

The curve of the left common iliac artery is not included in the figure for its values are so similar to those of the right common iliac artery that they could not be clearly represented upon the combined graph.

The growth curves of the vessels which supply the body only show the same type of increment which is characteristic of the growth of most of the organs and parts of the body. These vessels have the short period of slow growth in early fetal life, followed by a more rapid increase during the rest of the fetal period.

The curves of the vessels which supply *both* the body and placenta are characterized by a relatively long period of slow growth followed by a short period of more rapid growth during the latter part of prenatal life. This is a preliminary report.

¹ Seammon, R. E., and Calkins, L. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1924, xx, 353.

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Observations on the Mechanism of Circulatory Failure in Diphtheria.

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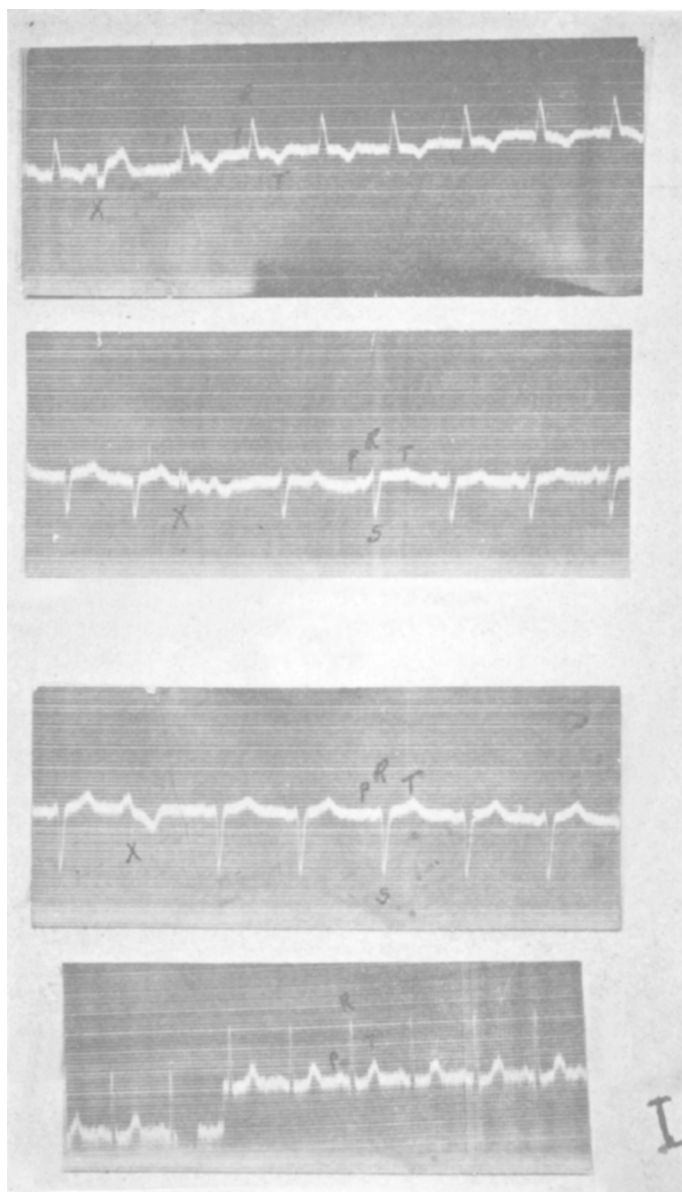
This report consists of study by means of the string galvanometer of the effects of diphtheria toxin upon the heart. It has long been known that a circulatory collapse may occur in diphtheria, which frequently results in death. There is still considerable uncertainty, however, as to whether it is the heart or the vasomotor apparatus which is primarily effected.

In the present study electrocardiographic observations were carried out (1) on a series of diphtheria patients (2) on animals injected with diphtheria toxin.

Previous observers^{1, 2, 3, 4} have noted electrocardiographic changes indicating myocardial injury during the acute stage of diphtheria. The present investigation was made during the convalescent or late stage of the disease, since circulatory failure may occur during this period also.

