INFLUENCE OF RIBOFLAVIN, NICOTINIC AND ASCORBIC ACIDS, AND TESTOSTERONE PROPIONATE ON EXPERIMENTAL TOXIC MYOCARDITIS

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A part of our work consists of studies on multiple experimental therapies for various types of myocarditis produced in our laboratory. In the course of such work we investigated the effect of a therapeutic mixture consisting of riboflavin, nicotinic and ascorbic acids, and testosterone propionate on the course of experimental toxic myocarditis.

In the acute period of experimental myocarditis in rabbits there occurs primarily in heart muscle but also in liver, kidney and brain a sharp depression in dehydrogenation capacity [8, 9, 10].

Clinical and laboratory observations have shown that nicotinic acid increases activity of reductive reactions in tissues and evidences especially in coronary insufficiency a vasodilatory action [15].

Steroid hormones activate cardiac function and respiration as well as central and sympathetic nervous systems increasing metabolism and absorption of nitrogen by the organism and raising cardiac output [4, 5, 11, 14, 18].

Experimental myocarditis has been produced not only by injecting caffein, ephedrin, theophyline and adrenaline but also by infection with bacterial cultures and the injection of various toxins [2, 3, 6, 7, 16, 17, 19, 20].

Numerous infectious processes and also scarlet fever toxin produce a reduction in thiamin, riboflavin, cyanocobalamine, and ascorbic and nicotinic acid content of the organism [12].

EXPERIMENTAL METHOD

Experimental myocarditis was produced by injection of staphylococcus toxin (series 72, N. F. Gamalei Epidemiological and Microbiological Institute). The principle of this procedure has been described previously [1]. Animals were studied for 21 to 26 days following intravenous administration of toxin. Electrocardiographic and histological methods were used. In all, 150 albino rats were used. Three series of experiments were performed using 50 rats each (25 controls and 25 experimental).

To produce experimental myocarditis staphylococcus toxin was injected into the left ventricle and thereafter given intravenously at 5 different intervals: on the day following, and then at 3, 7, 12, and 14 days.

Treatment was begun on the day after the intravenous injection. In series I and II experiments the rats received subcutaneous injections each day (16 times) of the complex preparation consisting of 0.5 mg testosterone propionate, 1 mg riboflavin, 6 mg nicotinic acid and 8 mg ascorbic acid. For series II experiments the testosterone propionate was omitted from the mixture. In series III experiments the animals received injections only every other day for 9 times but with double the above concentration of testosterone propionate and riboflavin.

EXPERIMENTAL RESULTS

After toxin injection into the heart electrocardiographic changes were observed in a relatively small group: in 10 rats of series I, 14 of series II, and 17 of series III, in all 41 animals. These occurred from the second day and through the following 9 days. The EKG changed in only one animal after 2 days, but in 12 after 3 days, in 5 after 4 days, in 2 after 5 days, in 4 after 6 days, in 3 after 7 days, in 8 after 10 days, and in 6 after 11 days.

