CHANGES IN THE ELECTROCARDIOGRAM AFTER BILATERAL ADRENALECTOMY IN DOGS

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It is well known from clinical observations and experimental research that the hormones of the adrenal glands affect many aspects of the activity of the body, including—and this to a very great degree—the cardiovascular system. Nevertheless the reports in the literature on the character and, especially, on the causes of the changes in the functional state of the heart in response to functional disturbances of the adrenal glands are contradictory.

The changes in the ECG in Addison's disease and in experimental interference with the function of the adrenal glands in animals have been described by several authors [3, 10, 13, 15, 17, 20, 22 and others]. Some of these [3, 9, 10, 12, 23] associate the changes in the heart's activity when adrenal function is disturbed with interference with the electrolyte balance (Na and K); other workers do not find this connection [14, 15, 21].

Other investigations have been made which indicate that the adrenal hormones affect the carbohydrate and protein metabolism of cardiac muscle. Removal of the adrenals leads to a considerable fall in the glycogen, ATP and creatine phosphate contents of the heart muscle. Administration of corticotonin (a physiologically active preparation obtained from the adrenal cortex by V. P. Komissarenko's method [4]) to an animal increases the glucose requirements of the muscle of the isolated heart and increases the content of energy-producing compounds in the cardiac muscle [5, 11]. These facts, it seems to us, do not support the assertion that the changes in the activity of the heart in adrenal insufficiency are due only to disturbances of the electrolyte metabolism.

We studied the activity of the heart (by the method of electrocardiography) in dogs after removal of the adrenals. By tracing the development of the ECG changes in adrenalectomized dogs, we tried to discover any possibility of compensation for these changes.

EXPERIMENTAL METHOD

Experiments were carried out on 9 dogs. After bilateral adrenalectomy (in two stages at intervals of 2 to 8 weeks) the animals were kept alive for a long period (from 2 to 20 months and even longer) by administration of desoxycorticosterone and saline solution, closely resembling plasma in its composition. As a result of this, the absence of adrenal cortical hormones regulating the water-salt metabolism was partially compensated, and the Na: K balance was not disturbed in these animals in a state of compensation. The animals received no glucocorticoids. In their outward appearance and behavior, these dogs were indistinguishable from normal.

In these animals which, thanks to the replacement therapy, were in a state of relative compensation, acute adrenal failure was caused by a change in the therapy. This was accompained by sluggishness, adynamia,