Readings were taken of 15 diphtheria patients during the period of convalescence, beginning usually in the 3rd or 4th week of their illness. In all cases, the local throat condition had entirely cleared

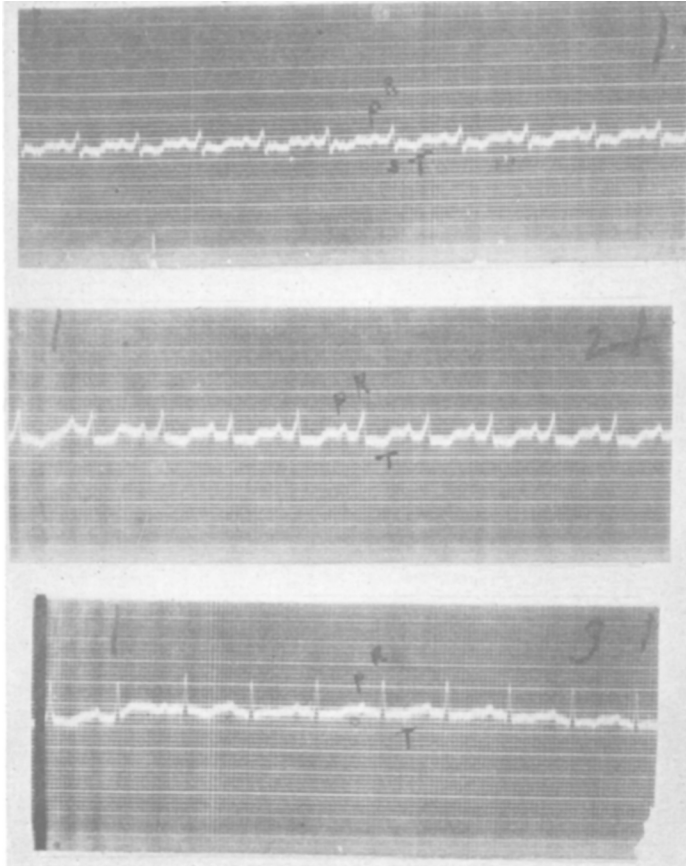
Fig. 1.



Electrocardiogram of a patient with multiple neuritis in the fourth week of convalescence. Inversion of T in lead one and ventricular extrasystoles. The lowest record shows lead 1, 3 months later with normal T.

up, and the cultures for the diphtheria bacillus were negative. The general symptoms of toxemia had disappeared, and practically the only abnormality was a heart which increased in rate very easily. Of the 15 cases, 8 had suffered a severe type of infection and of these, 7 showed significant abnormalities in the electrocardiogram. A summary of the readings shows the following: There was an absence of high-grade irregularities, occasional ventricular extrasystoles being the only arrhythmia noted in two cases. There was no evidence of prolonged auriculoventricular or intraventricular conduction. The longest P-R interval was .18 second and the

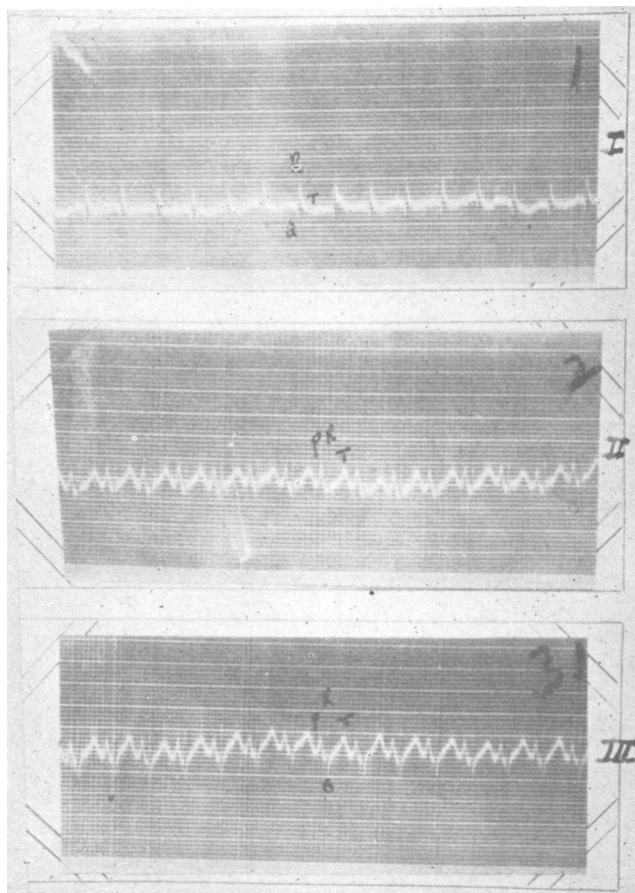
FIG. 2.



Inversion of T in all leads in the 4th week. The patient apparently in good condition, sat up to reach for a pitcher of water, 7 days after the record was taken, and died within a few minutes.

Q. R. S. complex was not altered in any case. The chief significant change was in the T wave. A definite inversion of the T was present in all. In one instance, the T was inverted in lead one, in another, in leads 1 and 2. In 3 cases, the change occurred in leads 2 and 3 and in 2, in all leads. In addition, 4 electrocardiograms showed a right preponderance, and 2 a left preponderance. In the 2 cases showing inverted T in all leads, sudden death occurred within a week after the readings were taken. The remaining 5 have recovered and with recovery the T wave has become upright. The change was a gradual one, the T first becoming less negative, then isoelectric and later positive. The earliest evidence of return to

FIG. 3.



