The presence or absence of the adrenal glands modifies the survival of the eviscerated and the eviscerated-nephrectomized rat either with or without insulin. This effect of adrenalectomy can be observed within 2 hours following operation. The data do not permit a differentiation between the relative importance of the adrenal medulla and the adrenal cortex in effecting the survival of the eviscerated rat.

Summary. The survival of the eviscerated rat is shortened by either nephrectomy or insulin. Insulin shortens the survival of the eviscerated-nephrectomized rat. Adrenalectomy at the time of evisceration shortens the survival of the eviscerated and eviscerated-nephrectomized rat either with or without insulin.

15817

Enhancement and Depression of Neuromuscular Transmission by Intra-arterial Injection of Potassium Chloride in the Dog.

SHEPPARD M. WALKER. (Introduced by A. S. Gilson, Jr.)

From the Department of Physiology, Washington University School of Medicine, St. Louis, Mo.

Rosenblueth and Cannon[1] observed that intra-arterial injection of KCl, during indirect stimulation of muscle in the cat at a high frequency, produced marked depression of muscle tension. More recent studies[2,3] have shown that intraperitoneal injection of KCl improved neuromuscular transmission in the rat and that intra-arterial injection of KCl in the nerve-muscle preparation from the frog first augmented and then depressed neuromuscular transmission. The present paper is concerned with the effect of varied rates of intra-arterial injection of KCl on the development and maintenance of muscle tension during stimulation of the nerve at a high frequency. Nine dogs anesthetized with sodium barbital were used in the experiments. Both *Triceps surae* were prepared as previously described for the rat.[2] Spring levels were used for the recording of muscle tension. The muscles of each leg were stimulated simultaneously through the cut sciatic nerves with electrodes connected in parallel and led from a Thyratron stimulator. The stimulus strength was about 6 times threshold and the frequency of stimulation was 275 to 300 shocks per second. The duration of stimulation was usually 5 or 10 seconds with an equal interval of rest between periods of stimulation. In some experiments stimulation was continuous during the period of injection. In a few experiments the muscles were stimulated with single shocks during the period of injection. Injections were made into the femoral artery. Two rates of injection were employed: slow, 2 to 3 mg of KCl (1.12% solution) per second; fast, 15 mg of KCl (4.2% solution) per second.

Results. During indirect stimulation at 300 shocks per second the peak of tetanic tension was followed immediately by a rapid decline of tension to a much lower level which was either maintained or slightly increased during continued stimulation (Fig. 1, 1A). Slow injection of KCl gradually reduced the rate and the extent of decline of tension in the perfused muscles during successive periods of stimulation. The maximal enhancement of tetanic tension was attained approximately one minute after the beginning of injection (Fig. 1, 1B). In the contralateral muscles, not subjected to KCl perfusion, little change in the tension curve occurred during the same interval (cf. 2A and 2B of Fig. 1). By the end of 2 minutes of slow injection

1 Rosenblueth, A., and Cannon, W. B., *Am. J. Physiol.*, 1940, **130**, 205.

2 Walker, S. M., *Am. J. Physiol.*, 1947, **149**, 7.

3 Walker, S. M., and Laporte, Y., *J. Neurophysiol.*, 1947, **10**, 79.

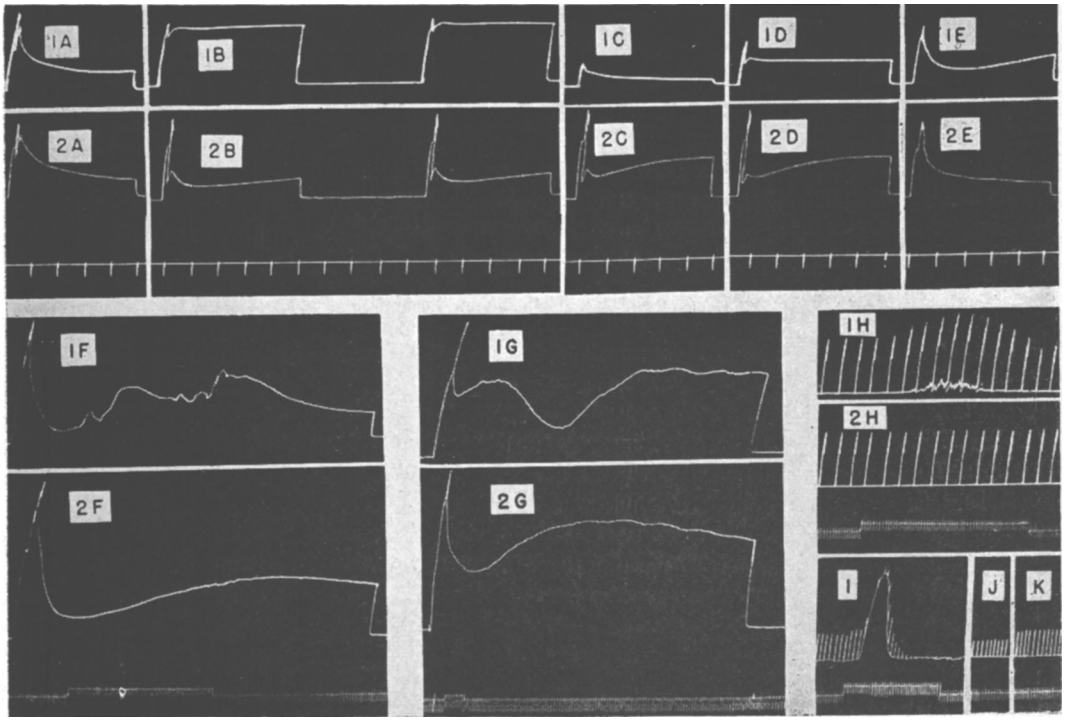

Fig. 1. Myograms showing the effect of intra-arterial injection of KCl on the response of the *Triceps surae* to electric stimulation of the cut sciatic nerve. Time signal: 1-second intervals. Elevations of the time line show periods of injection.

