thus, the reflex changes of the heart during stimulation of the chemoreceptors of the gastro-intestinal tract with acetyl choline in our experiments can be explained by changes in the general reactivity in the presence of experimental myocarditis and by a pathological process in the cardiac muscle itself. In conclusion, it seems necessary to us to stop at two moments.

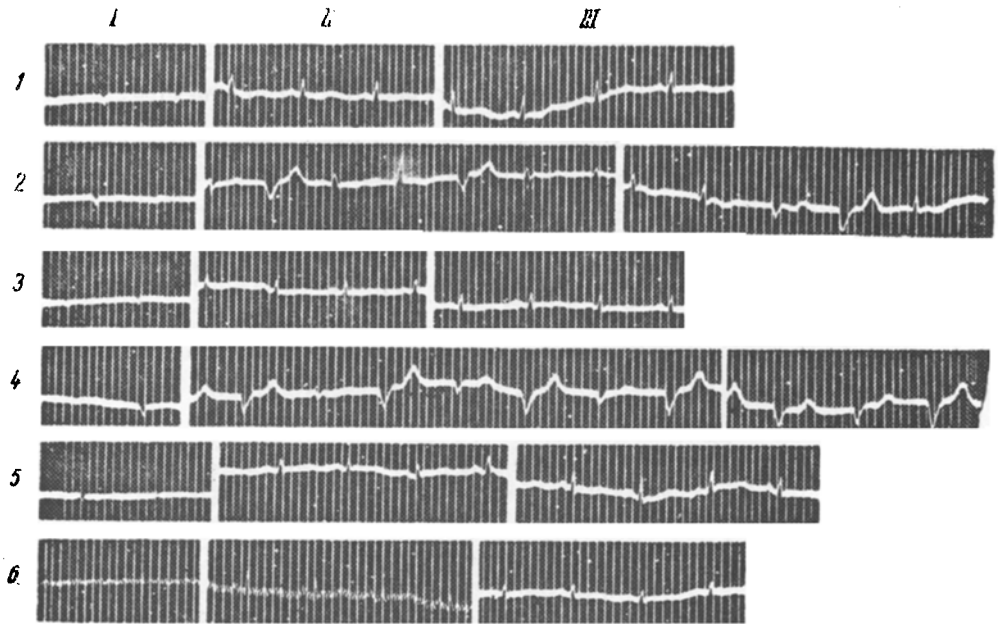

Fig. 2. Electrocardiogram of animal No. 9 - experimental myocarditis.
1) against a background of perfusion; 2) during administration of 20γ acetyl choline into the intestinal blood vessels; 3) 10 minutes after acetylcholine administration; 4) during administration of 50γ acetyl choline into the intestinal blood vessels; 5) 10 minutes after administration of acetyl choline; 6) on administration of 50γ acetyl choline into the intestinal blood vessels against a background of preliminary administration of 2 ml of 1% solution novocaine. I, II, III) leads.

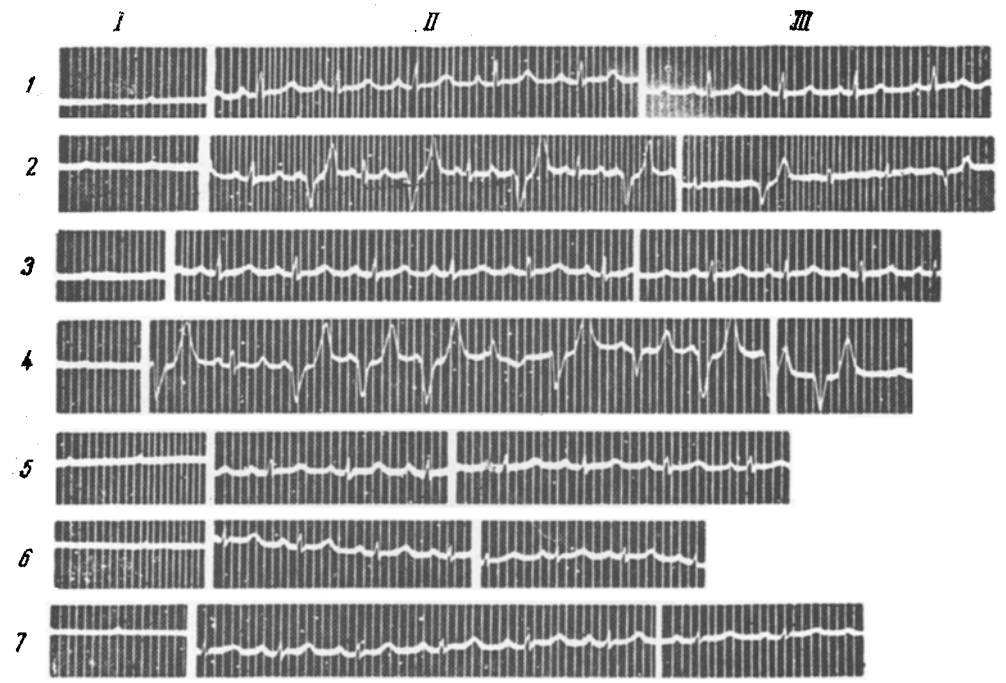

Fig. 3. Electrocardiogram of animal No. 21 - experimental myocarditis.
1) against a background of perfusion; 2) during administration of 20γ acetyl choline into the intestinal blood vessels; 3) 10 minutes after acetyl choline administration; 4) during administration of 50γ acetyl choline into the intestinal blood vessels; 5) 10 minutes after acetyl choline administration, 6) on administration of 2 ml of 1% novocaine solution into the intestinal blood vessels against a novocaine background; I, II, III) leads.

First, there are differences between the EKG changes occurring on stimulation of the chemoreceptors of intestines changed by a pathological process in the presence of a healthy heart (I. E. Ganelina, 1955) and the EKG changes observed in the presence of pathology of the heart and with healthy intestines.

In the first case, changes in the final part of the ventricular complex were registered primarily; extrasystole was not observed once. In the majority of cases pronounced EKG changes were observed on perfusion of the intestinal loop with oxygenated Tyrode's solution. Apparently, the nature of the reflex changes is connected to a considerable extent with part of the reflex arc which is affected: the afferent or the efferent.

Secondly, it is necessary to observe that the EKG changes which we observed during the administration of acetyl choline into the blood vessels of the perfused intestines differed substantially from the changes which were described when acetyl choline acted directly on the heart [19]. We did not observe a shortening of the S-T segment nor an elongation of the auriculo-ventricular conductivity.

The results of this work are confirmed by our clinical observations that when pathosis of the cardio-vascular system is present, the reflexes from the chemoreceptors of the gastro-intestinal tract on the heart can cause substantial changes in the latter.

SUMMARY

Reflex influences from intestinal chemoreceptors on the heart were studied on cats according to the methods of V. N. Chernigovsky. Chemoreceptors of an isolated loop of intestine were stimulated by acetyl-choline (10-50 γ). In normal cats there were no essential changes in EKG. Cats with experimental myocarditis showed some reflex changes in cardiac action (single, extrasystoles bigeminia group polytopic extrasystoles, negativation of the T-wave).

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