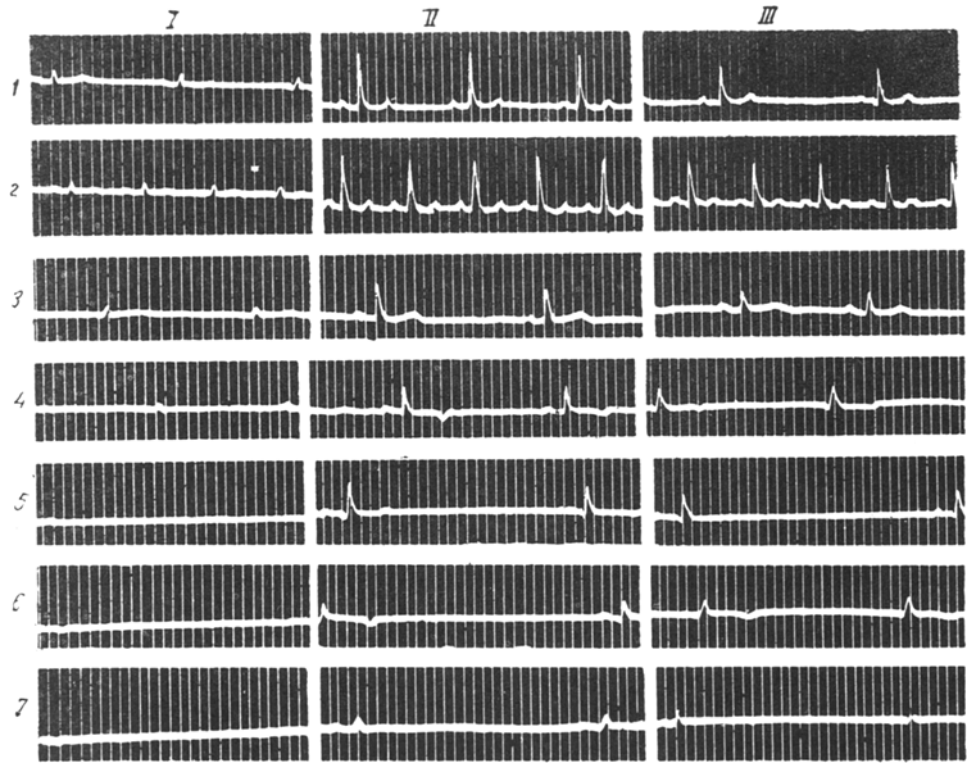

Fig. 1. Changes in the ECG of the dog Brovko after bilateral adrenalectomy. (In all the figures the ECG is shown for the 3 leads—I, II and III.) For explanation see text.

diarrhea, vomiting, a fall in the blood pressure, hemoconcentration, slowing of the bloof flow, an increase in the plasma potassium and loss of weight. Repetition of the course of replacement therapy brought the animal out of its crisis. Some animals endured several crises.

The ECG was studied before operation, after removal of one adrenal, after removal of the second and until the end of the animal's life. The changes in the ECG were studied in a state of compensation and during crisis. The ECG was recorded with the three classic leads, bythe usual method, by means of an EKP-4 apparatus.

EXPERIMENTAL RESULTS

The ECG was unchanged after the removal of one adrenal. The small variations which were due to the operation itself lasted one or two days. Removal of the second adrenal was accompanied in some animals by sharp, but brief, changes in the ECG mainly of the T wave: this was either greatly elevated or it became negative. In many animals marked tachycardia (up to 165-170 beats per minute) was observed in the course of one or two days after removal of the second adrenal.

Replacement therapy was given from the day of removal of the second adrenal, but, in spite of this, significant changes gradually developed in the ECG. In the first place the T wave and the S-T interval were affected. The change in the other components of the ECG took place much later. Very severe changes in the ECG were found only in the last days, and sometimes only in the last hours of the animal's life. Under these circumstances all the waves of the ECG were diminished, and especially the R wave (by 6-14 mm). The T wave was lowered and flattened; it often became negative and, in some cases, biphasic. In the last days of the animal's life the P wave, and sometimes the T wave also, disappeared. Thanks to the sharp fall in the main waves, the whole ECG at this time acquired an extremely flat and monotonous character. In the majority of the animals severe bradycardia developed (the heart rate did not exceed 50-40 per minute). The P-Q intervals were lengthened by 0.02- 0.06 seconds and the S-T intervals by 0.05-0.12 seconds. Replacement therapy did not prevent the changes in the ECG but merely retarded their development.

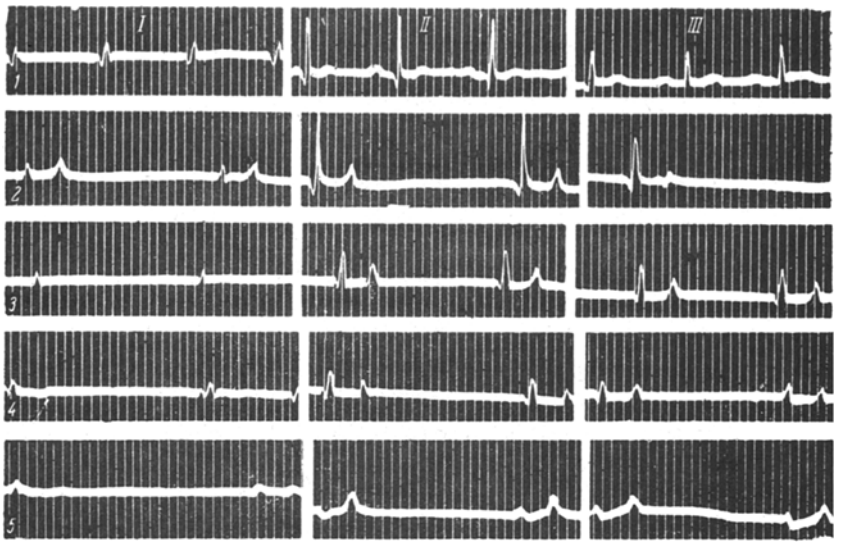

Fig. 2. Development of changes in the ECG during the last 4 days of life of the dog Pushok. For explanation see text.