Cat 3, before diphtheria toxin.

normal was noted 6 weeks after the onset of the disease. The return of the T wave to normal in the cases that recovered is of interest. It is still believed by some that diphtheria is a cause of cardiac failure in later life. The above observations strongly suggest that the effect is entirely a transient one, and that there is a restoration of normal myocardial function.

Rohmer,¹ in the course of an investigation upon the problem of whether diphtheria toxin possessed any special affinity for the conducting tissue of the heart, injected diphtheria toxin into 4 rabbits. In a brief paragraph, he merely states that he found no evidence of delayed conduction. He makes no note of any other changes. This seems to be the only previous report on the use of the string galvanometer in the study of experimental diphtheria.

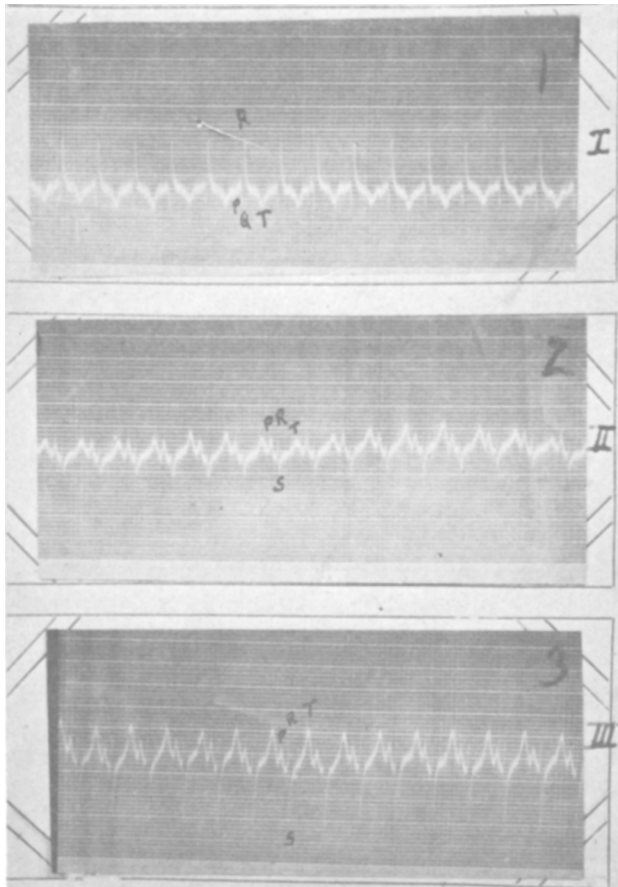
In the present study, cats were used, and diphtheria toxin* injected subcutaneously. The dose of toxin varied from .03 cc. to .05 cc. diluted to 2.5 cc. in sterile saline. The records were taken with the animal under light ether anesthesia. After a control record was taken and the toxin injected, subsequent readings were made at 48 hours and at varying intervals following this, if the animals remained alive. All the animals exhibited definite evidence of intoxication. The effect was usually noted on the second day following the injection. The animals became apathetic, moved about very little and refused their food. A small amount of anesthetic was necessary in taking the subsequent readings as they offered but slight resistance. A very frequent observation was a weakness and stiffness of the hind legs which was almost a constant finding. This usually occurred on the 2nd or 3rd day.

Of 7 satisfactory experiments, electrocardiographic changes were observed in 6 after the injection of the toxin. These may be summarized as follows: No definite arrhythmias occurred. Definite changes in the P-R interval and Q. R. S. complex were present in but one case. In this animal, 6 hours before death, the record showed a P-R interval of .12 second, where it had previously been .06 second. At the same time the Q. R. S. had markedly increased in amplitude and had widened from .02 to .06 second. The most constant and striking alterations were in the T wave. There was a definite flattening and inversion of the T in one or more leads in all cases, as early as 48 hours following the injection of the toxin. The change was present in lead 1 alone, in 2 cats, and in leads 1 and 2 in one animal. In the remaining 3, the inversion was present in

* The toxin was supplied by Dr. W. P. Larson of the Department of Bacteriology. ML dose equals 0.4 cc.

leads 2 and 3. In 2 cats in whom it was possible to follow for 7 and 10 days, a tendency for return of the T to normal appeared between the 3rd and 6th day in one instance; and between the 5th and 8th day in the other. In addition, in 2 animals, there was a definite change in ventricular preponderance, both within 48 hours, following the injection of toxin. In both cases a definite left ventricular preponderance developed. Similar rapid changes in preponderance are reported by McCulloch² and Marvin⁴ in their clinical cases. In one case, a definite flaccid paralysis of the hind extremities was present on the 10th day, when the electrocardiographic changes were returning to normal. This is of interest since clinically, diphtheretic paral-