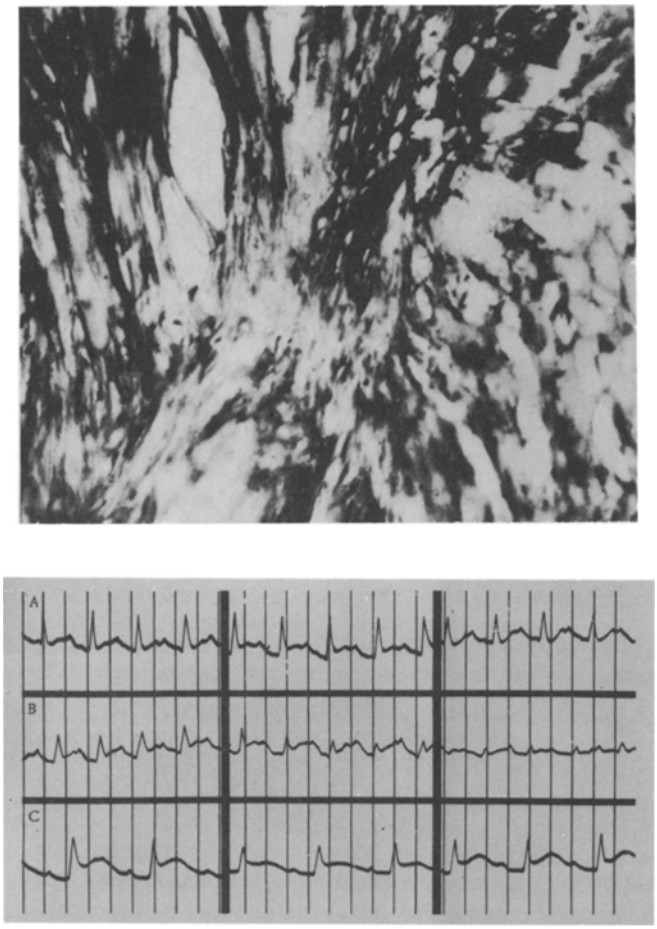
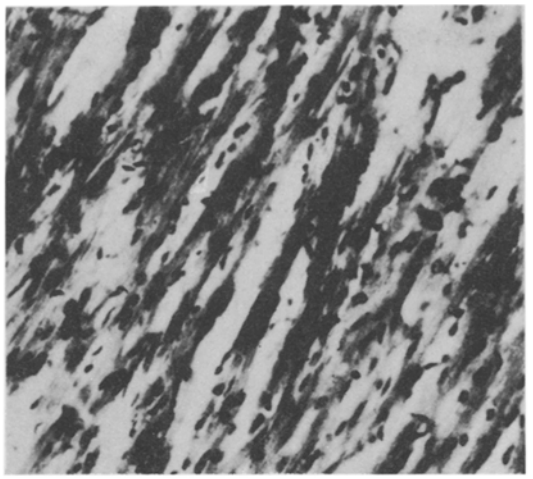


Fig. 1. Photomicrograph. Staphylococcus toxin administered (rat No. 400 control). Cardiosclerosis of right ventricle wall and septum. Pyrofuchsin. obj. 20x, occular 7x. EKG: A) original; B) decreased voltage of R wave 2 days after givin toxin intravenously in II, III and chest leads, monophasic rise of ST interval; C) slowed rhythm to 333 (RR = 0.18; PG = 0.05; QT = 0.10; systolic index 56), after 22 days (before sacrifice) monophasic rise of ST interval.

Most frequently an elevation in the ST segment was noticed in the II, III, and chest leads, a transition of the R wave directly to the high T wave without an ST interval, inverted T wave in the II and chest leads, a deepening of the S_3 wave.

Disturbance in cardiac function following intravenous administration of staphylococcus toxin appeared with series I in 36 rats, with series II in 33, and with series III in 30, or 99 rats total. In 68 of the experimental and control rats the EKG became pathological within the first 6 days after intravenous toxin administration. In series II and III experiments EKG disturbances were observed in approximately half as many rats (31) in the course of the subsequent days until the 16th day; in series I experiments after 9 days EKG changes did not occur either in control or experimental animals.

After intravenous toxin administration shifts in EKG, as expected, increased in comparison with disturbances appearing after injecting toxin into the heart. ST interval displacement was observed in 38 rats, ST interval displacement and other changes in 27, decreased R voltage in 21, levogram in 12, deep S wave in 9, increased R voltage in 9, negative T wave in 8, pathological Q wave and decrease of voltage in 5 rats.