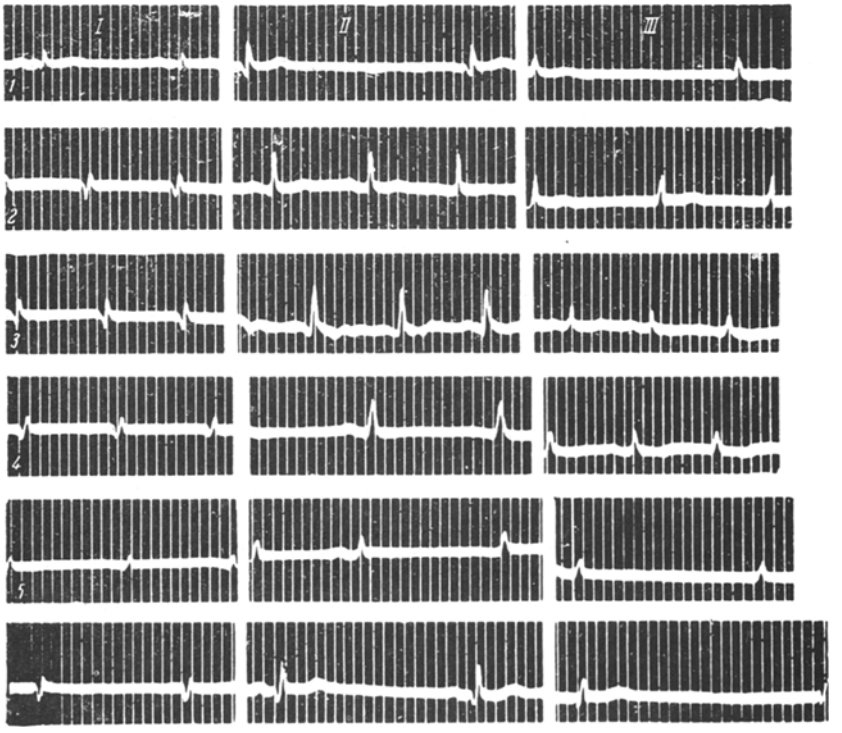

Fig. 3. Changes in the ECG in the period of development of and emergence from a repeated crisis in the dog Shalun. 1) ECG before discontinuation of replacement therapy; 2, 3, 4) ECG 5,7 and 10 days after discontinuation of replacement therapy; 5,6) ECG 3 and 8 days after resumption of the course of replacement therapy.

Fig. 1 illustrates the changes in the ECG after removal of the second adrenal from the dog Brovko. Cuts 1 and 2 show the ECG the day before (1) and the day after (2) operation; cut 3, the ECG 35 days after removal of the second adrenal (it kept this character throughout the whole time). Forty days after operation, 14 days

before the death of the animal, significant changes developed in the ECG (cut 4). During the next 10 days there was little change in the ECG (cut 6), and only in the 10-12 hours before the animal's death were the changes in the ECG greatly intensified (cut 7).

In Fig. 2 are shown the changes in the ECG in the last 4 days of life of the dog Pushok. During the 55 days after removal of the second adrenal, the character of of the ECG was almost unchanged (cut 1). Marked changes appeared only 3 days before the animal's death—the P wave disappeared, the character of the T wave was changed (cut 2). Subsequently the ECG changed every day (cuts 3, 4), and the changes reached their maximum degree 30-40 minutes before the animal's death (cut 5).

Both dogs received replacement therapy throughout this time.