1A to 1E: Recordings of tension from muscles perfused with 2 mg of KCl (1.12% solution) per second for 2 minutes and stimulated during alternate 5-second intervals with 300 shocks per second. 1A: Before injection. 1B: After 1 minute of injection. 1C: After 2 minutes of injection. 1D: One minute after injection was stopped. 1E: Ten minutes after injection was stopped. 2A to 2E: Recordings of tension from the contralateral muscles stimulated in parallel with the muscles recorded in 1A to 1E.

1F: Muscles perfused with 3 mg of KCl (1.12% solution) per second for 54 seconds during continuous stimulation at 275 shocks per second. 2F: The contralateral muscle stimulated in parallel.

1G: Muscles perfused with 15 mg of KCl (4.2% solution) per second for 7 seconds during continuous stimulation at 275 shocks per second. 2G: The contralateral muscles stimulated in parallel.

1H: Muscles perfused with 3 mg of KCl (1.12% solution) per second for 68 seconds during stimulation at 1 shock per 5 seconds. 2H: The contralateral muscles stimulated in parallel.

I: Muscles perfused with 15 mg of KCl (4.2% solution) per second for 40 seconds during stimulation at 1 shock per 1.5 seconds. J: The same muscles recorded in I showing partial recovery of neuromuscular transmission 20 minutes after the injection. K: The same muscles recorded in I showing complete recovery of transmission 25 minutes after the injection.

the perfused muscles showed marked depression of tetanic tension, while the response of the contralateral muscles showed only slight change (Fig. 1, 1C and 2C). At this point injection was discontinued. An increase of tetanic tension occurred in each successive period of stimulation of the muscles which had received intra-arterial injection of KCl (Fig. 1, 1D). Ten minutes after injection was stopped the tension curve was almost normal (Fig. 1, 1E).

Slow injections made during continuous stimulation at 275 shocks per second produced an increase of tension followed by a decline (Fig. 1, 1F). If injections were stopped shortly after the decline began another rise of tension occurred. If, on the other hand, injections were continued for several seconds after the decline appeared no increase of tension occurred after cessation of injection. When fast injections were given during stimulation a depression of tension be-

gan a few seconds after the start of injection. If the duration of injections was only 6 to 8 seconds an increase of tension followed shortly after the cessation of injection (Fig. 1, 1G). Longer periods of injection produced either a prolonged depression of tension or complete neuromuscular block.

The typical potentiation of muscle response to single shocks was produced by slow injections (Fig. 1, 1H). It is of interest to note that continuation of slow injection induced slight contracture which was followed shortly by diminution of response to single shocks. When injection was stopped at the onset of depression recovery of the normal response occurred within 10 to 20 seconds. Marked contracture and complete neuromuscular block were produced by prolonged fast injections (Fig. 1I). Twenty to 25 minutes were required for recovery of the response to single indirect stimuli (Fig. 1, J and K). It was shown that the quantity of KCl required to produce complete neuromuscular block did not impair the contractile strength of the muscle stimulated directly with single or with high-frequency shocks.

Discussion. Direct stimulation in the curarized muscle of the rat[4] has shown that KCl-treatment does not increase tetanic tension. Therefore, it is assumed that all enhancement of tetanic tension observed in this study, except increases resulting from contracture, is due to improvement of neuromuscular transmission. The presence of contracture usually could be recognized by irregularities in the tension curve (Fig. 1, 1F). The slowest rate of injection of KCl (2 mg per second) produced no contracture although marked augmentation of tetanic tension occurred (cf. 1A and 1B of Fig. 1). Moreover, it seems likely that the contracture during injection of 3 mg per second of KCl produced only a small portion of the increased tension observed at a high frequency of stimulation (cf. the slight increase of tension induced by contracture in 1H with the marked increase of tension during KCl injection in 1F).

The observation that neuromuscular transmission is facilitated by intra-arterial injection of small quantities of KCl confirmed the results obtained by intraperitoneal injection of KCl in the rat.[2] Furthermore, the failure of the injection to induce similar changes in the contralateral muscles showed that the results were not attributable to central effects on the circulation or respiration. The observations of enhancement of neuromuscular transmission with small amounts of KCl and of depression with large amounts are in agreement with the findings in the curarized nerve-muscle preparation from the frog.[3] Moreover, the present results in the dog have shown that both the augmenting effect and the depressant action of K on neuromuscular transmission occur in uncurarized muscle.

Summary. 1. Continuous slow injection of KCl (2 to 3 mg per second of 1.12% solution) produced initial enhancement and subsequent depression of neuromuscular transmission in muscle stimulated indirectly at 275 to 300 shocks per second.

2. Fast injection of KCl (15 mg per second of 4.2% solution) produced a prompt depression of neuromuscular transmission. Continued injection produced marked contracture and complete neuromuscular block.

3. Enhancement of neuromuscular transmission may occur in the absence of contracture or in the presence of mild contracture. Amounts of K sufficient to induce marked contracture usually produced complete neuromuscular block.

4. During complete neuromuscular block by KCl injection the response of the muscle to direct stimulation was unimpaired.

[4] Walker, S. M., unpublished data.