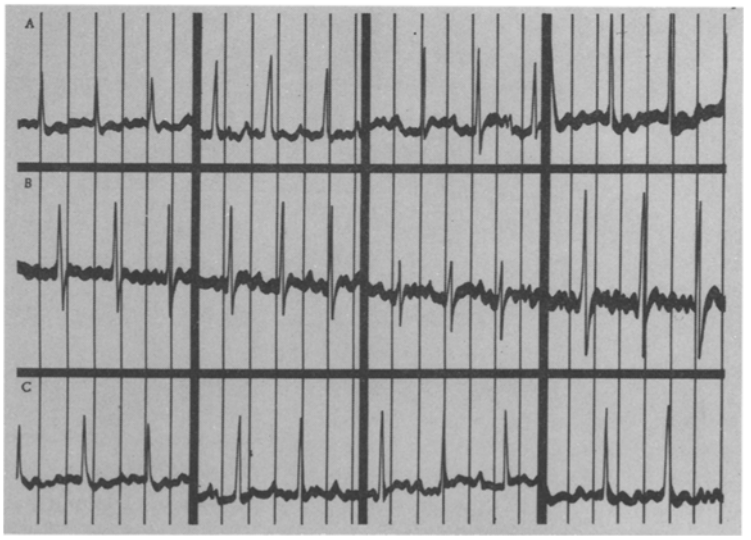


Fig. 2. Photomicrograph. Staphylococcus toxin administered (rat No. 465, experimental), treated with testosterone propionate and riboflavin. Myocardium unchanged. Pyrofuchsin. obj. 20x, occular 7x. EKG: A) original; B) appearance of deep S wave in all leads 2 days after intravenous toxin administration; C) normalized EKG after 22 days (before sacrifice).

Thus EKG changes were encountered in all animals taken for experiment. Administering staphylococcus toxin into the heart produced various EKG disturbances in notably lower numbers of animals (27%) than did intravenous injection (66%).

The EKG changes indicated in the control animals not only persisted for a long time but notably worsened.

Histological changes in the rat hearts were characterized by signs of cardiosclerosis and vasculitis; diffuse changes were not observed in any instance (Figs. 1 and 2).

The use of the therapeutic complex (T + B_2 + Nic + C) in series I experimental animals led to EKG normalization in 7 rats. Among series II experimental animals heart function was returned to its original pattern in 11 rats and among series III experimental animals 10 were restored to normal (Table 1).

TABLE 1. EKG Normalization in Animals in Relation to the Number of Therapeutic Mixture Injections

Test series	No. of animals	Therapeutic mixture	Times complex injected	Days after intravenous toxin began
I	1	T + B_2 + Nic + C	5	8
	2		10—12	12—15
	4		16	22—24
	1		8	10
II	7	B_2 + Nic + C	10—14	13—17
	3		17	21
	1		1	2
III	5	T+B_2*	6—7	13—17
	4		9	22—25

* In series III experiments the therapeutic mixture was given in double dosage.

TABLE 2. Changes in EKG under the Influence of Therapy during Experimental Myocarditis in Rats

Result of therapy	Test series					
	I		II		III	
	T+B_2+Nic+C	control	B_2+Nic+C	Control	T+B_2	Control
EKG normalized	7		11	2	10	3
EKG Partially normalized	9	7	8	9	9	9
EKG not normalized	8	15	5	12	5	11
p	<0,05		<0,05		<0,05	

* Incomplete normalization includes EKG disturbances in which small changes are retained in one or two leads.

In series I heart function did not become normal in any control rats, in series II the EKG turned normal in two control animals on the 16th and 21st days respectively, in series III controls two normalized on the 14th day and one on the 23rd day after intravenous toxin (Table 2).

Despite the fact that the number of therapeutic injections, the dosage and length of observation were nearly the same in the I and the II series, the return to normal of the bioelectric heart activity in animals of series I experiments was somewhat less pronounced than in series II. This may be attributed to the use in series I of a mixture consisting of testosterone propionate, riboflavin, nicotinic and ascorbic acids. In series III experimental animals injected every other day with double the testosterone propionate and riboflavin the curative results were close to those observed in the series I experiments.

The best results according to electrocardiographic data were obtained by giving the second mixture, the poorest were obtained from the third. Statistical analysis confirmed the reliability of the data.

Thus, the most effective therapeutic complex appeared to be the vitamin mixture without testosterone propionate. Apparently therapeutic complex treatment gave the best results during the subacute period of experimental myocarditis depending on treatment of long duration.

It will be necessary to make further investigations to define the effective application of steroid hormones in experimental myocarditis.

SUMMARY

Experimental toxic myocarditis was obtained in albino rats by administration of staphylococcus toxin into the left cardiac ventricle at first and then by intravenous administration of it at 5 different intervals on the next day, in 3, 7, 12, and 14 days. The preexperimental series (150 rats) a study was made of the effect produced by therapeutic complexes, consisting of riboflavine, nicotinic and ascorbic acids, and testosterone-propionate. The best therapeutic results were obtained by using riboflavine, nicotinic and ascorbic acids.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