When the animal's condition was good and the ECG kept its normal appearance, we temporarily ceased giving the saline solution and desoxycorticosterone, so that the role of the replacement therapy and the possibility of compensation for the changes in the ECG could be brought to light. Discontinuation of the replacement therapy led to severe and rapidly increasing changes in the ECG. On the 2nd-3rd day the heart rate rose to 150-170 per minute; on the 4th-5th day, still before the appearance of any external signs of crisis, changes occurred in the ECG (the T wave baceme negative and the S-T interval was shortened by 0.02-0.27 seconds); the ECG waves later diminished in size and they all gradually became smoothed out. On resumption of the replacement therapy the animal emerged from the crisis, although the changes in the ECG persisted for the first few days. The ECG regained its original form after 5-8 days.

Fig. 3 illustrates the characteristic changes in the ECG in the period of development of and emergence from a repeated crisis in the dog Shalun. Three days after discontinuation of the therapy, the heart rate rose from 60-68 to 100, and 6-7 days after, to 133-155 beats per minute. After 7 days, significant changes were observed in the ECG (cut 3); after 10 days these became more profound (cut 4). The animal's condition remained good during almost the whole of this time, and only 9 days after discontinuation of the therapy was slight sluggishness of its movement apparent. With the resumption of the course of replacement therapy, the changes in the ECG showed no weakening for one or two days (cut 5). The ECG regained its original appearance 8 days after the resumption of the therapy (cut 6).

During repeated crises the pattern of the changes in the ECG and of its return to its original appearance as the result of resumption of therapy was reproduced with remarkable accuracy. The only exception was the fact that after repeated crises the changes arose more rapidly and reached their maximun development in shorter periods of time than in the early crises. With resumption of the replacement therapy, the ECG regained its original appearance more slowly than after the previous crises. It seems to us that these factors indicate growing changes in the cardiac muscle after bilateral adrenalectomy, in spite of replacement therapy.

It must be pointed out that the rapidity of development and the depth of the changes in the ECG after bilateral adrenalectomy were not the same in the different dogs. Whereas some dogs lived a comparatively long time, maintaining a constant ECG in the period of compensation (Shalun — over 20 months), others died quite quickly (Kashtan lived 29 days, Orlik 14 days); under these circumstances the changes in their ECG in the day or two before death were either very weak or even absent altogether.

The results which we obtained testify to the high power of adaptation of the heart muscle to changes in the endocrine background of the utmost importance to the action of the heart. This is indicated by the maintenance of the constant character of the ECG for a long period of time in association with the profound disturbances of metabolism accompanying bilateral adrenalectomy. In this respect the results of our experiments agree with clinical observations, according to which, in the majority of cases of Addison's disease, significant changes are apparent in the last stages of the disease [9].

Our findings also suggest that the profound changes which develop eventually in the ECG of adrenalectomized dogs cannot be entirely explained by disturbances of mineral metabolism. The latter are compensated by the administration of saline and desoxycorticosterone. In a state of compensation the relative proportions of sodium and potassium in the serum were not disturbed. The possibility that relative compensation is, in fact, obtained with replacement therapy is shown by the sharp aggravation of the ECG changes when the therapy is discontinued and their disappearance soon after the therapy is resumed.

Replacement therapy did not, however, produce full compensation, for, although it was given for long periods of time, the dogs eventually developed significant ECG changes after bilateral adrenalectomy. These changes were evidently associated with interference with carbohydrate and protein metabolism, as a result of the absence of glucocorticoids. This is also confirmed by direct experiments [1, 2] showing that the protein and carbohydrate metabolism is considerably upset in adrenalectomized dogs on replacement therapy.

We have referred previously to the work of V. S. Lusenko [5], who showed that the content of glycogen, creatine phospahte and ATP in the heart muscle falls after adrenalectomy.