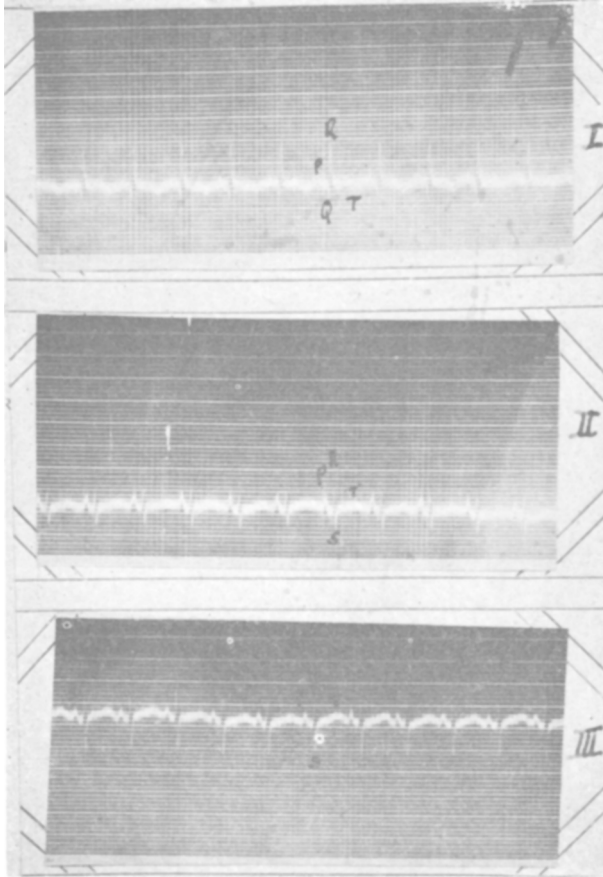
FIG. 4.



Cat 3, forty-eight hours after diphtheria toxin. Deep inversion of T in lead one and left preponderance.

ysis and circulatory failure are often associated, and attempts have been made to explain both on a nervous mechanism. Here we have an instance of paralysis occurring at a time when there is evidence of recovery in the heart.

FIG. 5.



Six days after diphtheria toxin. Partial return to normal.

Figures 3, 4 and 5 illustrate the changes in an experiment.

Cat 3 was electrocardiographed (Fig. 3) on February 22nd and .05 cc. of toxin injected subcutaneously. On February 24th the animal appeared inactive and listless but otherwise seemed normal. Fig. 4 shows the deep inversion of the T wave in lead one and the marked left preponderance which has developed. On February 26th the animal seemed very apathetic and refused its food. On Febru-

ary 28th the general condition was better, but it still refused food. Electrocardiogram on that date (Fig. 5) showed a lesser degree of T wave inversion and less marked left preponderance.

¹ Rohmer, P., *Z. Exp. Path. u. Therap.*, 1912, xi, 426.

² McCulloch, H., *Am. J. Dis. Child.*, 1920, xx, 89.

³ Smith, S. C., *J. Am. Med. Assn.*, 1921, lxvii, 765.

⁴ Marvin, H. M., *Am. J. Dis. Child.*, 1925, xxix, 433.

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Work of the Left Ventricle in Normal, Hypertension and Arteriosclerosis.

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It is very probable that increased work of any chamber of the heart is followed after some time by hypertrophy and dilation of that chamber. It is of interest to know the exact increase in work for the left ventricle of the heart in hypertension and in generalized arteriosclerosis.

The work of the left ventricle per beat is represented by the equation:

$$\int_{P_1}^{P_2} P dV + \frac{Sv^2}{2g}$$

where P is the pressure of the blood in the aorta, P₁ the diastolic and P₂ the systolic pressures, respectively; V the volume of the arterial system, corresponding to the pressure P, and dV an infinitesimal change in the volume when a small amount of blood is ejected from the left ventricle and the pressure increased by the amount dP. S is the stroke volume, v the velocity of the blood in the aorta and g the constant of gravity. The second term may be neglected in our problem because it makes up only 1 or 2 per cent of the work of the left ventricle and is constant for equal stroke volumes and velocities in the aorta.

If we can find the relation between P and V we can integrate the first term of the work equation and can thus find the work of the left ventricle per beat. Bramwell, Downing and Hill¹ have determined the relation between the volume and pressure in the "mean normal" artery of man. The curve, Fig. 1, is a reproduction of their curve of this relation. If we assume that in the "normal" person the diastolic blood pressure is 80 and the systolic 120, then, ac-