Finally, the character of the changes in the ECG after adrenalectomy may also serve as indirect evidence of changes in the metabolism of cardiac muscle. As we have pointed out above, the components of the ECG to be altered first after adrenalectomy were those which, in the opinion of many workers, are to some extent connected with metabolic processes, and according to A. I. Smirnov [7, 8], with restorative processes in heart muscle. This applies to the T wave, changes in which, in our experiments, appeared earlier and were more profound than in the other components of the ECG.

The association between the T wave of the ECG with metabolic processes has been shown by a number of special experiments in which authors have brought about changes in the carbohydrate and phosphorus metabolism of cardiac muscle and have observed changes mainly in the T wave [6, 8, 18, 19 and others].

Our results thus do not support the view that the profound changes which eventually develop in the ECG of adrenalectomized dogs are the result of interference with the mineral metabolism alone.

SUMMARY

The electrocardiographic changes developing in dogs following bilateral two-stage adrenalectomy were studied. The animal's life was maintained by desoxycorticosterone and saline solution administration. Changes appeared in the ECG only after the removal of the second adrenal gland, and were mainly revealed in the T wave and the S-T interval. In an animal in a compensated condition, these changes developed slowly and would become marked only during the last days, and, sometimes, even hours of its life. The ECG changes progressed more rapidly during the development of the crisis caused by the interruption of the replacement therapy. They could be revealed before the appearance of the external signs of the crisis.

LITERATURE CITED

[1] T. K. Valueva, Fiziologichnii Zhur., 1, No. 4 (1955).

[2] T. K. Valueva, I. P. Maevskaya, Fiziologichnii Zhur., 2, No. 3 (1956).

[3] G. Ya. Dekhtyar', Electrocardiography, Moscow, 1955 [In Russian].

[4] V. P. Komissarenko, The Adrenal Cortical Hormones and Their Role in the Physiological and Pathological Processes of the Body. Kiev, 1956 [In Russian].

[5] V. S. Lusenko, K. S. Klimenko, Proceedings of a Scientific Meeting of the All Union Intitute of Endocrinology. Moscow, 1956 [In Russian].

[6] M. S. Raiskina, Uspekhi Sovremennoi Biol., 33, 1, 173 (1952).

[7] A. I. Smirnov, Fiziol. Zhur. SSSR, 30, 4, 504 (1941).

[8] A. I. Smirnov, Fiziol. Zhur. SSSR, 35, 6, 675 (1949).

[9] L. I. Fogel'son, Diseases of the Heart and Vessels, Moscow, 1951 [In Russian].

[10] L. I. Fogel'son, Clinical Electrocardiography, Moscow, 1957 [In Russian].

[11] Z. L. Chernogorova, V. S. Lusenko, Med. Zhur. Akad. Nauk Ukrainsk. SSR, 22, 3, 12 (1952).

[12] C. Hall, H. Diserens, et al., Am. J. Physiol. 183, 3, 550-554 (1955).

[13] G. Harrop, et al., J. Exper. Med. v. 58, No. 17 (1933).

[14] H. Ljunggren, J. Exper. Med. v. 45, No. 2 p. 216-227 (1953).

[15] B. Lown and W. L. Arons , Am. Heart J. v. 50, No. 5, p. 760-769 (1955).

[16] B. F. Massell , New Engl. J. Med. v. 251, p. 221 (1954).

[17] K. Roberts , Proc. Soc. Exp. Biol. and Med. v. 79, No. 1, p. 32-34 (1952).

[18] H. Schumann, (cited by M. E. Raiskina [6]) (1942).

[19] K. Siegel and Z. Unna, Ztschr. f. ges. Exper. Med. Bd. 78, No. 3-4, S. 287 (1931).

[20] W. Sommerville, H. D. Levine and G. N. Thorn, Medicine, v. 30, p. 40-21 (1951).

[21] I. M. Weller and B. Lown , Circulation, v. 11, No. 1, p. 44-52 (1955).

[22] G. M. Wilson and H. Miller , Clin. Sc. v. 12, p. 113 (1953).

[23] L. Wyman, G. Fulton, F. Sudak and G. Patterson, Proc. Soc. Exp. Biol. and Med. v. 84, No. 2 p. 280-283 (1953).